Implementing an ISO 13485 Quality Management System for Medical Devices

Ann Goodall

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Ann Goodall, Ph.D.

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Chapter 1 – Introduction

Overview

The standard ISO 13485, *Medical devices — Quality management systems — Requirements for regulatory purposes* is now becoming the certification standard of choice for medical device manufacturers. All the requirements are specific to organizations that provide medical devices and do not depend on the size or type of the organization. ISO 13485 supports regulatory compliance in several countries, including the countries of the EU (CE marking), Canada, Australia and Taiwan.

Medical devices include active, non-active, implantable and non-implantable medical devices and in vitro diagnostic medical devices. The standard can be used by organizations that design, produce, install and service medical devices. It can be used by both internal and external parties to assess an organization's quality management system.

The purpose of ISO 13485 is to provide quality management system requirements that are applicable to the medical device industry, that are interpretive and not prescriptive, and that will serve as a basis for regulatory compliance, contractual relationships and third-party certifications.

This book provides practical guidance for implementing a quality management system that can be certified to ISO 13485 and maintaining ongoing certification.

The aims of this book are to:

- explain the scope and structure of ISO 13485;
- consider the key aspects of the implementation process, from the perspectives of planning and implementing the requirements;
- explain how to understand, interpret and apply the requirements of the standard in an organization;
- consider the development of the processes, policies, objectives and documentation and the development of measurement techniques;
- consider the resources required for implementing and maintaining a certified quality management system;
- consider the systems that are required to implement an ISO 13485 quality management system;

- explain how to ensure that the ISO 13485 requirements are effectively implemented to allow the organization's quality management system to be certified;
- discuss the proposed future changes to ISO 13485.

ISO 13485 is a quality management system standard for medical devices designed specifically for regulatory purposes. While it is based on ISO 9001 (the standard for quality management systems), ISO 13485 is a stand-alone standard.

ISO 13485 has eight clauses:

- Clauses 1 to 3 cover the scope, normative references and terms and definitions;
- Clause 4 contains the requirements for the quality management system;
- Clause 5 details the requirements for management responsibility;
- Clause 6 covers resource management;
- Clause 7 details the requirements for product realization;
- Clause 8 contains the requirements for measurement, analysis and improvement.

The book is organized in the order of the clauses in the standard. For each clause of the standard it includes discussion on the approach to be taken to implement and maintain the requirements of ISO 13485:

- Chapter 2 reviews the benefits of using ISO 13485 and its use for regulatory compliance;
- Chapter 3 looks at the process of planning the implementation an ISO 13485 quality management system;
- Chapters 4 to 8 discuss, from a practical perspective, how to implement the requirements for Clauses 1 to 8 of ISO 13485;
- Chapter 9 discusses the process of having a quality management system certified to ISO 13485 by a third-party certification body and the importance of ensuring that the quality management system is maintained in compliance with ISO 13485; it also looks to the future of ISO 13485.

Definitions

The definition of a medical device is included in ISO 13485, Clause 3.7. It states that a medical device is:

> *any instrument, apparatus, implement, machine, appliance, implant, in vitro reagent or calibrator, software, material or other similar or related article, intended by the manufacturer to be used, alone or in*

combination, for human beings for one or more of the specific purpose(s) of

- diagnosis, prevention, monitoring, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury,
- investigation, replacement, modification, or support of the anatomy or of a physiological process,
- supporting or sustaining life,
- control of conception,
- disinfection of medical devices,
- providing information for medical purposes by means of in vitro examination of specimens derived from the human body,

and which does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means.

(ISO 13485, Clause 3.7)

There are additional terms, and definitions of those terms, in ISO 9000:2005, which are used throughout ISO 13485; it is a useful standard for organizations implementing ISO 13485.

ISO 9000:2005, Quality management systems — Fundamentals and vocabulary is the top-level quality management system standard, which sets out the common terms and approach that are used in the standards relating to quality management systems. Throughout this book various terms will be used, for which the following definitions are taken from ISO 9000:2005, in addition to the definitions in ISO 13485. These include:

- **quality**

  degree to which a set of inherent characteristics…fulfils requirements…

  NOTE 1 The term "quality" can be used with adjectives such as poor, good or excellent.

  NOTE 2 "Inherent", as opposed to "assigned", means existing in something, especially as a permanent characteristic.

  (ISO 9000:2005, Clause 3.1.1)

- **requirement**

  need or expectation that is stated, generally implied or obligatory

  NOTE 1 "Generally implied" means that it is custom or common practice for the organization…, its customers…and other interested parties…, that the need or expectation under consideration is implied.

NOTE 2 A qualifier can be used to denote a specific type of requirement, e.g. product requirement, quality management requirement, customer requirement.

NOTE 3 A specified requirement is one that is stated, for example in a document....

NOTE 4 Requirements can be generated by different interested parties....

(ISO 9000:2005, Clause 3.1.2)

- **management**

  coordinated activities to direct and control an organization...

  NOTE In English, the term "management" sometimes refers to people, i.e. a person or group of people with authority and responsibility for the conduct and control of an organization. When "management" is used in this sense, it should always be used with some form of qualifier to avoid confusion with the concept "management" defined above. For example, "management shall..." is deprecated whereas "top management...shall..." is acceptable.

  (ISO 9000:2005, Clause 3.2.6)

- **organization**

  group of people and facilities with an arrangement of responsibilities, authorities and relationships...

  NOTE 1 The arrangement is generally orderly.

  NOTE 2 An organization can be public or private.

  (ISO 9000:2005, Clause 3.3.1)

Examples of organizations are a manufacturer, distributor, 'Company, corporation, firm, enterprise, institution, charity, sole trader, [or] association...' (ISO 9000:2005, Clause 3.3.1).

- **product [or service]**

  result of a process...

  NOTE 1 There are four generic product categories, as follows:

  - services (e.g. transport);
  - software (e.g. computer program, dictionary);
  - hardware (e.g. engine mechanical part);
  - processed materials (e.g. lubricant).

Many products comprise elements belonging to different generic product categories. Whether the product is then called service, software, hardware or processed material depends on the dominant element. For example, the offered product "automobile" consists of hardware (e.g. tyres), processed materials (e.g. fuel, cooling liquid), software (e.g. engine control software, driver's manual), and service (e.g. operating explanations given by the salesman).

NOTE 2 Service is the result of at least one activity necessarily performed at the interface between the supplier…and customer…and is generally intangible. Provision of a service can involve, for example, the following:

- an activity performed on a customer-supplied tangible product (e.g. automobile to be repaired);
- an activity performed on a customer-supplied intangible product (e.g. the income statement needed to prepare a tax return);
- the delivery of an intangible product (e.g. the delivery of information in the context of knowledge transmission);
- the creation of ambience for the customer (e.g. in hotels and restaurants).

Software consists of information and is generally intangible and can be in the form of approaches, transactions or procedures….

Hardware is generally tangible and its amount is a countable characteristic [i.e. quantifiable]….Processed materials are generally tangible and their amount is a continuous characteristic [i.e. quantifiable]. Hardware and processed materials often are referred to as goods.

NOTE 3 Quality assurance…is mainly focused on intended product.

(ISO 9000:2005, Clause 3.4.2)

- **supplier**

  organization…or person that provides a product…

  EXAMPLE Producer, distributor, retailer or vendor of a product, or provider of a service or information.

  NOTE 1 A supplier can be internal or external to the organization.

  NOTE 2 In a contractual situation, a supplier is sometimes called "contractor".

  (ISO 9000:2005, Clause 3.3.6)

Another useful document for organizations implementing ISO 13485 is a technical report published by the International Organization for Standardization (ISO). Technical report ISO/TR 14969:2004, Medical devices — Quality management systems — Guidance on the application of

ISO 13485:2003 provides guidance to help manufacturers in developing, implementing and maintaining an ISO 13485 quality management system.

Now that ISO 13485 has been outlined, the following chapters will focus on how to put ISO 13485 quality management systems into place and how to ensure that the requirements continue to be met.

Chapter 2 – ISO 13485

This chapter describes the background and relationship of ISO 13485 with ISO 9001, together with the use of ISO 13485:2003 for regulatory purposes.

The chapter focuses on:

- the relationship between ISO 9001 and ISO 13485;
- ISO/TR 14969;
- benefits of implementing a certified ISO 13485 quality management system;
- ISO 13485 and regulatory requirements.

The relationship between ISO 9001 and ISO 13485

The ISO 13485 standard for medical devices is based on the ISO 9001 standard but is a stand-alone standard. The structure of ISO 13485 is the same as other standards in this family, including ISO 14001 and OHSAS 18001.

The particular requirements for customer satisfaction and continual improvement have been modified from the requirements in ISO 9001. ISO 13485 requires processes for ensuring continuing effectiveness of the quality management system to meet customer requirements; it also promotes active systems for customer feedback related to whether the organization is meeting customer requirements.

ISO 13485 is a quality management system for medical devices specifically for regulatory purposes. ISO 13485 has the same format as ISO 9001:2000 and most of the requirements are the same.

The main differences between ISO 9001 and ISO 13485 are:

- that requirements for 'customer satisfaction' are changed to 'customer feedback';
- that requirements for 'continual improvement' are changed to 'continual improvement of the quality management system';
- the increased requirements for procedures;
- the increased requirements for records;

- the inclusion of specific regulatory topics related to medical devices, including post-production review, advisory notices and adverse events.

'Customer satisfaction' and 'continual improvement' are not included in ISO 13485 because these concepts are not appropriate for regulatory purposes.

The modification that has removed 'customer satisfaction' and 'continual improvement' from ISO 13485:2003 means that conformance with ISO 13485:2003 does not provide conformity with ISO 9001:2008.

In practice, an ISO 13485:2003 standard states what has to be done. The quality management system standard specifies the processes that will maintain compliance to the system and how they are to be carried out. The organization then needs to have internal audits to ensure that the requirements of the quality management system standard are being completed as intended. This includes conforming to the regulatory requirements that have been included in the quality management system standard and that are intended to be fulfilled as part of it. There are systems to verify that the processes are being managed effectively and to ensure that the organization is fully in control of its activities. This gives the customers of an organization confidence in the quality capabilities of the organization.

When an organization has certification to ISO 13485 by a certification body this gives an organization the credibility of an independent assessment. This certificate will be reviewed by customers, which could mean that they might not consider it necessary to audit the organization for themselves. The number of audits that an organization must have may therefore be reduced, and audits that are required might be less rigorous than before. The certificate can be a reference for customers and can show conformity for regulatory requirements.

ISO 13485 applies to organizations in the medical device industry. This includes organizations that design and develop devices, manufacture devices, install devices, service devices and provide services that are related to medical devices.

ISO 13485 includes definitions that are specific to the medical device industry, including a definition of a medical device (see Chapter 1) and other terms that will be used. 'This definition has been developed by the Global Harmonization Task Force (GHTF)' (ISO 13485:2003, Clause 3.7). The definition establishes that to be a medical device the instrument or the in vitro reagent (for example) must have a medically intended purpose.

ISO/TR 14969

ISO/TR 14969 is a technical report that is intended to provide guidance for the application of ISO 13485:2003. It is a very useful document for any organization that is implementing or maintaining an ISO 13485 quality management system. It provides guidance on how the requirements of ISO 13485 can be met, and is recommended reading for those involved in implementing ISO 13485.

ISO/TR 14969:2004 states that it:

> provides guidance to assist in the development, implementation and maintenance of quality management systems that aim to meet the requirements of ISO 13485 for organizations that design and develop, produce, install and service medical devices, or that design, develop and provide related services. It provides guidance related to quality management systems for a wide variety of medical devices and related services. Such medical devices include active, non-active, implantable and non-implantable medical devices and in vitro diagnostic medical devices.
>
> (ISO/TR 14969:2004, Clause 0.1.1)

The guidance in ISO/TR 14969:2004 has considered requirements and guidance from the following organizations:

- the Global Harmonization Task Force (GHTF);
- the International Organization for Standardization (ISO);
- the European Committee for Standardization (CEN) and the European Committee for Electrotechnical Standardization (CENELEC); and
- national regulatory bodies.

Compatibility with other management systems is discussed in Clause 0.4 of the introduction to ISO 13485.

Conforming to the requirements of ISO 13485 does not mean that the organization conforms to the national or regional regulatory requirements. It is the responsibility of the organization to identify and establish the requirements needed to ensure compliance with the regulatory requirements.

The relationship between the standards, guidance and regulations interrelates and overlaps. The background and evolution of ISO 13485 is described in the Appendix.

Benefits of implementing a certified ISO 13485 quality management system

There are many good reasons why an organization may choose to implement an ISO 13485 quality management system and then to certify that quality management system to ISO 13485. These include a quality management system being required to meet regulatory requirements when registering medical devices worldwide.

Initially, quality was very much based on quality control, but with the development of quality management systems the emphasis has moved to quality assurance. Quality control is reactive; examples of quality control are conformity checks and product testing to detect defects. Quality assurance is preventive; it is a proactive approach to identifying and preventing problems.

A well-implemented ISO 13485-based quality management system 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 provide the basis for monitoring, managing or potentially improving the performance of suppliers.

In addition, it might help to increase the organization's competitive edge. It makes good business sense and forms an excellent basis for an efficient and effective business, to be certified against ISO 13485.

There are many benefits to implementing ISO 13485, which include:

- the enhanced reputation of the organization;
- it will result in an engaged workforce who understand their roles in the business, as it introduces a structure for the organization;
- it helps with the tender process to have an independently certified quality management system;
- it can be an expectation of customers, and be part of customer requirements worldwide to have certification to an internationally recognized standard;
- it drives improvement in the quality management system;
- it supports any internal business need to move forward into a new business sector;
- it helps with meeting regulatory requirements. For example, ISO 13485 is a harmonized standard for EU medical devices directives.

ISO 13485 and regulatory requirements

ISO 13485 supports regulatory compliance in several countries, including the countries of the EU (CE marking), Australia, Canada and Taiwan.

Various regulators use ISO 13485 as a basis for showing conformity to their regulatory requirements, and for compliance with regulations, including those in force in Canada, the European Economic Area and Australia.

In Europe, a quality management system is required for CE marking of a medical device that is placed on the market in the EU. Under the medical devices directives, including Council Directive 90/385/EEC [the Active Implantable Medical Devices Directive (AIMD)] and Directive 98/79/EC [the In Vitro Diagnostic Medical Devices Directive (IVDD)], ISO 13485:2003 is a harmonized standard that can be used by organizations to show conformity of their quality management system to the requirements of the directives. EN ISO 13485:2012 was harmonized for use with the EU directives in August 2012 to replace EN ISO 13485:2003 as the harmonized standard. EN ISO 13485:2012 provides a framework to enable a manufacturer to meet some of the quality management system requirements for an EC Declaration of Conformity [Annex 2 and Annex 5 of the AIMD; Annex II, V and VI of Council Directive 93/42/EEC [the Medical Devices Directive (MDD)]; or Annex III, IV and VII of the IVDD]. As the EU harmonized standard for medical device quality management systems, it is an essential tool that allows medical device manufacturers to provide evidence of compliance to EU legislation, based on a sound regulatory interpretation, through its implementation in their quality management system.

In Australia it is a regulatory requirement that the manufacturer's quality management system has to meet the requirements of ISO 13485:2003.

In Canada, ISO 13485:2003 certification is part of the requirements of the Medical Devices Regulations. Manufacturers of Class II or higher-class medical devices have to have an ISO 13485:2003 quality management system that is certified to the Canadian Medical Devices Conformity Assessment System (CMDCAS).

In Taiwan the Good Manufacturing Practice requirements are based on certification to ISO 13485:2003.

In Japan, ISO 13485:2003 is an option, not a requirement, but it is the basis of compliance to the regulations. Japan requires the establishment of a quality management system that conforms to the Ministry of Health, Labor and Welfare (MHLW) Ministerial Ordinance No. 169, 2004, which is similar to ISO 13485.

In the United States the medical device organizations have to establish a quality management system that meets the requirements of the Quality System (QS) regulation, Code of Federal Regulations Title 21 (21 CFR) part 820 as published in the Federal Register. ISO 13485 is an option but is not a requirement. Many of the requirements in the QS regulation are similar to ISO 13485 but there are additional requirements that have to be met

for medical devices that are sold in the United States. The United States Food and Drug Administration (FDA) has been co-operating closely with the development of ISO 13485, in an attempt to further align ISO 13485 and QS regulation requirements.

With the growing interest in regulation in the Middle East, Asia, Africa and Latin America, many more regulatory requirements are added when doing business in these regions. ISO 13485 certification is an excellent tool to harmonize the various quality management system requirements from all these existing and developing legislations, as it is easy for national regulators to add country-specific requirements to the general framework provided in the global standard.

Summary

In summary, when an organization uses ISO 13485 as the basis for its quality management system, this can support the business and ensure that the regulatory requirements in the intended markets for the medical devices will be met.

Chapter 3 – Getting started

This chapter discusses the issues that should be considered when planning the implementation of an ISO 13485 quality management system.

The focus will be on:

- quality management systems;
- principles of quality management;
- a process approach;
- planning the implementation;
- a 10-step implementation process;
- key elements of getting started.

This chapter considers the planning of the initial activities that have to be undertaken before an organization can start to implement a quality management system that meets the requirements of ISO 13485. It also explains the principles of quality management and the process approach to quality management systems. The chapter will include issues that need to be considered when implementing an ISO 13485 quality management system and some tools that can be used to help the implementation.

Quality management systems

A quality management system should be aligned with the business objectives of the organization that it is supporting; it should provide a framework that enables the organization to manage the achievement of those objectives. The quality management system should be designed to meet the stakeholders' needs and to enhance the reputation and image of the organization, so it needs to be applicable to all teams and activities in an organization. It can be used as a framework for improving the business and for managing changes to that business. It should be implemented in a way that is built around the way the organization works; it should be flexible and allow for change.

A quality management system should not just be implemented for the sake of having certification to a standard. It should not be all about paper, a checklist or box-ticking activities; it should be more than simply conformance to the requirements of the standard that the organization is implementing.

There are benefits to having quality management systems for both large and small organizations. An organization can implement a quality management system to improve its efficiency and effectiveness, and to manage the way activities are completed; this means that issues are considered and activities do not get left out. The quality management system establishes clear lines of responsibility: it describes what has to be done, when it should be done, how it should be done, and where it should be completed. This means that there is a systematic approach, ensuring a consistent approach without personnel all doing things in their own way.

ISO quality management systems standards make this good management practice available to organizations of all sizes in all sectors.

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.

The quality management system links:

- quality planning – policies, objectives, processes, controls;
- quality assurance – proactive;
- quality control – reactive, detection, conformity;
- quality improvement – effectiveness, efficiency, capability.

These elements are linked through policies of the quality management system, using the ISO 13485 standard and the quality management system principles to give consistency.

ISO 13485 and ISO 9001 are from the same family of ISO standards. The benefit that is gained from being part of a family of standards is that they can be used as part of an integrated set. ISO 13485 follows the same format as ISO 9001:2000. Other standards in the same family are ISO 14001 (for environmental management systems) and OHSAS 18001 (for health and safety management systems).

Principles of quality management

There are eight principles of quality management.

These are the shared elements of organizational structure, authorities and responsibilities, methods and processes, data management, resources, training, maintenance, customer requirements, product quality and continuous improvement. They are the basis of an ISO 13485 quality management system. The list below discusses each of these elements and how they are part of the quality management system.

1. Customer and regulatory focus

It is important that there is an understanding of current and future customer needs so that the organization can meet its requirements, including ensuring that all known applicable regulations are applied. In order to do so, the organization must know the requirements of its customers and understand the regulatory requirements of the markets in the countries where the product or service is to be sold. This may be a changing environment.

2. Leadership on purpose and direction

Leaders, by establishing a common purpose and direction for the organization, create and maintain the internal environment in which people can become fully involved in achieving the organization's objectives. In ISO 13485, the leadership is referred to as 'top management' – this being the senior management of the organization or of the site that owns the quality management system.

3. Involvement of people at all levels

A key element of any organization is its people. Their full involvement enables best performance in the organization; it is important to involve all the people in the organization in implementing and then maintaining a quality management system.

4. Process approach to resources and activities

Every organization uses processes for deploying its resources and performing the activities for the product or service that it is supplying. ISO 13485 as a quality management standard is based on a process approach. Various tools can be used as a basis for a process approach; an approach that is commonly used is the Plan–Do–Check–Act (PDCA) cycle. This will be described in more detail later in this chapter.

5. Systems approach to management

An important element to ensuring the smooth running of any quality management system is identifying, understanding and managing its interrelated processes. This contributes to the organization's effectiveness and efficiency in achieving its objectives and reducing overall process risks.

6. Factual approach to decision making

Decisions based on analysis of data and information – facts and data – are typically more effective than decisions that are not supported in this way. Monitoring and measuring of product and processes will allow an organization to understand its ability to supply a safe and effective product and service based on the facts and data that have been determined.

7. Mutually beneficial supplier relationships

An organization is responsible for ensuring control of its outsourced processes. With increasing regulatory pressure, supply chain management has become one of the keys to success of any organization. In order to be able to supply its product or service the organization is very dependent on receiving product or services at the right time and of the right quality. Without this, the organization will not be able to meet its own customers' needs. Hence, mutually beneficial working relationships with suppliers is a principle of any quality management system.

8. Improvement as an ongoing objective

There has been much discussion in the medical device industry about the extent of continual improvement that can take place. The focus of the industry has been on improvement of the effectiveness of the quality management system. This does not negate the need for product improvement. Legislation is now changing to stimulate product improvement in a continuous effort, but it is recognized that for some product a basic product may need the customer's and regulatory requirements. This is in contrast to ISO 9001:2008 where there is a continuing requirement to improve product and processes.

ISO 9000 and ISO 13485 family of quality management standards

In addition to the eight quality management principles, ISO 9001:2008 and ISO 13485 are both based on the PDCA cycle. They share the primary objective of ensuring that an organization meets customer, statutory and regulatory requirements.

The standards encourage organizations to continually improve their quality management systems in an ISO 13485 way. In ISO 9001:2008 there is a wider emphasis on continual improvement, which, in addition to benefiting the organization's quality management system, will also benefit customers, suppliers and other interested parties; this is not

included in ISO 13485. The standards also assist organizations to establish controls to deal with the threats, risks and opportunities that are encountered in maintaining a quality management system and meeting customer requirements.

Process approach

ISO 13485 is based on a process approach to quality management system management. It suggests the use of a process approach for the development, implementation and improvement of the effectiveness of a quality management system, with the aim of providing medical devices that meet customer and regulatory requirements. The quality management system should be regarded as a process with several processes within it.

A process is defined as a 'set of interrelated or interacting activities which transforms inputs into outputs' (ISO 9000:2005, Clause 3.4.1). Any activity that receives inputs and converts them to outputs is considered to be a process. (See Figure 1.)

For an organization to function efficiently it has to identify and manage numerous linked processes. The output from one process often forms the input to the next process. This application of a system of processes in an organization, using the identification and interaction of these processes, is called the process approach. A process approach is defined as the systematic identification and management of the linkages, combination and interaction of a system of processes within an organization.

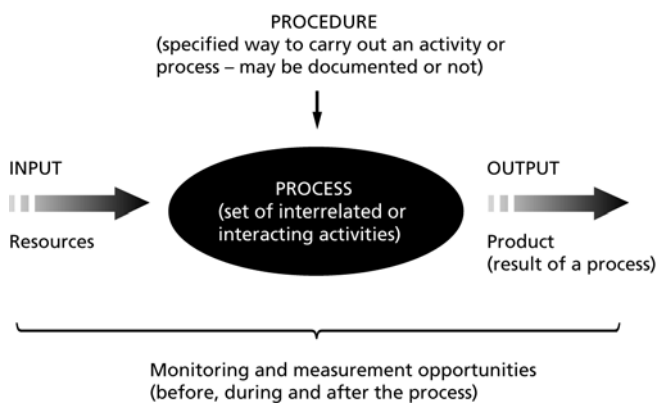


Figure 1 – The elements of a process

The process approach as outlined in ISO/TR 14969 considers the importance in understanding and meeting requirements. It looks at processes in terms of the value that the process can add, measuring the performance of processes and determining if that process is effective, and the use of the objective measurement of processes to improve those processes.

Plan–Do–Check–Act methodology

The PDCA cycle (also known as the Deming cycle) can be applied to all processes. (See Figure 2.)

It can be described as follows.

Plan: establish the objectives and processes necessary to deliver results in accordance with customer requirements and the organization's policies.

Do: implement the processes.

Check: monitor and measure processes and product against policies, objectives and requirements for the product and report the results.

Act: take actions to improve processes' performance.

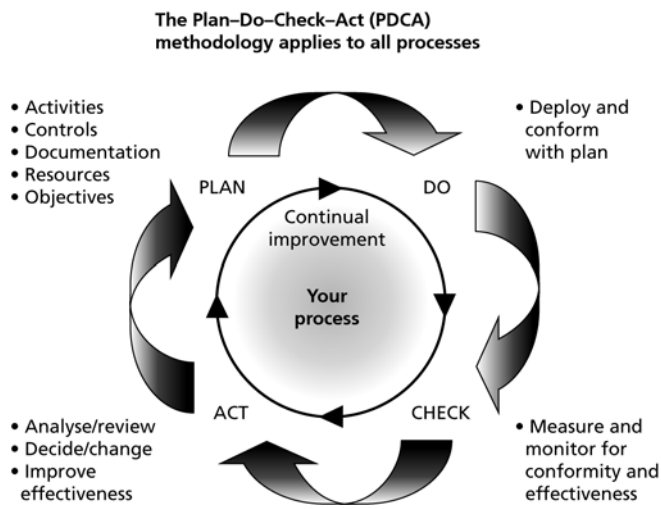


Figure 2 – The Plan–Do–Check–Act (PDCA) cycle

ISO 13485 process model

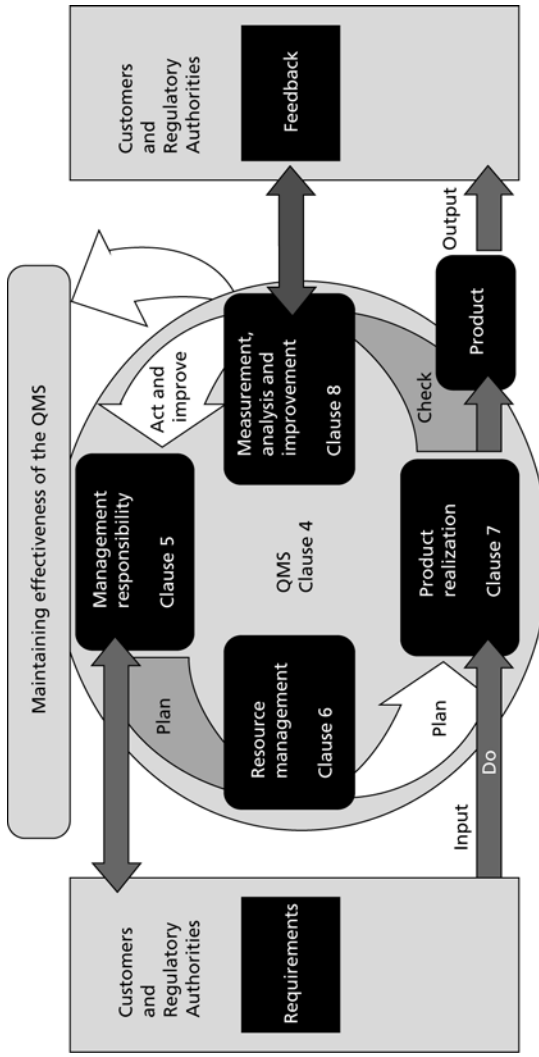
The process model of the PDCA cycle is used in ISO 13485 to link Clauses 4 to 8 of the standard. It is used to show how the requirements of customers and regulatory authorities can be met. (See Figure 3.)

The continual process starts with the 'Customers and regulatory authorities' requirements box. An organization has to take into account two sets of a customer's information. These are information from the customer at a strategic level and information from the same customer at a detailed level. The difference is that the strategic requirements are what the top management of the organization should identify, for what the customer wants now and also for what the customer might want in the future. These strategic requirements might also relate to the level of service supplied now and in the future. The organization's top management should take this feedback into account when it is setting the organization's policies and objectives, and when planning for the future (Clause 5.2). The detailed requirements are those very specific requirements from the customer for a specific product or service (Clause 7.2).

There is a link in the quality management system between the two customer boxes. The management system is related to Clause 4. Clause 4.1 is one of the most important clauses of the standard. It is this clause that sets out the foundations for the management system, with special emphasis placed upon processes and their measurement and improvement.

There is a link with the 'Management responsibility' box (Clause 5). The organization's top management should have overall control of the management system.

There is an arrow between the 'Management responsibility' box and the 'Customers and regulatory authorities' requirements box. This arrow relates to Clause 5.2 mentioned above and top management's relationship between the organization and its customers.



(source: based on ISO/TR 14969:2004, Figure 1)

Figure 3 – ISO 13485 process model

There is a link with the 'Resource management' box (Clause 6). When top management has determined its policies and objectives from customer requirements and what it is prepared to provide, then the organization will need resources in order to provide the product/service to the customer.

There is a 'Plan' arrow, as all the activities of management and resources are 'planning' the management system to meet customers' requirements, which then flows to the 'Product realization' box (Clause 7). These are the requirements that actually provide the product/service to the customer.

The 'Do' arrow takes the detailed customer requirements that are dealt with in the 'Product realization' box and delivers the product/service to the customer.

The 'Check' arrow links up to the 'Measurement, analysis and improvement' box (Clause 8). The main feature for this stage of the process is the 'Measurement' activity. The standard requires process, product and customer satisfaction to be measured, as well as requiring internal audits to take place.

The arrow from the 'Measurement, analysis and improvement' box to the 'Customers and regulatory authorities – Feedback' box shows that one of the primary intentions of the standard is to meet or exceed customer requirements and expectations.

The 'Act and improve' arrow completes the PDCA process. All the information established from the measuring activities should be analysed for points where improvements can be made.

This stage completes the circle and then the process starts again. This is the basis of continuing to maintain the effectiveness of the quality management system.

Planning the implementation

Planning the implementation process is important. It ensures that everyone understands the goal and that the appropriate level of resources and support are available to complete the project.

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 the quality management system and the underlying causes or views, such as supply chain requirements or regulatory requirements.

Some initial general steps for a successful implementation effort would include:

- knowing how to interpret the ISO 13485 requirements for a specific organization's system;
- ensuring team members are knowledgeable about the current system in the organization;
- ensuring management commitment to the implementation process and quality management system; and
- developing a comprehensive project plan that 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, getting ready for continually improving the system, where regulatory requirements allow. The ultimate assessment and verification of the first implementation comprises a round of internal audits followed by a management review to confirm the effectiveness of the quality management system.

Planning is essential to implementing a quality management system. An important part of that planning is making sure that all the key players and stakeholders in the organization have an understanding of the requirements and the implementation process.

When planning the implementation of ISO 13485 it is important for the organization to consider what aspects of a quality management system are already in place. The planning team will need to complete a gap analysis against the requirements of ISO 13485.

There are various ways in which a gap analysis can be done. It should be performed by those involved in developing the requirements; this will help them to have buy-in to any changes that will be needed for their procedures to be implemented and then followed.

Training on the requirements is an important part of the implementation activities; various levels of training should be considered. Training should be part of the implementation plan.

Ten-step implementation process

An approach that can be taken to planning the implementation of ISO 13485 is as follows.

Step 1: Top management commitment

Top management involvement in the implementation and continuing certification to ISO 13485 is important. Top management must be able to demonstrate that it fully supports the implementation of the ISO 13485 quality management system requirements. To support this, it should have training in the requirements of the standard to fully understand its responsibilities. Without the commitment of top management, the implementation will not succeed.

To demonstrate top management commitment to the implementation, it must start the process of implementation by defining roles and responsibilities, which will include covering the following areas:

- ensuring the provision of resources to implement and maintain the quality management system;
- determining and communicating the objectives of the quality management system;
- establishing a quality policy appropriate to the organization;
- ensuring that customer requirements have been determined and met;
- appointing a management representative for top management. This role cannot be filled by a team of people: an individual has to be appointed to the position.

Top management commitment can be demonstrated in a formal way by management reviews taking place at appropriate intervals during the implementation process.

Step 2: Appoint an implementation team

Depending on the size of the organization implementing the quality management system, most organizations will usually have a team of people involved in implementing the system. It requires more than one person to successfully fulfil the implementation initiative.

Top management will need to appoint a person to lead the team. This could be the management representative. In a large organization a steering committee may be required to co-ordinate the implementation; there may also be teams related to either functional areas or subsystems in the quality management system.

It is important that the implementation team has training in ISO 13485 to ensure that all those involved in the implementation understand the requirements of the standard. This training will need to be in greater depth than the training given to top management.

Step 3: Promote awareness

All employees need to understand the intention behind implementing the ISO 13485 quality management system standard. They need to understand what their role will be during the implementation process and when the system will be fully operational. This awareness-raising is important, to get 'buy in' from all personnel during the planning and the implementation process. It should include promoting the benefits of the quality management system to staff and to customers.

Step 4: Perform a gap analysis

Unless the organization is a start-up business it will have some existing policies, procedures and processes, which may or may not be compatible with the requirements of the standard.

It is important to review existing systems to determine which meet the requirements of ISO 13485, and can therefore be used unchanged, and which will require amendment. As part of the gap analysis, the action to be taken to close the gap should be determined, together with who will be responsible for the action and the timescale in which the action should be completed.

Various formats can be used; an example is shown below (Table 1).

Table 1 – Example table of responsibilities for closing gaps

ISO 13485:2003 Clause	ISO 13485:2003 requirement	Gap	Action	Who is responsible
5.5.1	Has top management ensured that the responsibilities and authorities are defined, documented and communicated within the organization?	*1.Responsibilities have not been defined or documented*	*1. Senior management team to document responsibilities for inclusion in the quality manual by xx/yy/zzzz*	*1. Senior management team*
		2. Responsibilities	*2. The quality manual will*	*2. Team leaders*

ISO 13485:2003 Clause	ISO 13485:2003 requirement	Gap	Action	Who is responsible
		have not been communicated	*be discussed at team meetings in the functional areas within two weeks of issue*	

Step 5: Develop the implementation plan

Now that it is known what has to be achieved (from the gap analysis) an implementation plan can be developed.

The implementation plan does not have to be complicated but should identify the tasks that need to be completed. This may be at a high level, but, as a minimum, it should define timing and resources, which should be documented in a formalized plan.

Depending on the size of the organization and the project management skills available, it may be appropriate to appoint a project leader to manage the gap analysis process and completion of the actions and the implementation plan, on a part-time or full-time basis.

It is also important for the organization to consider the costs and resource requirements that will be necessary to implement a quality management system that meets the requirements of ISO 13485. The time frames for completion and achieving certification, which will be dependent on the amount of resources that can be given to the project, can also be defined and included in the plan.

The time taken for implementation will depend on the size of the organization, but it could vary from six to twelve months, taking into account the complexity of the organization's processes and whether a quality management system is already in place.

Step 6: Approve the implementation plan

For any plan it is important that there is shown to be 'buy-in' from the leadership of the organization. Top management should review the implementation plan and decide if it is appropriate to proceed. It should then approve the plan. This may be at the site or it may be at a

corporate level, if the organization operates at several sites. Approving the plan shows its commitment to implementing and maintaining the requirements of an ISO 13485 quality management system, as it is agreeing to provide the resources to ensure successful implementation of the plan.

Step 7: Implement the plan

Work begins, to implement the plan and to meet the requirements of the standard. The quality management system may be implemented in stages; examples of the stages that might be included in an implementation plan are:

- developing the documentation system;
- creating policies – this will include the quality policy;
- developing procedures and processes;
- conducting training – this should include all employees in the organization as they will all have a part to play in the quality management system;
- implementing processes and procedures, including records of the activities required by the standard;
- progressing to certification by contacting a certification body (if the quality management system is to be certified).

In the following chapters of this book the detailed implementation will be discussed in relation to the requirements of ISO 13485.

Step 8: Operate and assess the quality management system

Once implemented, the quality management system should be evaluated to determine if it is working as expected and achieving the identified goals. There should be measurement of the processes that need to be monitored, to identify whether improvements can be made.

A schedule of internal audits should be established to review and monitor that the processes are taking place in line with the procedures that have been documented, and that the records are being completed as defined by the quality management system. The internal audits will also be a review to check that the requirements defined in ISO 13485 have been appropriately implemented, and to give top management a report on the progress of implementation.

Top management should conduct a management review to evaluate the effectiveness of the quality management system that has been implemented.

Step 9: Improve the system

Top management and all parts of the organization must recognize that the quality management system will have to be constantly developed in order to maintain its effectiveness. This process will continue after implementation, based on the PDCA cycle.

Step 10: Certification and registration

Not all organizations will implement a certified ISO 13485 system. This will be a decision for the organization's top management.

If an organization is to have its system certified by a third party, the project team will need to plan for this external assessment. This will include selecting a certification body. It is normal for a system to be operating for six months before assessment by a certification body.

Receiving the certificate is not the end of the project; it is the beginning of a continual cycle of maintaining the effectiveness of the quality management system.

Throughout steps 8, 9 and 10 it may be useful to revisit and keep the gap analysis up to date. Requirements move on and the organization's quality management system may change, so this is a useful record to maintain to ensure that requirements of the standard continue to be met.

Key elements of getting started

When getting started with an ISO 13485 quality management system, there are various elements that should be considered. This includes checking that the following elements are in place:

- Is top management supporting the implementation?
- Are the required resources available, including training and sufficient resources across the various functions in the organization?
- Do those involved in the implementation have the appropriate knowledge of ISO 13485 for their roles in the implementation?
- Is there sufficient time in the plan to implement and monitor the ISO 13485 quality management system?
- Is there appropriate infrastructure in place, including workplaces, buildings, equipment, communications and supplier control?
- Are the processes defined?
- Are the processes documented?
- Are the required records in place?
- Have there been internal audits of the processes? If so, do these give valuable information to help the implementation process?

Summary

In summary, by considering the topics discussed in this chapter, the organization will now be in a position to develop the plan and to proceed with the implementation of ISO 13485 requirements. The following chapters of this book include more detail related to implementing the practical requirements of ISO 13485. These will need to be considered as part of the implementation of the quality management system and also to maintain the system once it is implemented, to ensure that it remains effective.

Chapter 4 – Quality management system: meeting the requirements of Clauses 1, 2, 3 and 4 of ISO 13485

This chapter discusses the issues that need to be considered when implementing the requirements of Clauses 1, 2, 3 and 4 of ISO 13485.

The focus of this chapter will be on:

- scope, exclusions and non-applicability;
- quality management system elements;
- document and record control processes.

The first four clauses of ISO 13485 cover the scope, normative references, the terms and definitions that are used in the standard, and the general requirements for an ISO 13485 quality management system; they set the scene for Clauses 5 to 8.

Scope (Clause 1)

Clause 1 details the scope and the application of the standard, and specifies the requirements for organizations that wish to use the standard for their quality management system. The organization must be able to demonstrate its ability to provide medical devices and related services that meet customer and regulatory requirements. An aim of the standard is to facilitate harmonized regulatory requirements for medical devices.

The scope of an organization's quality management system must relate to medical devices for an organization to be able to use ISO 13485.

An example of an acceptable scope for an organization that is meeting the requirements of ISO 13485 is: 'Design and manufacture of in vitro blood glucose monitors', as this clearly identifies the medical device in the scope. An example of a scope that may not be applicable without further clarification is: 'The provision of a microbiological testing and consulting service'. With this scope it is not clear that the service is for a medical purpose.

It may be that an organization is not placing a finished medical device on the market but is supplying a product or service. ISO 13485 can be used for this type of organization. For example, undertaking repackaging for a medical device or sterilizing a medical device is within the scope of ISO 13485.

Exclusions and non-applicability

ISO 13485 can be applied to any organization, whatever its 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 organization's quality management system, typically in the quality manual.

If any requirement of Clause 7 is not applicable to the organization (due to the nature of the medical device), then that requirement does not have to be included in the organization's quality management system, but it must be justified. An example of this is sterilization: this requirement can be excluded if the manufacturer does not produce sterile medical devices or if an organization is not servicing or installing an instrument for a customer.

The terms 'if appropriate' and 'where appropriate' are used several times in ISO 13485. 'When a requirement is qualified by either of these phrases, it is deemed to be "appropriate" unless the organization can document a justification otherwise' (ISO 13485:2003, Clause 1.2).

Normative references (Clause 2)

ISO 9000:2000, Quality management systems — Fundamentals and vocabulary should be used in conjunction with ISO 13485:2003. This standard gives useful information that can be used when implementing ISO 13485.

Terms and definitions (Clause 3)

This clause of ISO 13485:2003 gives terms and definitions that are used in the standard. There are some changes in the terms that are used from the ISO 13485:1996 version of the standard. The term 'organization' relates to the company/manufacturer that is implementing ISO 13485:2003.

This is a useful clause to use when starting to implement an ISO 13485 quality management system to ensure that the organization uses terms and definitions consistently.

Quality management system (Clause 4)

Clause 4 of ISO 13485 defines the general requirements related to the quality management system, documentation requirements and requirements for records. This sets the scene for the following clauses of ISO 13485.

General requirements (Clause 4.1)

As part of this requirement an organization has to put into place a documented quality management system, use this system and then make sure the effectiveness of the system is maintained.

To do this the organization has to:

- identify the processes;
- determine the sequence of the processes and how they interact;
- put the methods and criteria in place for monitoring these processes, so that the processes can then be monitored and measured;
- make sure resources are available;
- monitor and measure the effectiveness of those processes;
- put in place a system for identifying where improvements can be made.

Often this is done with process flow diagrams for the organization's processes. The processes included should relate to the business and how the business processes interact, not just to the way the quality management system manages those processes.

The Figure 4 shows how the processes in ISO 13485 interact.

This links the following clause (Clause 5) of ISO 13485 from management responsibility, to resource management, to product realization through to measurement, analysis and improvement, and then back round again.

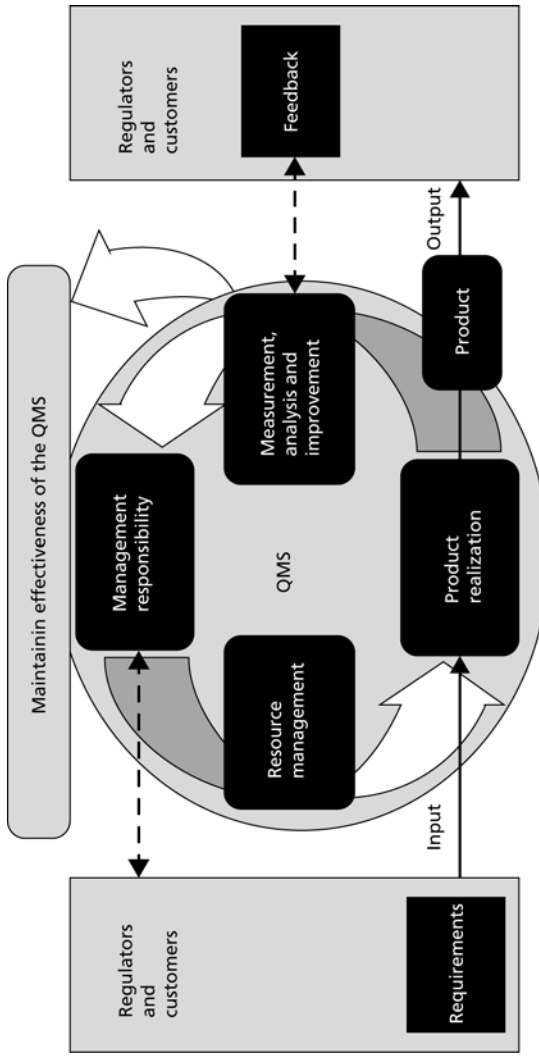


Figure 4 – How the processes in ISO 13485 interact (source: based on ISO/TR 14969:2004, Figure 1)

Outsourcing

The only place in ISO 13485 where outsourcing is referred to is in Clause 4.1. There is a great variety in the types of processes that an organization can outsource, such as rare reagent manufacture, distribution, calibration, servicing/maintenance, regulatory affairs, IT and vigilance/medical affairs support.

Some organizations are virtual organizations, where most of the activities are outsourced, including design and manufacture.

The supplier of the outsourced processes should be managed in the same way as any other service or material that is purchased from a supplier. This is covered in more detail in Chapter 7.

When an organization outsources a process it still remains responsible for that process. It must ensure that the processes remain suitable and effective as part of the quality management system. Once an outsourced process has been identified, then the mode of control should be identified and documented. The organization will need to ensure that the product requirements are not affected as a result of outsourcing that process. For example, if the design process is being outsourced, the business that is outsourcing the process would need to be involved in defining the design inputs to ensure that the customer and regulatory requirements are met.

Documentation requirements (Clause 4.2)

This clause includes general requirements, what should be included in a quality manual, and the requirements for the control of documents and records that are used to support the quality management system.

To be efficient and effective an organization has to manage how to ensure that those working in that organization carry out processes in a consistent way. This includes both large and small organizations. In large organizations it means that tasks are completed in the same systematic way; large organizations, or those with complicated processes, cannot function well without documented management systems.

General requirements (Clause 4.2.1)

Within the quality management system there should be various types of documents, including:

- a quality policy and objectives;
- a quality manual and documented procedures as required by ISO 13485;

- the documents that are necessary for the planning, operation and control of processes;
- required records, including those required to support regulatory requirements.

These documents and records have to be controlled and maintained as part of the quality management system.

The requirements for documented procedures are referenced in at least 27 places in ISO 13485, including requirements for: document control, control of records, monitoring environmental conditions, design and development planning, purchased product requirements, servicing, validation of software, validation of sterilization, identification of product, traceability of product, preservation of product, control of product with limited shelf life, control of monitoring and measuring of equipment, a feedback system, internal audits, nonconforming product, the analysis of data, advisory notices, corrective action and preventive action.

What should be included in a procedure?

These are examples of the typical sections that a procedure can include:

- purpose;
- reason for the procedure;
- scope:
  - boundaries for the procedure;
  - which activities are covered;
  - used by which organizations;
  - applicable to which product lines;
- definitions:
  - definitions of terms not readily understood;
  - explanations of any abbreviations; or
  - hyperlink from procedure to glossary terms;
- responsibilities:
  - job titles of personnel who perform the activities;
  - summary of the responsibilities and authority;
- references:
  - documents mentioned during the procedure;
  - list of related procedures and/or instructions;
  - indication if any references are attached;
- procedure:
  - description of the actions to perform a process;
  - conveyed in logical sequence of activities;
  - corresponds to the process flowchart;
  - covers what, when, where and by whom;
  - considers inputs, outputs and measurements;
  - describes quality criteria and deviation steps;

  - identifies the process suppliers and customers;
- history:
  - revision log;
  - detailed changes to content.

Documented requirements are referenced in at least 16 places in ISO 13485, including: maintenance activities, health, cleanliness and clothing, work environment conditions, cleanliness of product, risk management, contamination control and installation activities. These are situations where it may not be necessary to have procedures, but where the requirements have to be detailed. For example, when maintenance of a piece of equipment is carried out, the measurements that have to be checked or the tasks that have to be completed may be written in a document that provides a record of the activities. They do not have to be detailed in a procedure as they are carried out, because the personnel doing the work are trained in the task.

The quality policy and quality objectives will be covered in the discussion relating to Clause 5 (in Chapter 5). Throughout the book, where documented procedures are required, they will be reviewed in relation to the relevant clause of the standard.

Quality manual (Clause 4.2.2)

A quality manual is a requirement of ISO 13485. The standard does not specify how to write a quality manual or its format, but it does have some requirements. A quality manual is an outline of the organization's quality management system and how the system meets the requirements of the standard. Many organizations write their quality manual to follow the clauses of the standard, but this is not a requirement.

The scope of the quality management system has to be included. This should clarify all of the activities carried out by the organization; the scope should also detail if more than one site of an organization is covered by the quality management system.

The quality manual also has to state what has been excluded from the organization's system and any parts of the standard that are not applicable to the system. The justification for these exclusions and parts that are not applicable must also be stated in the quality manual. Most organizations cover this when they describe the scope of their system; if there are no exclusions or parts of the standard that are not applicable, it is helpful to state this for clarity.

The quality manual should refer to the documented procedures that are required by the quality management system and ISO 13485. It must include 'a description of the interaction between the processes' (ISO 13485, Clause 4.2.2) that make up the quality management system.

The best approach to describing the interaction of the processes is to use process maps; these maps should reflect the processes that are used throughout the business. They should be there to help the business and include all functions in that business.

Some organizations base their process maps on the PDCA cycle that is used in ISO 13485 to provide an overview of the clauses of the standard. However, this is only part of the way in which process maps can be used; in addition, they should be used as a top-level map to demonstrate the processes that make up the organization. Process maps may be used in all of an organization's procedures to give an overview of those procedures; this will help to explain the process at a top level to those using or being trained in the process.

It is important for these process maps to show the interaction between the processes and, within a quality management system, to help the users understand the processes they use day in, day out. It is especially important to understand where these processes interact with other processes in the organization. This is why it is a requirement of ISO 13485 to ensure that the quality manual describes the interaction of the processes throughout the organization.

The process approach was described in Chapter 3; in the quality manual this should be used to support the description of the interaction between the processes.

In the quality manual there should be a description of 'the structure of the documentation used in the quality management system' (ISO 13485, Clause 4.2.2). This may be a reference about how the procedures are organized, for example:

- if they are presented separately as policies, processes and procedures;
- if there is only one type of document in addition to the quality manual;
- if the quality policy is documented with standard operating procedures (SOPs);
- how the manufacturing documentation is organized:
    - manufacturing documentation and forms to record the results;
    - manufacturing procedure in which personnel complete the required information for it to become a record of the activities that have taken place;
- a separate set of procedures that are used to state how equipment should be used, often called Equipment operating procedures (EOPs).

Organizations may use the pyramid diagram, as shown in Figure 5, to describe the structure of the documentation in their quality manual. The elements of the quality management system documentation can be represented as shown in Figure 5, in a hierarchy.

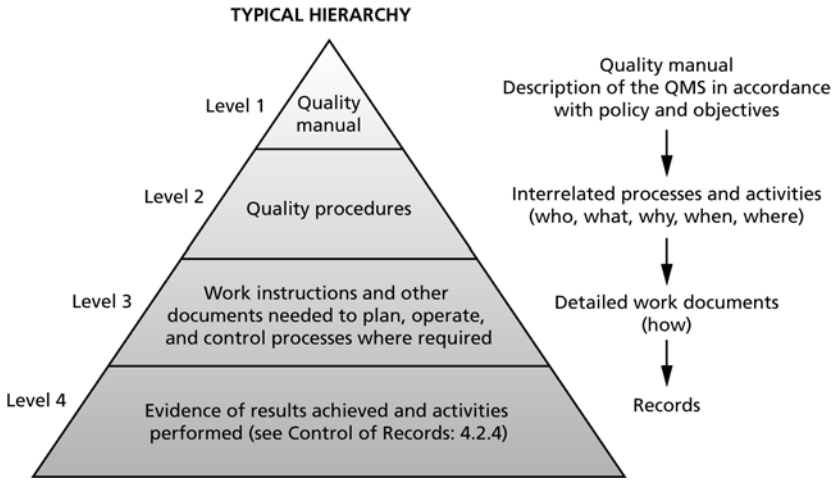


Figure 5 – Pyramid hierarchy of documentation

Level 1 – Quality manual:

- overview of the organization and its product and services;
- agreement to comply with applicable ISO 13485 requirements;
- system scope;
- exclusions;
- sequence and interaction of processes;
- procedures or reference to them.

Level 2 – Quality procedures: the 'who, what, why, when and where' of meeting customers' requirements. Processes and procedures have to be interactive to enable the quality management system to work. In ISO 13485, there are at least 29 references to documented procedures.

Level 3 – Work instructions and other documents needed to plan, operate and control processes where required: 'how' activities are carried out from the processes. These documents should be balanced with the skills of the personnel conducting the activity. In theory, the organization does not need any procedures if it is confident that all its personnel know how to do their job. This level may include quality plans, work instructions, drawings, flowcharts, workmanship standards and product specifications. There are 16 references to documented requirements in ISO 13485.

Level 4 – Evidence of results achieved and activities performed: these should include any record in the organization that has been generated to meet the customers' requirements. Records may be mandatory or implied for each ISO 13485 clause.

Control of documents (Clause 4.2.3)

Control of documents is a key process for any organization that has a quality management system. It includes requirements that they should be legible (particularly important if they are handwritten), and about how they should be approved and retained.

Documents and records can be viewed in the following way:

- document what has to be done;
- do what is documented;
- document what is done.

A procedure is required for the control of documents.

All documents that are part of the quality management system have to be controlled. This is to ensure that the users of the documents are using the most current version.

Organizations may have several procedures to manage various types of documents. For example, as follows.

- There can be procedures covering the processes that are used for general quality management system activities, for example, training. These are commonly known as standard operating procedures (SOPs) or operating procedures (OPs). These tend to detail the processes at the level below the quality manual.
- Other types of procedures detail the manufacturing processes, sometimes called manufacturing instructions or process operating instructions. Organizations often manage these through a separate system with a separate document control procedure. In addition, the organization may have other facilities for document control systems and human resource (HR) systems. It is preferable not to have too many different systems, as this can be confusing to the users and could lead to errors that could be picked up in audits as nonconformities.

The system for document control has to address the following points, amongst others:

- how documents are approved, to make sure they are correct and adequate for the task for which they are to be used, before they are approved for use;
- how documents are reviewed to make sure they are still appropriate, and then updated if required;
- how documents are re-approved before they are put to use.

Changes to documents

When a revised document is being approved it must normally be approved by the functions that approved the previous version of the document.

There are scenarios when the function may have changed. When a product is initially placed on the market it may be the research and development (R&D) function that signs off the manufacturing procedures, but once the product is in routine manufacture it may be a technical group (part of manufacturing) that approves subsequent documents. Any changes to the function that approves the documents must be clear in the document control procedure. The requirement from the perspective of the standard is, when a procedure has been put in place, it must be clear in the quality management system who should be signing which documents. These points must also be addressed:

- how changes are identified for the users of the document. How will they know the document has changed? If changes are made to a document, the version number of the document should be changed. There needs to be a system that is understood by the users. The document could have a number that is retained and then the version is identified by a letter. It also needs to be clear in the system about what types of changes require the version of the document to be changed. Is it necessary to change the version of a document if a spelling mistake is corrected? This would need to be defined in the document control system;
- the process for rapid changes. Sometimes an organization has to make changes to a document quickly. A process for doing this should be included in its document control procedure, especially in relation to manufacturing documents. There could be a concession or deviation system for a specific amount of time before a permanent change is implemented. What is important is that the temporary change is not in place for a prolonged period. The temporary change must be approved by the same functions that would have approved the procedure;
- access to updated documents. Relevant documents should be available where they are used. Often the procedures are held electronically, so that all users can access these procedures. In some areas of manufacturing this may not be possible; hard copy procedures may have to be used so that the procedure can be available at the point of use. For example, the procedure may be laminated and attached to the wall. This is often done where personnel are entering a changing area in manufacturing. Here it is helpful to have illustrations included in the procedure to demonstrate how the clothing should be worn. The use of illustrations and diagrams in procedures often makes them easier to understand, ensuring that they are understood in the same way by all users;

- documents have to be legible and readily identifiable. This may mean that in certain areas they need to be laminated so that they are not damaged by the activities taking place in the area. To ensure documents are identifiable they have to have some unique identifier on each page of the document. This is important if pages from a document become separated and muddled with another document. It is also important that it is clear when users have reached the end of a document. It is preferable to do this by using a numbering convention for the pages, such as 'x of y' (e.g. page 6 of 8). Some organizations put 'end of document' at the end of the document but this is not as clear as using the system 'x of y' for page numbering.
- documents of external origin, including copies of standards such as ISO 13485, also have to be controlled. Organizations have to ensure that they have only 'legal' copies of standards and other regulations that are used in relation to the quality management system. A way of doing this is to have one person responsible in the organization for the control of these standards and regulations, using a system that tracks when a standard is revised – for example, ISO 13485:2003 replacing ISO 13485:1996. When these changes occur, all the copies of the standard that may be held in the organization must be replaced. If internal auditors have copies of the standard they would need to be provided with the updated copy of the standard. For this reason the standards and regulations used by the organization have to be controlled. If previous versions of standards and regulations are kept by the organization after they have been superseded, they must be clearly marked to show that they are obsolete.
- superseded documents. When a document is replaced with a new version it is important that all copies of the previous version are removed from circulation, and are no longer used. If an electronic document control system is not being used, the organization needs to have another system to ensure that previous copies are replaced. This may be the responsibility of the manager of the area where the documents are being used, or it may be the responsibility of the document controller; this should be defined in the document control procedure. Electronic document control systems use different ways to identify documents that are superseded. For example, when documents are printed there might be a date of printing together with a statement that the document can only be used for a short period of time, such as one or three days.

Whether the system is electronic or paper, all users of the system need to understand that they cannot keep copies of procedures that are past their 'use by date', and that these must not be used for manufacturing or for processes in the quality management system.

There may be a reason why a user needs to keep a previous version of a document. If this is the situation, the document must be clearly marked

to show that it is superseded – this can be done electronically with a watermark or by stamping or writing on the hard copy of the procedure.

Superseded versions of documents need to be retained, normally by the document control function. This is important for when the system is being audited, because the assessor may want to see the procedure that was in use at the time an activity was completed – which may be a couple of years previously. These superseded documents also need to be retrievable in a timely way during an assessment; this is easier with an electronic documentation system than a paper system.

- retaining out-of-date documents. Documents, even when they have been superseded, must be available for the lifetime of the product to which they relate. So, for procedures relating to the design and development of a medical device they would need to be retained until that product is no longer being used by the customer; this may be several years after the last unit of that product was sold. For a medical device such as a hip implant, the lifetime of the device may be as long as 30 or even 50 years after the device has been implanted into the patient. For in vitro diagnostic medical devices the lifetime of the product is usually the expiry date of the reagents; however, the consequence of the result of the test (the information) on the patient may have to be considered, so the documents (and records) will need to be retained for an appropriate period after the testing has been completed.

Organizations tend to be conservative when they define how long they will retain documents for, and some documents relating to the design of a device might be retained indefinitely. When the retention period is defined, regulatory requirements for the countries that the medical device is sold in should be considered. The retention period of the document should also take account of the legal liabilities related to the product.

There is further discussion on the lifetime of the device in relation to risk management in Chapter 7.

Use of electronic document management systems

Organizations more and more are using electronic document management systems to control their documents. When using electronic systems it is important to consider any national and regional regulatory requirements relating to electronic systems; these may cover, for example, access and storage of electronic procedures, audit trails and requirements for electronic signatures. An example of this is the US requirements in Electronic Records: Electronic Signatures, 21 CFR part 11.

Even with electronic systems, some paper copies of documents are still required. These may be in areas where it is not possible to have electronic copies available when the task is being completed (as discussed above).

Device master records

The FDA QS regulation, 21 CFR 820.181, requires that manufacturers have a device master record (DMR); this comprises the same documentation specified in the last paragraph of ISO 13485, Clause 4.2.1. The DMR should contain (or make reference to by index) the location of the required documents. The same document file can do double duty in fulfilling the intent of Clause 4.2.1. The documents contained in the DMR are subject to the same document controls as in the procedures from Clause 4.2.3.

Control of records (Clause 4.2.4)

Quality records are an important part of any quality management system. In ISO 13485 they are the evidence that the required activities have been completed.

Records are a special type of document. Documents can become records. For example, in a manufacturing area the instructions for the process are in a controlled document; this document becomes the record when the information that is recorded during the process is included. Clause 4.2.4 details which types of records have to be managed and controlled.

In ISO 13485 records requirements are referenced in at least 50 places, including: training, maintenance, risk management throughout product realization, design and development inputs and outputs, design reviews, design and development verification and validation, design changes, supplier evaluations, verification of purchased product, installation, servicing, results of validation of software, sterilization process validation, process validation plans, unique identification of product, special storage conditions, calibration of equipment, internal audits, nonconformities, results of analysis of data, customer complaint investigations, corrective action investigations and effectiveness, preventive action investigations and effectiveness, records required by regulatory requirements, management reviews, and evidence that product realization and the resulting product meet the specified requirements and traceability. Many organizations will have the need for records for other aspects of the system due to the nature of their business.

Retention of records

In Clause 4.2.4 of ISO 13485 there are requirements for the control of quality records, including completion, '…storage, protection, retrieval…and disposition of [quality] records' (ISO 13485, Clause 4.2.4).

The purpose of the records is to show evidence of conformity to the requirements in ISO 13485, and to demonstrate that the system is operating effectively.

ISO/TR 14969:2004 identifies three categories of records:

a) those that relate to the design, and the manufacturing processes, affecting all medical devices of a particular type;
b) those that relate to the manufacture or distribution of an individual medical device or batch of medical devices [these should be kept for the lifetime of the particular device to which they relate];
c) those that demonstrate the effective operation of the overall quality management system (system records) [these will need to be kept for the periods defined in the quality management system].

(ISO/TR 14969:2004, Clause 4.2.4.1)

There are various ways in which organizations document how long they will retain records. Some will detail this information in the procedure relating to a specific activity; others will have an overall procedure that details how long all records are to be retained. The latter may be easier because then there is one place to go to find the information.

Completion of quality records

Maintaining good records relating to a medical device is important, not just because it is a requirement of the quality management system. It may also be helpful in investigating any issues or complaints that may subsequently occur during the lifetime of the medical device.

Handwritten records have to be completed in such a way that they are permanent, so they must not be completed in pencil. The problem with completing a record in pencil is that it can be erased, and this means that the record could be changed without this being recognized. Records should be completed in ink. Traditionally, this has been black or blue ink, mainly because if a record was photocopied, any other colour may not have been visible, but with the advent of digital scanning and improved copiers this is no longer such an issue.

In the record it should be clear who has completed the record. There are various practices for recording who has completed the record; sometimes there are initials or a signature. There needs to be some means of knowing who the initials or the signature represents; some organizations

keep a record of the signatures and initials of all members of staff. For manufacturing, validation, design and other records the person who is completing the record has to print their name alongside their signature at one place in the record.

It is preferable for the date to be recorded in the record along with the signature. If the date is not recorded, the sequence in which activities were completed may not then be clear. It should be remembered that, if the date is written in numerals only, different countries have different conventions for writing the date; this can be confusing. If a date is written 04/06/2011, this would be 4 June 2011 in the UK and 6 April 2011 in the United States. It is preferable to write the date in alphanumeric style for organizations that operate in several countries; if an organization is audited by an assessor from a different country it may otherwise be necessary to explain the date format that is used in the organization.

When completing a record there are best practices for recording the information. The data should be added to the record as the activities are completed. Records should not be pre- or post-dated and another person's signature must never be used. A form should be fully completed.

When data is recorded separately, if the data is transcribed to the record sheet, that transcribed data must be checked or countersigned to confirm that it has been transcribed correctly, or the original data must be retained. Printouts from some equipment may fade over time due to the combination of the ink and paper, and it is suggested that these should be photocopied and retained.

If an error is found in a record it is important that it is corrected in the right way to ensure that the original record can be seen and is not concealed by the correction. The error should be crossed through with a single line and the correct entry written alongside; this is then signed and dated, with a reason given for the correction. The signature is to show who made the change and whether they had the authority to make that change. It is preferable to date the correction and give a reason, because this makes clear when the record was reviewed in the sequence of events and why it was changed. It should be ensured that the reason given makes it clear why the change has been made, to someone seeing the document who has never read it before. This may be a considerable time later; just stating that it was an error does not tell a subsequent reviewer anything to support the change and may make them question the change further. It is sometimes difficult to give a reason, but the more informative this is, the more it will help the review of the record – which could be several years later if it is a manufacturing record and the medical device has a lifetime of several years.

Storage and retrieval of quality records

Records have to be protected to ensure that they can be retrieved when required. This may be for an audit or because the record contains relevant information relating to an investigation of a complaint.

Paper records (if this is the only way the record can be stored) need to be protected from flood, fire and theft – or just from being misplaced. Nowadays, records, even if they are paper, are often scanned for storage. It is just as important with scanned records as it is with paper records to index and store them in a way that enables them to be readily retrieved. How often has it been said that an item stored electronically cannot be found because the user is not sure which folder it has been placed in? This is equally important for the archiving of paper records. During an audit the assessor has a finite time in which a record can be found, so it is important that the system of retrieval and storage is understood.

Summary

In summary, Clauses 1 to 3 are the clauses that set the framework for the quality management system. Clause 4 details the top-level requirements for the quality management system that are developed further in Clauses 5, 6, 7 and 8. Having good record and document control systems will also be the basis for ensuring that all the requirements in Clauses 5, 6, 7 and 8 are correctly implemented and maintained.

Chapter 5 – Management responsibility: meeting the requirements of Clause 5 of ISO 13485

This chapter discusses the issues that need to be considered when implementing the requirements of Clause 5 of ISO 13485.

The focus will be on:

- management commitment;
- customer focus;
- the quality policy;
- planning;
- responsibility, authority and communication;
- management review.

ISO 13485 places great emphasis on the involvement of the organization's top management (senior or executive management), its commitment and leadership in supporting an ISO 13485 quality management system and the business of the organization. These requirements are detailed in Clause 5.

Management commitment (Clause 5.1)

It is important that the most senior managers of the organization show their management commitment. Top management can demonstrate the maintenance of this commitment by fulfilling several requirements in ISO 13485. The senior management in the organization has to ensure that those working in the organization are aware of the statutory and regulatory requirements that must be met to place the product or services of the organization on the market. This includes meeting customer requirements.

Top management for the organization has to be defined; most organizations usually do this in their quality manual. This is normally the leadership team in an organization, although it does not have to be; whatever the case, the organization's definition of 'top management' must be clearly documented.

A quality policy has to be written for the organization. Although others in the organization may develop the policy, it is top management's responsibility to make sure it is established and appropriate for the organization. A way of demonstrating this is that the most senior manager of the organization signs the quality policy. If this is a multi-site organization, it will depend on whether the quality management system is independent of the other sites; if so, then the senior manager for that site will sign it.

When assessing this clause of the standard, the assessor will interview the managing director, the site director or the chief executive officer – whoever is the most senior person – to determine whether top management is committed to the development and implementation of the quality management system and how its effectiveness is being maintained. The assessor will also try to determine whether the quality objectives have been established and whether these have taken into account whether there are adequate resources. The assessor is looking to confirm that top management has demonstrated its commitment by the actions it has taken in the organization. This may be demonstrated in several ways:

- top management ensures that there are sufficient resources to maintain the quality management system;
- top management ensures that the quality policy and objectives are communicated throughout the organization;
- top management has an understanding of customer and regulatory requirements.

A quality management system is a set of interrelated processes. Part of reviewing the management responsibility is an assessment of whether top management is ensuring that there is a coordinated system in which the processes operate.

When reviewing if the processes are working effectively, top management should be considering the extent to which:

- planned results are being achieved effectively. The sequence of the processes and how they interrelate ensures that the planned results of the processes are being achieved;
- the inputs, outputs and activities covered by the process are understood. This can be demonstrated by using process maps for the key processes of the organization. Top-level process flows or process maps are often included in the quality manual and in the top-level procedures supporting the quality manual;
- key performance indicators (KPIs) or measures are used to monitor the individual processes to ensure that they are operating effectively;
- the hazards and risks associated with a process are identified;
- the improvement of processes is facilitated by analysing the data from the processes. A four-up diagram is a useful technique for this

purpose. This is where a page is divided into four segments, each detailing an aspects of that metric (for example, a graphical representation in one segment, listing actions in another segment and progress against those actions from a previous review in a third segment). This makes it easy for top management to quickly gain an understanding of the issues, either positive or negative, related to the metric;
- for each process, a process owner is identified who has the responsibility and authority for the process;
- each process is being managed to achieve its objectives.

Top management in the organization must have an overview of the processes, to ensure that they all have owners and that the objectives are being met. This overview may take place as part of a regular top management review, but if the organization's top management review occurs only annually this may not be frequent enough. Organizations often review their key metrics at their regular management meetings for the business, reporting to top management as required. This demonstrates that top management has a regular overview of the business and that the use of quality management system principles supports the management of the business and the organization.

Customer focus (Clause 5.2)

Top management needs to have an understanding of customer requirements. It is the top management team's responsibility to ensure that the requirements of customers are met. Meeting these requirements links to other clauses:

- customer-related processes – determination of requirements related to the product (Clause 7.2.1);
- customer feedback (Clause 8.2.1).

In Clause 5.2, the emphasis is on understanding the customer focus from a strategic/business focus, which then supports the more specific activities required by Clause 7.2.1 and Clause 8.2.1. The standard links these clauses as pointers to how these requirements can be fulfilled. This demonstrates an important aspect of the standard: the clauses are all interrelated. When reviewing to check that all the requirements of ISO 13485 have been implemented, this cannot be done until all aspects of the standard have been reviewed. It also demonstrates that there may be many ways of fulfilling the requirements; the standard does not specify how to fulfil the requirements but only what the requirements are. Hence, it is top management's responsibility to ensure that these requirements are fulfilled in a way that aligns with the business needs of the organization.

Top management must understand the needs of the organization's customers. For any business to be successful it is important to know how

its markets are changing. This information may come directly from customers, from affiliated organizations, or from distributors of the organization's product or services.

Another aspect of customer focus also needs to be considered: whether any specific regulatory requirements need to be fulfilled in the markets where the product or service is to be supplied. Without fulfilling these regulatory requirements, it will not be possible to fulfil the customer requirements.

Quality policy (Clause 5.3)

Every organization has to have a quality policy; it is top management's responsibility to ensure this policy is defined and appropriate for the organization. This is the 'road map' or vision of the organization. The quality policy should relate to the business operations of the organization; it is not just related to quality. This is where the quality management systems and the business systems become one and organizations should adopt this principle when preparing their overall set of policies.

A quality policy can be a simple one-line statement or more complex. It must include the commitment of top management and the organization to meet the requirements of ISO 13485 and regulatory requirements in relation to markets for the organization's product. There must also be a statement of commitment in the quality policy to maintain the effectiveness of the quality management system.

The quality policy provides a framework for reviewing and establishing the quality objectives. It establishes the context for the quality objectives.

Commitment to the quality policy is demonstrated by communicating the policy to all members of the organization. This may be by discussing the quality policy at management meetings and reviewing changes at team meetings, or by teams discussing how their roles in the organization relate to the quality policy. During an ISO 13485 assessment, members of the organization will be asked if they know what is in the quality policy. They will not be expected to know it word-for-word, but will be expected to demonstrate that they understand how the policy relates to their role in the organization.

Another way in which an organization can demonstrate that the quality policy has been communicated is by displaying signed copies of the quality policy in various locations across the site. It is important to ensure that these copies are controlled: if the quality policy changes, all copies will need to be updated.

Top management should ensure that the quality policy is reviewed to make sure that it remains current in relation to the quality-related goals and objectives of the organization. This is often done by including the quality policy as a standard agenda item in a management review.

Examples of acceptable quality policies are as follows.

- ABC Medical is committed to complying with customer requirements, as well as regulatory requirements, and to continually improving the effectiveness of our quality management system. Our organization has decided to achieve quality objectives as set out in the documented statement of quality objectives. The top management of our organization reviews the quality management system in meetings of the board of directors, at least once every six months. Our quality management system is designed to ensure the maintenance of product quality through evaluation, inspection and verification processes at all stages of production.
- QRSO Inc. is committed to the highest level of quality in the manufacture, sale and support of our product. Product quality, compliance to all applicable regulatory requirements and continuous improvement shall underpin all of our efforts in development, manufacturing, advertising, sales, shipping and technical support.

An example of a quality policy that is not acceptable, because it does not include the commitment to meet regulatory requirements, is shown below.

> XYZ Medical is committed to providing quality product and services that meet or exceed the expectations of our customers, and which have significant scientific and clinical benefit. The needs of the customer and the patient are central to all our efforts. The contribution and commitment to quality of each employee is critical to the success of the entire company – the foundation of XYZ Medical's success is our employees. We are committed to performing all of our activities in an ethical manner.

Planning (Clause 5.4)

Top management has responsibility for planning the quality objectives, and for planning to ensure that the quality management system is appropriately implemented and effectively maintained.

Quality objectives (Clause 5.4.1)

The quality objectives are the way in which top management puts the quality policy into operation in the organization. These objectives need to be clearly defined so that they can be understood by all staff; they

must be linked to the personal objectives of all those working in the organization. They are typically established annually.

The actions related to the quality objectives do not have to be the personal objectives of top management, but it is top management's responsibility to ensure that they are completed. It is typical that the quality objectives are cascaded down in an organization so that everyone in the organization can relate them to their day-to-day activities. Not all the top-level quality objectives will apply for all functions, but some objectives will cover the whole organization. It is important that top management can explain to assessors of its ISO 13485 system how the quality objectives relate to the quality policy and how they are cascaded to everyone in the organization.

Quality objectives need to be SMART (specific, measurable, achievable, realistic and timely), like any other objectives, and it is particularly important that they have time frames. The quality objectives are not only for the quality management system but also should relate to the medical devices and/or services that the organization provides. This is linked to the planning of product realization. (This will be covered in more detail in Chapter 7.) They should relate to both customer requirements and regulatory requirements, as well as ensuring an effective quality management system is maintained.

Examples of quality objectives are:

- reduce the cost of nonconforming materials (scrap and rework) by 15 per cent;
- product returns due to nonconformity to requirements will represent less than 1 per cent of sales;
- Improve on-time performance to 97 per cent of product;
- internal audit corrective actions to be completed by their due date.

Objectives are best if they are quantified, for example:

- test rate = tests passed/tests planned;
- scrap rate = products rejected/products produced;
- complaint rate = received complaints/total customers;
- on-time delivery = deliveries by due date/deliveries scheduled.

Having quality objectives established is a way in which everyone in the organization can understand the aim of their role and give a focus for the organization. When goals are measured regularly, it is a monitor of the performance of the organization as a whole, and the performance of teams and individuals in the organization. There is a saying that is often used: 'What gets measured gets done'.

Quality management system planning (Clause 5.4.2)

This is the process by which the organization translates its quality objectives and other inputs into activities, to make sure they happen. This relates to general overall planning, rather than the more detailed planning that is required, for example, for product realization or resource management.

The quality objectives are only one of the inputs into the planning. Other examples of planning inputs are the organization's quality policy and regulatory requirements related to the markets in which the medical devices are sold.

Examples of outputs from planning are:

- the quality manual – this shows how the requirements of the quality management system are to be achieved;
- gap analysis, for example, if there is a new regulation that affects the quality management system: to identify any changes that may have to be made, the action plans and the results of these actions.

These are often documented as quality plans. Organizations will often have quality plans that identify the areas of focus (usually improvement) for a given period – typically, a calendar year. It is important that quality plans fit with the business goals of the organization.

Examples of quality plans are:

- A reduction in the number of nonconformities for specific processes;
- The redevelopment of a product to resolve specific customer complaints;
- implementing new regulatory requirements.

The ideal approach to quality planning is to include it in the budget cycle, so that it is run in parallel with the financial planning process. This ensures that there is appropriate funding for the quality plans and the priorities align with the organization's business priorities.

Responsibility, authority and communication (Clause 5.5)

Responsibility and authority (Clause 5.5.1)

It is the responsibility of top management to ensure that responsibilities and authorities for quality management are defined and communicated throughout the organization. These responsibilities of top management are often defined in the quality manual. The interrelationship of roles in

the organization has to be established, particularly separation of responsibilities for the personnel whose work could affect the quality of the medical device.

Most organizations define the responsibilities and authorities of their staff with job descriptions for the various roles that are required. These are not necessarily individual job descriptions; they could be for a group of personnel who all perform the same role. The job description would include the responsibilities and authorities of the role; it may also include the competencies the jobholder would require for their role.

Organization charts should be maintained to show all personnel in the organization and their interrelationships; these charts should identify the person who is the management representative.

The job descriptions and the organization charts are quality records, so they have to be controlled and any changes to them must be managed. Changes to organization charts often highlight the linkages between the functions; this is particularly useful where matrix management is used by an organization.

It is also necessary to have a system for delegation of responsibilities, and how this is managed. Some organizations do this by memos that are held on file; others make it clear in documented procedures how responsibilities are to be delegated and to whom, if an individual is absent.

If there are specific functions with specific responsibilities (e.g. internal auditors or the independent reviewer in a design review), these responsibilities could be defined in the procedures related to the activity.

Management representative (Clause 5.5.2)

The management representative is a key role. Only one person can be the management representative – the role cannot be shared. The management representative has to be appointed to the role by top management. This must be documented, typically in the management review minutes, and stated in the job description of the person appointed to the role. The person can have any functional responsibility in the organization, although it is usually the quality manager. If the management representative is not from the quality function, they must have independence to ensure there is no conflict of interest between their function and maintaining the quality management system.

In ISO 13485 there are specific responsibilities defined for the management representative:

- the 'processes needed for the quality management system…[must be] established, implemented and maintained' (ISO 13485:2003, Clause 5.5.2);
- the performance of the quality management system must be reported to top management by the management representative; this should include proposals for improvement where required. This is typically done by the management representative as part of a management review;
- the management representative must promote awareness of the regulatory and customer requirements throughout the organization.

In addition to these responsibilities, the management representative is often the person who is responsible for liaising with external parties about the quality management system. This could include managing audits by certification bodies, by notified bodies (if the organization is manufacturing the higher-risk medical devices that require notified body approval before they are placed on the market) and by the FDA (if the product is being sold in the United States and an assessment is taking place relating to the quality management system regulation). Some organizations have procedures for how these assessments are to be managed.

Internal communication (Clause 5.5.3)

Communicating the requirements of the quality management system is a responsibility of top management in the requirements of ISO 13485. The processes for communicating the effectiveness of the quality management system must be established in the system, so that all the members of the organization are aware of their role.

Different organizations establish different systems for communication. Examples of the ways in which communication occurs are:

- organizational meetings;
- team briefings, where information is cascaded down from top management through the organization to teams;
- emails throughout the organization (but it is important to remember those who do not regularly access their email);
- posting information on noticeboards;
- monthly bulletins that are given to each member of the organization.

The types of topics that would be communicated include:

- feedback from external assessments, such as surveillance visits for ISO certification;
- feedback following regulatory inspection from organizations such as the FDA(United States), Agência Nacional de Vigilância Sanitária (ANVISA) (Brazil), Therapeutic Goods Administration (TGA) (Australia), a notified body for CE marking;
- trends from internal audits, if there are any issues that need to be communicated organization-wide;
- an overview of the actions and conclusions from a management review;
- the organization's financial performance, if appropriate;
- quality objectives at the top level;
- quality plans and progress against those plans.
- changes to the external environment – for example, new regulatory requirements that have to be met, which will have an impact throughout the organization;
- changes to the organization's quality policy;

The methods of communication must be appropriate to the organization, so that everyone who needs to know about the information communicated understands it. This may mean that different methods of communication are used for different levels in the organization.

The systems of communication must be effective, open to all and regular. During an assessment the assessor may ask any members of the organization whether they understand how the effectiveness of the quality management system is communicated to them. The assessor will also check that the view of top management about internal communications is the same as the view of staff who are receiving the communication.

The information that is communicated should relate to top management expectations about the performance of the quality management system. It is important that this information relates to the quality management activities undertaken by the people who receive the communication. For example, a person who works on manufacturing tasks, such as packing the medical devices into their outer packaging, will need to understand how their role relates to the system: following procedures so that the process is completed consistently, completing the records of the process correctly, and wearing appropriate clothing for the area in which they are working. This information would include feedback from any external audit that the organization has had, and the impact of any nonconformities on their activities. For a person working in a quality or regulatory role, the information from an external audit would be communicated in more detail, because this person is responsible for helping to maintain the quality management system, and regulatory requirements related to it, across the whole organization.

Management review (Clause 5.6)

Management review is an important part of top management's responsibility. It is a top-level review, which ensures that the effectiveness of the quality management system is maintained. Top management must take an active part in this review.

Inputs to management review (Clause 5.6.2)

ISO 13485 specifies a series of inputs to the management review (as listed below). A way of making sure these are all covered is to define an agenda in a procedure or a form that covers both the required inputs and the required outputs.

Many of the inputs are interrelated and may not fall under one specific heading. The relationships between inputs will also depend on how the tasks are managed functionally in the organization. Inputs specified by ISO 13485, Clause 5.6.2 are:

a) 'results of audits':
   i. review of internal audits, including progress to the schedule and whether appropriate resources were available to complete the audit;
   ii. surveillance or re-certification audits to ISO 13485;
   iii. regulatory body, for example, the FDA or notified body for CE marking;
   iv. audits by consultants.

The results of the audits should identify any trends in areas of weakness identified by the audits and make recommendations for corrective actions from the trends that have been identified. These trends should cover all the types of audits to look for generic trends;

b) 'customer feedback'

Proactive customer feedback for medical device organizations can be difficult to obtain, because there may be several customers in the chain that interface with the product.

Customer feedback would include a summary of customer complaints, to identify the key issues, and enquiries and service reports, or maintenance reports, for organizations that supply instruments or software.

Post-market surveillance should interface with customer feedback. For example, have there been any reportable events under vigilance or medical event reporting? Have any product or batches had to be recalled or any advisory notices issued?

c) 'process performance and product conformity'

This input reviews the status of the manufacturing processes or service delivery, including:

i. first or past acceptance for finished product;
ii. review of nonconformities;
iii. deviations from process in manufacturing, or providing the service;
iv. issues with process validation;
v. maintenance and calibration issues;
vi. supplier issues and incoming acceptance of product;
vii. KPIs for processes;

d) 'status of preventive and corrective actions'

The organization should have a system for monitoring and analysing corrective and preventive actions from all inputs throughout the organization. The input to management review should be a top-level analysis, identifying any areas of concern and actions, for example, whether there is a requirement for more resources in specific areas.

Checking the status of corrective and preventive actions should include whether:

i. actions are being completed in a timely way;
ii. root causes are being identified;
iii. actions being taken are effective;

e) 'follow-up actions from previous management reviews'

It is important to ensure that any actions from previous management reviews have been completed, and have been recorded as having been completed. In addition, if corrective and/or preventive actions were required, these should be shown to be effective.

This can be done in several ways. The actions may be reviewed at the next meeting and their status recorded. If management reviews are only held annually, this may be too long a time interval to identify whether the actions are complete and effective. A separate log may be kept of the actions from management review, with a nominated person made responsible for following up with the owner of the action to ensure that they are on track for their due date of completion. If there are issues with completing the action, this nominated person would make sure that top management is aware of that. The log may be paper or electronic, but should be regarded as a formal record in the quality management system; it can be an input to the next management review and areas of concern discussed. Assessors are likely to review the process for how actions are tracked to completion, and how the process ensures that no actions are 'lost';

f) ‘changes that could affect the quality management system’

These changes, which could be internal or external to the organization, could include:

i. regulations;
ii. changing market environment;
iii. what competitors are doing;

g) ‘recommendations for improvement’

As each input is reviewed, recommendations should be made – these may be made by the process owner or by the management team. These are considered at management review to determine if they are appropriate. Top management will need to consider the priority of the different actions that have been identified and to ensure that there are appropriate resources available;

h) ‘new or revised regulatory requirements’

Any new regulatory requirements, or changes to any existing requirements, will be part of a management review. An example would be the changes that were put in place from 2010 to the Medical Devices Directive (MDD) and how the organization has ensured that these have been implemented in the quality management system. If the organization is selling in new markets there may be specific requirements to meet; top management would be able to determine through management review if these have been adequately implemented. In the next few years there will be many changes to regulatory requirements, including the EU directives and those covered by ISO 13485. Organizations will need to ensure that these are considered by top management through management review;

i) other inputs

Other inputs may need to be considered at management review that have come from the analysis of data as required by Clause 8 of ISO 13485.

These could include:

i. training requirements in the organization;
ii. the interface with suppliers – checking that materials and services supplied are of the appropriate quality;
iii. any particular supply issues.

The review of these inputs will allow the organization to develop its business and quality plans for future activities.

The review meeting

- When should the management review take place?

ISO 13485 requires that management reviews take place at planned intervals. These intervals need to be defined by the organization, and should be documented in the procedure for document review or in the quality manual. The standard does not require a procedure for management review; it only requires that there are records of the review. However, in practice, most organizations do document the frequency of the management review, who will attend and what the agenda items will be.

The frequency of the management review varies from organization to organization and will depend on the maturity and size of the organization. Annual reviews may be frequent enough in some organizations, but typically there is a management review every three months or every six months. In certain circumstances, an organization may need a management review more frequently. For example, when an ISO 13485 system is being implemented it may be appropriate to have management reviews monthly to check the progress of implementation.

- Who should attend management reviews?

The most senior management – those defined as top management – of the organization should attend the management review. For some multinational or multi-site organizations this may mean that each site has its own management review, with the senior management from that site. This management review feeds into the management review for the complete organization; there may be attendees from the site at the corporate level and vice versa.

It is important that anyone who attends management reviews is able to contribute on topics that are within their sphere of functional responsibility, and that they are empowered to take action on any of the outcomes, if required.

What this usually means is that for some parts of the organization there will be more attendees at the meeting than for other functions. Quite often there will be several representatives for quality/regulatory functions or the operational functions in the organization, but Finance and HR may or may not attend, depending on the issues to be discussed. Whatever the circumstances, it is important that anyone who is defined as top management for the organization attends the review.

It would be unusual for the most senior person in the organization not to attend. In exceptional circumstances this may have to happen, but it

should not occur regularly, because then the assessor may view this as an indication of the organization's top management not taking its responsibilities seriously.

The meeting is usually chaired by either the most senior person in the organization or the management representative for the organization.

- How should the meeting take place?

There are various ways in which the management review meeting can be conducted; this will depend on the style of the organization.

  - It could be a formal meeting with a structured agenda, meeting minutes and action points.
  - It could be that the attendees are from various locations, so the meeting has to take place by conference call or by using weblinks.
  - There could be initial reviews by middle managers, reporting to top management with summarized information. Top management would review the output and come to conclusions about the effectiveness, suitability and adequacy of the quality management system.
- How should the information for the review be presented?

Yet again, how the information is presented will depend on the organization. One of the problems with management review is that those attending the review can be supplied with too much information. One way of making this easier is for the management representative to provide the meeting with an overview of the information that has been supplied for the meeting. This analysis can identify any interrelated issues that apply across the various inputs. The agenda can then identify the key comments/issues for each point of the agenda.

Another approach is that at the start of the report there can be a summary of not more than three bullet points for each area for which information/data has been presented. The people attending the review will understand the key points and then go into the detail of the report if they require more information.

Organizations have different approaches to how the information should be presented at the meeting. It may be preferable for the information to be supplied before the meeting, to give the opportunity for attendees to at least obtain an overview of the key points for discussion. The information can be presented as hard copy or as an on-screen presentation.

The people attending management reviews normally have very full diaries, and so the easier it is for them to understand the important

points, the better. The shorter and more focused the meeting, the more likely it is to be beneficial to the organization.

- What should be covered and in what depth?

The items that should be covered in the review are:

  - inputs, as defined above;
  - continued suitability of the quality policy and quality objectives for the organization;
  - any quality problems and the actions taken;
  - risk management, especially if the quality management system is aiming to meet the requirements of ISO 14971, Medical devices — Application of risk management to medical devices. This would lead to a review of any product safety issues.

The depth to which the various topics are discussed will be affected by how the information is presented. Management's time is precious, so the most productive management reviews are where the information is presented in such a way that management can get to the key issues quickly, without having to read through a lot of data. This is a challenge because, for even small- and medium-sized organizations, there is a lot of data to review. At times of change in the organization, the management review may have to be more in-depth (and possibly longer).

Output from the management review (Clause 5.6.3)

The records of the review meeting can be in various forms, for example, formal minutes or notes in a notebook. They can be held electronically or on paper, but whatever form they take the organization must expect that they will be reviewed by anyone assessing the system.

The records of management review should cover the key points of the discussion that took place at the meeting. The records should document any actions, including who is responsible for them.

There may be different types of actions, such as:

- corrective actions;
- preventive actions;
- actions given to a specific individual who has attended a management review.

It is important that:

- there are sufficient resources allocated to complete the actions;
- a person is responsible for completion of the actions;
- the timescales for completion of the actions have been defined during the management review;

- a system is in place to track the actions that are being progressed, through to the following management review meeting;
- actions are documented as an input that has been completed, or there is a clear idea about the progress that is being made with the action.

As part of the output from the management review, ISO 13485, Clause 5.6.3 requires that top management should make decisions on the following:

a) 'improvements needed to maintain the effectiveness of the quality management system and its processes'.

For example:

i. the output from the review should include a statement on the effectiveness of the organization's quality management system. This needs to be included in the minutes or the records of the meeting;
ii. there should also be confirmation that the quality policy has been reviewed and remains appropriate for the organization;
iii. an example of a change that may be made as a result of the management review is that the organization may decide to hold the management reviews more frequently or less frequently;
iv. it may be decided that there should be changes in the way training is given;

b) 'improvement of product related to customer requirements'

By considering product complaints, adverse events and new product that are in design and development, it may be decided that changes need to be made to existing product or the way it is manufactured.

For example, something has been identified from customer surveys that will result in product improvements. Enquiries related to product are often a good source of information about product and how it can be improved;

c) 'resource needs' of the organization

Considering the resource implications of the actions that have been defined from management review, or ensuring that there are adequate resources to ensure that the system remains effective, are aspects that are often forgotten in a formal way as an output from management review. Resources will often be discussed in the meeting, but it needs to be remembered that it is important to document resource requirements as an output from the meeting.

Summary

In conclusion, the points discussed above all relate to the leadership of senior management, and hence the leadership of the business, focusing both on customer and regulatory requirements, and on maintaining the effectiveness of the implemented quality management system. Leadership

by top management is one of the key elements of any quality management system, because without it the organization may fail to meet the defined requirements of the standard.

Chapter 6 – Resource management: meeting the requirements of Clause 6 of ISO 13485

This chapter discusses the issues that need to be considered when implementing the requirements of Clause 6 of ISO 13485.

The focus will be on the:

- human resources;
- infrastructure;
- work environment.

It is important for any organization to have adequate resources to be able to meet customer and regulatory requirements, and to ensure that the quality management system is effective. It is the role of top management to ensure that appropriate resources are available; this links back to the requirements in Clause 5 of ISO 13485.

There are many aspects to resources. These include people, infrastructure (buildings, utilities and facilities), work environment, information, suppliers and partners, and financial resources. Even if these resources are outsourced, they have to be managed by the organization, just like its processes.

Human resources (Clause 6.2)

The people who make up an organization are one of the most important parts of a quality management system. It is important that the personnel whose work can affect product quality have appropriate competences for the tasks that they undertake: the appropriate education, training, skills and experience for their role.

Personnel affect quality throughout the organization, and not just those people who interact directly with the product or service. In fact, most of the employees of an organization could have an impact on the quality of the product. For example, if an invoice is not paid promptly (and correctly) for materials that are being used to manufacture the product,

then the materials may not be available for use by the manufacturing team and it may not be possible to deliver the product by the date required by the customer.

Competence, awareness and training (Clause 6.2.2)

For any position in the organization, it has to be considered what skills and qualifications are required for that role at the points where the individual carries out work that can affect quality. The way that this is documented by many organizations is to have a job description for each of the roles. The same role may be undertaken by several people, who carry out the same job, so they will have the same job description; but there will also be individual roles where there is a job description for that person (position) only.

The job description should include the education, background and previous training that will be required of a person, to carry out that role, as well as a description of the tasks to be undertaken by the person doing that role. This should not be a 'wish list' related to the position, but genuine requirements that are achievable, because it has to be demonstrated that the person that fills that position meets the requirements included in the job description. However, the description must not be so specific as to make it impossible to employ anyone to fill that role. Often organizations will have a list of 'must haves' and a list of desirable attributes in the job description.

When a person joins an organization for a specific job role, or transfers within an organization to a new job role, they have to be able to demonstrate that they fulfil the requirements in terms of the skills and education that are required for that role. Where previously gained skills and previous education are being used to support the fulfilment of defined requirements, it is important that the organization can demonstrate evidence of this background by holding records of it on file.

Provision of training

The requirements in the job description can be translated into training plans for when the person starts the role. Training that has already been completed when they take up the role should also be considered. Even if a person comes to a role with considerable experience, they will still need to be trained in the processes for that organization. For example, a design and development scientist will join the organization with experience of many of the techniques that they will use in their new role, but they will need to be trained in the specific design control procedures of the organization.

Training can be carried out in many ways:

- by working with a person competent in the task;
- by a training course;
- by a detailed plan of work that includes defined tasks, which have to be completed to the appropriate standard.

Quality management system training

It is also important for ISO 13485 that personnel working in the organization should have had training in the standard and what it means for their role. The depth of this training will depend on their role but most employees will require some level of training.

This quality management system training would normally include:

- training on the quality policy and how that may relate to their role in the organization;
- what a quality management system is and the key aspects of the quality management system that affect their role;
- training on document control or record completion.

This training is normally given at regular intervals. The approach that can be taken is to have quality management system training when an employee joins the organization and then to repeat this annually. This training can then be delivered to work teams and should be fairly brief, but can then be related to the actual roles that they carry out for the organization. The training can also relate their role to the quality policy and the quality objectives of the organization.

Effectiveness of training

Many organizations find the process of how to measure the effectiveness of the training difficult to establish, but it is a requirement of ISO 13485. The process of determining effectiveness needs to be distinguished from personnel completing the training and giving feedback on the training. The aim is to show that the training has a long-term impact and is not short-lived, that the person who has been trained can then continue to perform the task for which they have been trained.

This is easier to show for practical tasks such as in manufacturing, where the normal approach to training is for the trainee initially to observe the task demonstrated by the trainer. Then they complete the task with the trainer; and the third time the task is completed by the trainee with the trainer observing. This last stage can be completed as many times as is necessary to demonstrate that the trainee is capable of completing the

task. Another example of this is when training an internal auditor: they will be asked to complete an audit while being observed by a trained auditor.

For activities that are not practical tasks it can be more difficult to measure whether the trainee is competent and whether the training has been effective. This may be done by tests of understanding, discussing the revised procedures in team meetings or discussing the revised procedure with a trainer.

Contribution to quality objectives

The organization has to ensure that its employees understand how their role has an impact on the quality objectives of the organization, and the importance of their role in achieving these objectives.

Records of education, training, skills and experience

Although there is no requirement in ISO 13485 to have procedures for competency, awareness and training, there is a requirement to have records. These records will need to cover all aspects.

How training is recorded is often defined by the type of training. The function responsible for maintaining the records of training varies from organization to organization. In some organizations this is the responsibility of the functional area; in other organizations it will be a site or even a corporate function. The important point is that, within a site, the approach to maintaining records is consistent across the site, with one procedure, even if the responsibility for the process is within the functional area. One reason for this is that personnel may move to jobs in a different function within the same organization, but their previous training will still be relevant to their new role.

Often the records of education, training, skills and experience are stored in the HR function or in the area where the person is working. When an assessor is checking that the requirements of ISO 13485:2003 have been fulfilled, these records of training related to the job and the records of education, skills and experience will have to be brought together.

Some organizations make the employee responsible for maintaining their own records of education, training, skills and experience. In this situation it is even more important that there is a clearly defined system and well-documented process, because otherwise there will be inconsistencies in the records when they are assessed during audits.

The records should include:

- the curriculum vitae of the individual, as this will show that the person fulfils the requirements of the job description, together with any certificates e.g. degree, technical training;
- records of training on internal procedures. These are often electronic;
- records of courses attended. For example, for ISO 13485 or risk management courses;
- the records of the personnel delivering the training to individuals, to ensure that they have the appropriate knowledge to deliver the training;
- records for training the trainers in the organization.

Keeping records of training has often been a weak process in many organizations, but it is a key process in supporting product quality. Without evidence of appropriately trained personnel, it cannot be demonstrated that the product can be manufactured as defined in quality procedures.

Infrastructure (Clause 6.3)

For any organization that is manufacturing a product or providing a service, it is important that the infrastructure is appropriate for that product or service, to maintain its quality.

When a manufacturing facility is being established, the organization will need to consider:

- how the facility is being constructed;
- how the equipment is being installed;
- how the equipment will be maintained properly;
- how the facility will be cleaned to the standard required for the product that is to be manufactured;
- the layout of the factory, to ensure that there is space to enable the product to be segregated properly, to prevent a mix-up from the various stages of the process;
- how the product will flow through the facility. Facilities are often designed around the flow of the product so that materials keep moving through the process from the location where the materials are received through to manufacturing and then to dispatch, if there is sufficient space to do this. The product never returns to an area in the facility that it was in previously, except perhaps for storage. Organizations have different ways of showing the product flow to employees, for example, by colour-coding the doors, walls or floor of each designated area;
- how the facility, utilities, equipment and cleaning will be checked and/or validated to ensure that they are adequate for the processes that are to be used. This is particularly important for sterile product

and needs to be considered when an area is being designed or refurbished. If a product is sterile or is to be sterilized before use, or there is a situation where it is important that there are no viable organisms, the organization must consider this as part of the manufacturing environment, to ensure that the environment facilitates this. Specifications should be defined for the manufacturing environment that are appropriate for the product quality.

Manufacturing equipment

The requirements for maintenance of the manufacturing equipment have to be defined and documented, with records of the activities that take place. The approach to this is often to have a form that can then be used to record the results of the maintenance. The interval at which the various maintenance activities must be completed should also be defined; this can be included on the form. In planning the activities to be included in maintenance, the organization must consider how the process/manufacturing equipment could affect the quality of the product to be manufactured. This should also include considering how the equipment is cleaned.

Qualification of manufacturing equipment should be completed before any product manufactured on the machine is released for sale. It is important to be able to demonstrate that the equipment is capable of the processes for which it will be used. This qualification task links to the validation of processes; without equipment that is fit for purpose, the process to be used on the equipment will not be capable of producing a product of the required quality.

Where there are measurements that require calibration, the organization will need to consider how this will take place, the equipment that will be used for the calibration and the impact that this could have on the product.

Further detail on monitoring and measuring equipment, and qualification of equipment in relation to process validation, is included in Chapter 7.

Work environment (Clause 6.4)

The work environment can influence product quality. The key aspects that need to be considered are:

- how the work environment is established;
- the process equipment that is used;
- the personnel working in that environment;

- relating the work environment to the product and the impact that environment can have on the product.

Many environmental parameters can affect the product that is being produced, for example, temperature, lighting and water quality. ISO 13485, Clause 6.4 specifies this as: 'The organization shall determine and manage the work environment needed to achieve conformity to product requirements'. Often organizations do not consider the impact the work environment can have on their product or service.

Environmental monitoring

There are many situations where the work environment can have an impact on product quality for medical devices. The medical devices that may be impacted include:

- product that is to be supplied labelled 'sterile', including devices that are to be labelled 'pyrogen free';
- devices that are to be supplied non-sterile but that are intended to be sterilized before use, where the device has a limited shelf life. This is particularly relevant for in vitro diagnostic medical devices, as these devices have a relatively short shelf life and often have a specific storage temperature (either frozen or refrigerated);
- products that have special handling or storage requirements – these may be due to safety issues related to the materials the device contains;
- products that are susceptible to electrostatic discharge (ESD) due to electronic microcircuits or embedded software;
- products that are affected in their use by microbiological and/or particulate contamination, or other environmental conditions.

Factors that could affect the work environment include:

- the temperature of the area. This has to be within a temperature range that does not affect the product. This can be particularly important for manufacturers of in vitro diagnostic medical devices, where the temperature the assay takes place at often needs to be within a defined temperature range;
- cleanliness of work surfaces. Cleaning processes may have to be validated to ensure that cleanliness of the appropriate level is maintained;
- humidity;
- water quality;
- air quality (for controlling microbial and particulate contamination);
- air ionization;
- pressure differentials and airflow;
- number of people in the work environment;
- lighting (both spectral content and intensity);

- noise levels and vibration.

All the parameters that have been defined as having a likely impact on the product will have to be monitored for that work environment. Organizations usually establish environmental monitoring programmes. Buildings often have building management systems to monitor temperature and pressure – monitoring not only the areas where product is produced, but also the areas where product is stored, if there are specific storage requirements and humidity conditions.

Microbial (bioburden) and particulate contamination are monitored using settle plates and air samplers. The processes that are used for monitoring this type of contamination should be validated.

Health, cleanliness and clothing of personnel

When medical devices are manufactured, the factors affecting their production need to be understood; this includes the health of the personnel involved in production.

- Health

If a person has a medical condition that could affect the product they must not be allowed to enter the manufacturing area. The organization has to define what type of conditions could affect the product, and then make sure that the personnel working in the area understand when they are not allowed to work in the area. This can be something as simple as not sneezing near the product. The risk might not necessarily be associated with a person who is infected; it could be that saliva has an impact on the product.

- Cleanliness

Cleanliness is particularly important for the manufacturing of medical devices that are sterile, or have to be sterilized before use, or where the microbial cleanliness is important to the product that is being manufactured.

Personnel are not allowed to wear make-up or jewellery in clean rooms, because of the possible impact on the product through the risk of contamination.

- Clothing

It is usual in medical device manufacturing that the personnel working in the area have specific protective clothing for that area, even if the product is not sterile. This clothing will be non-fibre shedding. (The last thing that a customer would expect to see is a fibre in the product they are using.) The extent of protection provided by the clothing will depend

on the impact that not having the clothing could have on the product. The minimum is normally coats, hats and gloves for personnel working in areas where they can come into direct contact with the product. Sometimes, manufacturing personnel wear all-in-one suits with hoods and shoes. Where hats are worn to cover the hair, it is important that beard covers are available so that men can cover their beards, if necessary. Face masks are also worn in many manufacturing areas where there is exposed product.

The order in which clothing is put on and how it is worn is important, because the purpose of this clothing is primarily to protect the product – not the wearer. In some circumstances, for safety reasons, clothing may be used to protect the personnel working in the manufacturing area, as well as the product, if potentially harmful materials are being used.

Staff normally place their hats on their heads before putting on their coats. This is to prevent debris from the hair falling on the outside of the coat. Often there are barriers in changing rooms and shoe coverings are placed on shoes before the shoe is placed on the floor on the 'clean' side of the barrier. It is important that clothing is worn properly – for example, all hair is to be confined inside the hat – so it is helpful to provide mirrors in the changing room. The organization must define a process for how the clothing is to be worn and the standards expected, and then ensure that all personnel using the area know what is expected of them. It is often easy for an assessor for ISO 13485:2003 to enter a manufacturing area and identify someone who is manufacturing product but not wearing their protective clothing as expected.

The requirements for health, cleanliness and clothing have to be documented; there should also be records of staff training in these requirements.

Environmental conditions

There must be documented requirements where the work conditions could have an impact on the product. The environment also has to be monitored. For sterile product it is important that the environment is appropriate to the product quality. This is linked to Clause 7.5.1.2.1.

Personnel

Personnel who are working in a special environment, even if they are visiting the area on a temporary basis, must follow the procedures of that area, to meet its requirements.

Many people may be going into these areas for many different reasons, in addition to the personnel who normally work in that manufacturing environment. These people could include:

- visitors;
- auditors;
- maintenance engineers;
- personnel from design and development functions who are working on the processes to be used in the area;
- quality assurance or quality control personnel;
- customers.

These personnel must be escorted and the organization should define how these visitors are to be trained for awareness about the specific procedures of the area. For example, it may be appropriate to provide a specific induction to an area if it has frequent visitors.

Many organizations design their manufacturing facilities so that visitors and staff can observe the processes without entering the area. For example, observation windows are often placed in the corridors surrounding the manufacturing area. Photographs or overviews of the processes may be displayed in the corridors so that equipment can be seen more closely and the processes described, in addition to looking at the area through the windows.

If temporary personnel are working in a manufacturing area, they must also be trained in the specific procedures relating to that area. The training should relate to how the activities that they are undertaking could affect the quality of the product. Temporary personnel should be accompanied and supervised by trained personnel if they have not completed the training for the area in which they are working.

Control of contaminated or potentially contaminated product

It is important to consider how to prevent the risk of contamination or cross-contamination of product from product that is known to be contaminated or which could become contaminated.

There are various situations in which this could occur in the work environment. For example, a product could be returned to an area for reworking, so there should be defined processes to ensure that the product being reworked does not come into contact with other product in the area. When cleaning an area, chemicals or materials may be used that could contaminate the product. There is a similar risk when maintenance takes place; oil and other materials could be used that might affect the quality of the product.

Summary

In summary, in order to be able to meet customer requirements and regulatory needs, and to implement and maintain an effective quality management system, an organization has to have appropriate resources in place. These resources include the people, their working environment and the systems that they use to ensure that the product and service are of appropriate quality. There is a relationship between the requirements in Clause 5, Management responsibility and those in Clause 6, Resource management, as it is the responsibility of top management to ensure that the appropriate resources are available. Once the resources are in place, the requirements for product realization can then proceed.

Chapter 7 – Product realization: meeting the requirements of Clause 7 of ISO 13485

This chapter discusses the issues that need to be considered when implementing the requirements of Clause 7 of ISO 13485.

Product realization includes all the processes that bring the product or service to the customer. These include: planning, understanding customer requirements, communicating with the customer, the design and development of the product or service, purchasing of the materials and services, production/manufacturing, delivery of the product/service, and calibration and maintenance of any equipment that is used in these processes.

It also includes some of the activities that support the product or service after delivery, for example, customer service, technical support, supply and servicing of equipment, and processes for maintaining any property of the customer that the organization holds.

The focus in this chapter will be on the following:

- planning of product realization:
- customer-related processes;
- design and development;
- purchasing;
- production and service provision:
- control of monitoring and measuring devices.

Planning of product realization (Clause 7.1)

Planning is a key element throughout product realization. It is important that the processes needed for product realization are planned and developed by the organization. Various aspects need to be considered; in particular, the planning of product realization must be consistent with the other processes that make up the quality management system. For any processes, if the planning is completed appropriately, then it is much easier to complete the activities that are required to deliver the product or service to the customer. As part of the planning activity, all the aspects

that are covered by Clause 7 of ISO 13485 need to be considered, as this is planning for the processes throughout product realization.

The following aspects related to the product or service need to be considered:

- the 'quality objectives and requirements for the product' (ISO 13485:2003, Clause 7.1) or service. These need to be defined as part of the planning;
- the processes and documents. These need to be established as part of the planning, as well as the resources that are specific to the product or service;
- the aspects of designing the product or service. These include the verification and validation activities, and the inspection and test activities, that will be completed on the materials used in the product or service and its components, as well as on the finished product or service;
- records. The organization will need to determine when records are required, to provide evidence of meeting the requirements of the product or service, and the activities that have taken place to produce the product or service.

It is also important that the output of the planning is compatible with how the organization manages its operations.

Risk management

The only place where risk management is identified in ISO 13485 is under the planning of product realization. Risk management is a requirement throughout product realization; the requirements for risk management must be documented and records of the risk management must be retained. Risk management ultimately forms the basis of the decision to place a product or service on the market or to discontinue a product or service for customers, depending on the outcome of a risk–benefit analysis.

Risk management is a topic in its own right, so this chapter covers the topic of risk management only at a high level in relation to medical devices.

A standard that gives guidance on risk management is ISO 14971, Medical devices — Application of risk management to medical devices. This standard represents the state-of-the-art approach to risk management. If compliance is claimed to this standard, audit organizations will expect compliance with the whole standard.

In accordance with ISO 14971, the manufacturer needs to consider the mechanisms by which information is gathered, know when standards

have been revised or a new standard has been issued, and know about relevant standards and information from similar devices; the manufacturer also needs to ensure that there is an evaluation and review process. The emphasis should be on any unforeseen hazards that may emerge, and assessments of their likely probability and severity of impact, and any errors that may become apparent during the use of the device.

Further guidance on how to integrate risk management throughout the entire quality management system can be found in GHTF guidance from Study Group 3 (SG3) (see References).

Risk management is the systematic application of management policies, procedures and practices to the tasks of identifying, analysing, evaluating, controlling and monitoring risk. Risk management is not about using an isolated failure mode and effects analysis (FMEA); this is not used by the quality management system to assist in making risk-based decisions. A risk analysis cannot be used in isolation – it has to be part of the risk management process.

Risk management is a structured approach to managing uncertainty related to a threat (risk). The options are:

- to transfer the risk to another party who is better placed to manage it
- avoid the risk by making a change;
- remove the risk;
- reduce the risk; or
- accept the risk.

If a risk is accepted, this has to be balanced against the benefit; if the benefit outweighs the risk, then this is recognized as being an acceptable risk.

Risk analysis is the science of understanding risks, their probability of occurring and the likely impact if they do materialize. This is followed by evaluation and together these form the risk assessment process. It is the systematic use of available information to identify hazards and to estimate the risk.

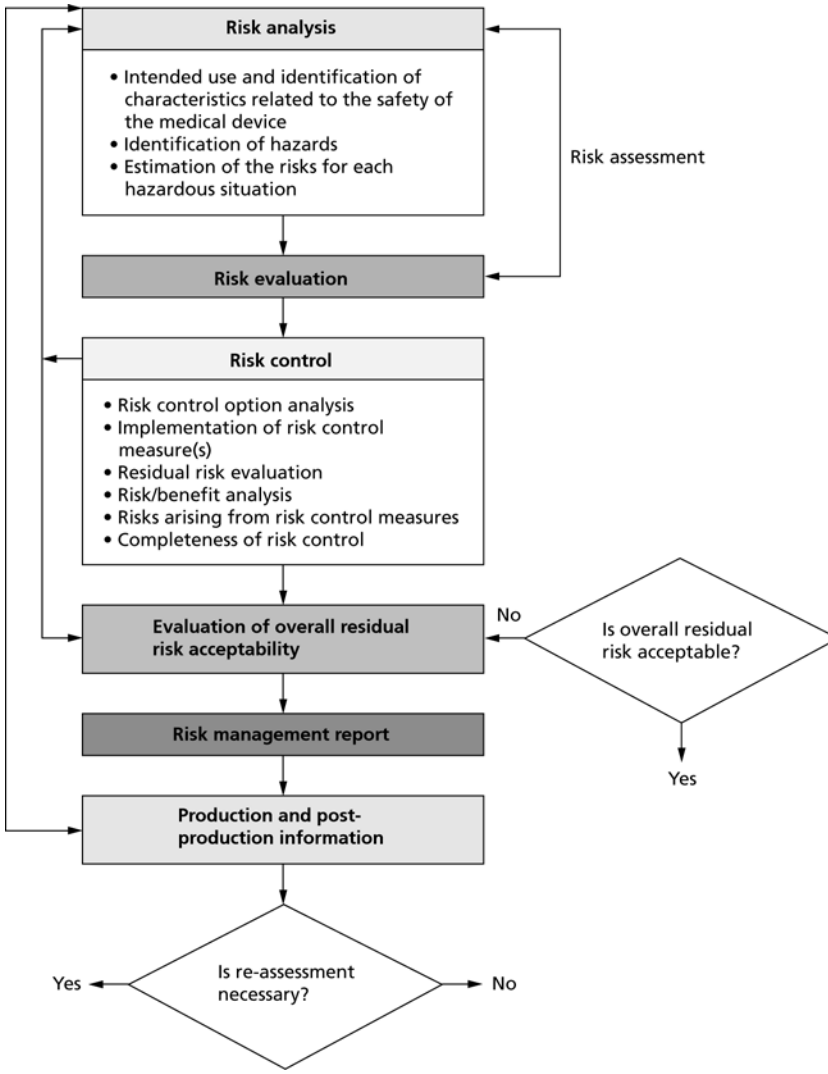
It is important to understand, for each medical device, its intended use/intended purpose, the identification of characteristics related to the safety of the medical device and the identification of hazards. It is also important that the risk analysis is completed by a cross-functional team. It will consider the various aspects of the medical device and also, through discussion, offer different perspectives on the device.

The topics that should be considered are:

- Has the intended use and intended purpose of the medical device been defined?

- Does the risk analysis consider any other uses?
- Does it warn against other uses?
- Have ISO 14971, Annexes C, E and H been considered?

Figure 6 is adapted from ISO 14971:2007: it is an overview of the risk management process.



(source: adapted from ISO 14971:2007, Figure 1)

Figure 6 – Overview of the risk management process

Risk management activities should be planned. The format of the plan could be an individual product plan or could be for a family of product.

The organization should have a procedure for how it describes and manages risk management activities. The procedure should describe the risk management activities throughout the life cycle of the medical device – including the decommissioning of the medical device, if this is a process that is required. The procedure should:

- assign authorities and responsibilities;
- define the risk acceptability criteria;
- include verification activities to ensure risk estimates are appropriate; and
- specify when the risk management file will be reviewed.

Risk evaluation is the process of comparing the estimated risk against given risk criteria to determine the acceptability of the risk. This includes the evaluation of hazardous situations. The organization should have definitions of probability of occurrence, severity of the potential harm (impact), plus detection if harm occurs. The process includes recording how an analysis was performed, how the scoring was applied and whether it was applied consistently (e.g. has the potential harm for a delayed result been applied consistently), and whether the frequency applied is realistic (e.g. based on the analysis of data).

Risk control is the process in which decisions are made and actions taken to reduce risks or maintain them within specified levels. The organization has to consider the type of control measures required, which could include: supplier control, incoming quality control inspections, testing of incoming materials, clean rooms, sterile consumables, filtration of components as a mode of control for bioburden contamination, control of mixing as a mode of control for homogeneity of batches, labelling, warnings and precautions.

The *risk management* report is a summary report of the key risk management information. This has to be in place before the product is launched or placed on the market; it confirms that the risk management plan has been implemented, the overall residual risk is acceptable and methods are in place to gather production and post-production information. The risk management report is included in the risk management file.

It is important that the risk management process is applied through the life cycle of the product.

Risk management is the initial estimate/best guess as to what will happen in real life, so it needs to be reviewed. When real-life experiences

become available, these estimates are either validated as correct or reassessed. It should be recognized if the risks increase and decrease with experience.

The organization should have a process (system) in place to gather data from production and post-production sources, to ensure that these risk-based decisions continue to be valid.

Lifetime of medical devices

A way of controlling the residual risks is by ensuring that the lifetime of the product is such that the residual risks are minimized. The lifetime of a medical device has to take into account the technical, commercial and legal aspects, as well as other considerations, related to the medical device.

As has been discussed earlier in relation to control of documents and records (Chapter 4), the lifetime of a product, as defined for the specific product, needs to be considered carefully as related to the use of the product, and not just when the product is no longer in date for use in a laboratory or by a patient.

For any medical device the basis of the lifetime of the device should be documented.

It is important to understand all the aspects that need to be considered in relation to the lifetime of the medical device, which will vary depending on the nature of the device. These aspects include:

- the shelf life of the medical device;
- the expiry date for a medical device or component that is subject to degradation over time;
- the impact of the stability of the packaging material, which might break down faster than the product. This can happen with some containers for storing chemicals or reagents; it would also be an important consideration for a medical device that is sterile;
- whether the device is for a single use or can be used for a number of cycles or over a period. This consideration would need to be based on testing that has been completed for the medical device;
- the results that have been determined during the design and development phase to forecast the degradation of the material;
- for implantable devices, the residual risk that results from the entire period that the device resides inside the patient's body;
- for sterile medical devices, the time that the medical device will remain sterile;
- the impact of any regulations;
- if the organization has an agreement to supply the medical device to another organization to place the device on the market. There may

be requirements in the contract about either party's ability/willingness or contractual or regulatory obligation to provide a support service;
- the availability or cost of spare parts;
- legal considerations, including liability. The use of the medical device, and the long-term use of results or information from the device, must be considered.

Customer-related processes (Clause 7.2)

There are three aspects to the requirements for customer-related processes:

1. identifying the requirements related to the product;
2. the review of the requirements related to the product;
3. communicating with the customers.

Determination of requirements related to the product (Clause 7.2.1)

This clause focuses on the requirements while the product is being designed and, subsequently, when it is on the market, including customer expectations related to the delivery of the product, and whether there are any special requirements from the customer when the product has been delivered.

For new product, the customer requirements need to be considered in line with Clause 7.3. It is also important to determine if there are any regulatory or legal requirements, for example, the CE marking of the product if it is to be sold in the EU, or the FDA requirements if it is to be sold in the United States. There may also be regulations relating to safety, for instruments. If the medical device is being produced for another organization, there will be some form of contract between the two organizations; this is another aspect of customer requirements related to the product. It is essential to ensure that any requirements specified are understood by the parts of the organization to which they relate , and not just by the manager who has signed the contract; this can be a particular issue in larger organizations. Some organizations develop specific quality agreements that are signed by the quality functions of both the manufacturer and the customer. These agreements would cover aspects such as the management of complaints, the investigation of nonconforming product, and the requirements for quality audits of the supplying organization.

At this point in developing an understanding of specific customer requirements, if any parts of the requirements related to the product cannot be fulfilled, then this should be identified and actions taken to resolve the issue with the customer.

For medical devices this includes understanding the intended use of the product and preventing any foreseeable misuse. This is particularly important when developing new medical devices and links back to the risk management process.

Review of requirements related to the product (Clause 7.2.2)

When the product requirements have been determined, the organization must have processes in place to review these requirements, to ensure that they can be fulfilled when an order is received.

Orders from the customer can be received in many ways: email, via a website, fax, telephone calls, or verbally to a sales representative. The requirements of the customer must be clearly understood by the organization; if there could be any confusion, processes must be in place to ensure that this confusion is resolved.

It is important for the organization to understand all parts of the customer's order (or the relevant part of the contract), and to be able to ensure that these requirements can be met. If the customer's requirements or expectations cannot be met, then these concerns must be discussed with the customer and agreement reached on what will be supplied instead.

This review should take place before the organization agrees to supply the product. These processes will differ depending on whether the product is an off-the-shelf item or a unique product that is being supplied to an agreed specification or contract.

Part of this review is to ensure that, if an order has been received, the organization has the product in stock so that it can be supplied to the customer or, if not available from stock, the product can be supplied by a certain date.

If it is an off-the-shelf item, this will mean that the customer is ordering this product against a catalogue number with no additional specific requirements. The required action is to confirm to the customer that the product is available and is being dispatched. If the product is not available, the customer will need to be informed, and provided with information about when the product will be available.

There are systems that will now do this task, automatically notifying the customer by email that their product is available to be dispatched when the order is processed, and then updating the customer that the order has been dispatched.

Where there is a specification or contract related to the item that is going to be supplied, the organization must have systems in place to ensure that the customer's specific requirements are fulfilled. This may be by an automatic link to that specification, but it needs to be available to the area that is producing the medical device for the customer. Quality agreements can be used to support the contract, and to ensure that all the requirements are known in the appropriate functions in the organization. These agreements will often define the named contacts in both the supplier organization and the organization purchasing the item. These agreements can be revised more easily than the contract.

Records must be maintained of these activities, including the review of the order, stating whether it can be fulfilled and when it has been fulfilled.

Customer communication (Clause 7.2.3)

The organization must determine and implement processes that are effective for communicating product information, information related to orders, customer feedback and advisory notices for customers.

The organization has to establish systems to ensure that customers are informed about information relating to the product supplied to them. This information varies from informing customers that the product they have ordered is available, when it will be supplied (as discussed above) and when there is additional information about a product, to when some aspect of the product needs to be corrected or amended – this is called an advisory notice. The definition of an advisory notice is included in ISO 13485 (Clause 3.3). Advisory notices are discussed further in Chapter 8.

Customer feedback can be customer complaints (see Chapter 8), or it can be an enquiry, where the customer needs some additional information about the product, but the communication does not relate to the product not performing correctly. Customer feedback can also be information received from the customer that is positive about the product or service.

Design and development (Clause 7.3)

The design and development process includes all the sub-processes, from developing the product or service from a concept or an idea, and

ensuring that it is in line with the user and regulatory requirements, through to manufacturing a finished product or service that is available to customers, and then establishing how any changes to that design are to be managed.

There are various aspects relating to the design and development process, which are identified in the requirements of ISO 13485. These are:

- planning;
- inputs;
- outputs;
- review;
- verification;
- validation;
- control of changes.

The linkages can be demonstrated as shown in Figure 7. The inputs are the user requirements (which include regulatory requirements); the product (or service) is part of the output.

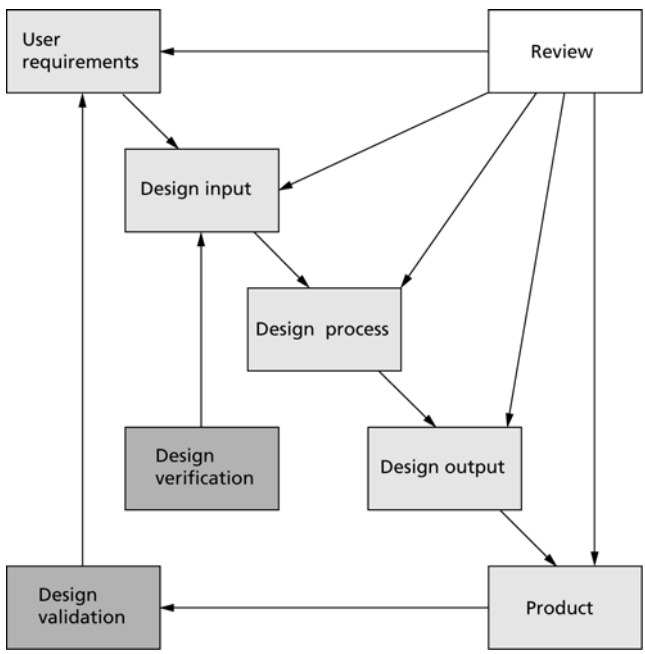


Figure 7 – Overview of the design and development process

Design and development planning (Clause 7.3.1)

The planning of design and development is important, to ensure that the design process is appropriately controlled by the organization. The objectives of the process need to be clear. Design and development planning covers all the other aspects that are listed above, which are part of an organization's plan to provide the product or service to its customer – a product or service that meets the requirements of the user of the medical device and also any regulatory requirements that are necessary for the medical device.

Organizations approach design and development planning in different ways. ISO 13485 requires the organization to define its specific procedures for design and development planning.

The aspects that need to be considered for inclusion in the design and development plan are:

- the aim – that is, the purpose of the medical device or service that is being developed. This may seem obvious but needs to be considered carefully to ensure that it meets user needs;
- which procedures of the organization's quality management system are needed as part of the plan;
- where the product or service is to be sold. This is important because where the product or service is to be sold will have an impact on the regulatory requirements that have to be fulfilled. If it is to be sold in the EU, the product will have to be CE marked, and all the activities that are needed to ensure that the essential requirements of the applicable medical device directive have been met will need to be included in the plan. If it is to be sold in the United States, the requirements of the QS regulation will have to be met;
- who is responsible for the various activities that are included in the plan. This links to the 'Responsibility and authority' part of Clause 5 (Clause 5.5.1);
- the major tasks that will need to be undertaken to complete the design and development process, and the order of the phases in which the tasks are to be completed. Many organizations have phases in their design and development plans, with milestones and activities documented that have to be completed before the next phase can be initiated. This links to the 'Design and development review' part of Clause 7.3 (Clause 7.3.4);
- who will be involved in the review teams and the procedures that should be followed for the reviews. This should include peer review;
- risk management. This has to be used throughout product realization and hence should be used throughout the design and development process. Where and when it is to be used should be defined in the plan. Risk assessment, in relation to the patient and end user of a medical device, is often done at a minimum of three points in the design and development plan: when the design inputs are defined,

before design validation (clinical studies or performance evaluation) and then, finally, before the product or service is available to be used by customers. Risk management is also used during other parts of the design and development process, for example, during process validation, or when there is an issue identified, risk analysis tools can be used to determine the impact of the issue;

- suppliers. Most design and development projects will need new suppliers, often for materials that will be critical to the product or services that are being developed. These suppliers may often be new to the organization, so their selection is an important factor in the project plan. The GHTF published guidance on this topic: GHTF/SG3/N17:2008, Quality Management System – Medical Devices – Guidance on the Control of Products and Services Obtained from Suppliers. This is discussed in more detail later in this chapter, in the section on purchasing, relating to Clause 7.4.

Some organizations develop checklists/plans that can be applied to any project. There is an added benefit to doing this, because the experiences that have been gained from previous projects can be applied to future projects; lessons learned are not dependent on a specific individual's knowledge.

The transfer of the device or service to manufacturing and/or installation for the user should be included in the plan. This needs to take place early enough in the process to ensure that all the aspects of producing the product or service have been taken into account, so that the capability and capacity to manufacture the product or service is confirmed before starting to sell it.

Design and development inputs (Clause 7.3.2)

To produce any product or service that will make money for an organization, the customer and regulatory requirements must be understood and then translated into the design inputs. The inputs should not be 'wish lists' but actual requirements that can be fulfilled.

Records of inputs are required by ISO 13485, which specifies some of the following inputs to be considered and included:

- how the device or service functions. This will include:
  - o the intended use of the device, including the performance claims that it will have to meet. This will link to the customer and regulatory requirements that have been defined for the product or service. The performance claims may be defined in an international standard for the product; if it is a high-risk in vitro diagnostic medical device that is going to be sold in Europe or in the EU, it will have to meet the requirements of the common technical requirements;

  - the indications for use of the medical device or service;
  - performance requirements (including normal use, storage, handling and maintenance), and user and patient requirements;
  - the physical characteristics of the product or service, including what will be included in the device. For in vitro diagnostic medical devices, this will include how many uses the device has and the number and size of the reagents included in the kit;
  - human factors/usability requirements;
  - safety and reliability requirements;
  - toxicity and biocompatibility requirements;
  - electromagnetic compatibility requirements;
- any applicable or statutory requirements. These could include:
  - regulatory and statutory requirements of the intended markets;
  - relevant voluntary standards (including industry standards and national, regional or international standards);
  - harmonized standards to the EU directives if the product is being sold in the EU. These are not statutory requirements but, in practice, most organizations choose to follow the requirements of the harmonized standards;
  - consensus (de facto) standards for the product or service that are used for certain countries;
  - specific regulatory requirements for the labelling of the device. Although labelling is now more harmonized and the use of symbols is widely accepted, there are still specific country requirements for labelling. Additional information relating to the use of symbols for medical devices is available in ISO 15223, EN 980–9 (which was no longer harmonized from January 2013), and ISO 18113-1 to ISO 18113-5;
- inputs from previous devices of a similar design:
  - the product or service being developed may be a redevelopment of an existing product or may be part of a family of products. It is important that historical data – information from these products or services – is considered as part of the design inputs;
- other aspects of design and development that are essential to the device or service that is being provided. For example, is the device compatible with the accessories and auxiliary devices that may be used with the product, and with the environment in which the product or service will be used? (For example, the instruments that are needed to implant a replacement hip.);
- the outputs of the risk management. These outputs should include consideration of complaints/failures or adverse events for previous product or services that have similar characteristics to the product or service that is being designed and developed. These may be the organization's own product or those of manufacturers that are producing similar product or services. The information relating to a similar product or service from other manufacturers could be derived from a review of the relevant scientific literature or where there have been Field Safety Corrective Actions or recalls associated with

the product. This information can be found on websites such as that of the FDA, Irish Medicines Board and the Medicines and Healthcare Products Regulatory Agency (MHRA);

- the packaging and labelling of the product, which should also be included as part of the design inputs. The device may need to be kept sterile or fragile. The packaging must be designed so that it is compatible with the device, so that the performance of the device meets its requirements when it is received by the user;
- how the product will be manufactured. Are there any specific manufacturing considerations that should be taken into account when the product is designed? There is no point in having an excellent design that cannot be manufactured in the quantity that is required, because the processes are not capable of manufacturing the product at such a scale;
- what will be required for customer/user training. How will it be documented and given to the customer? Will the customer have to have training from the manufacturer in how to use the device or service, or will they be able to use the device from the information supplied in the manual or the instructions for use?
- whether the device will need to be serviced. Is specific training required for the service engineers? Is there maintenance that the customer will have to carry out?
- whether the device will be economically viable. This question is critically important, from both a business perspective and a quality perspective.

The inputs must be clear– so that they will not be misunderstood – and one input should not contradict another. The inputs should be such that when the project is nearing completion they can be understood by people working on the project at that time, so that they can translate these to the design outputs and check that all the inputs have been fulfilled. They also need to cover all aspects of the device or service. An example of this is that the countries where the product is to be sold must be determined before the regulatory requirements can be defined in relation to the inputs.

The design inputs need to be as detailed as possible, to ensure that the product will meet the market and customer requirements. As with any process, it is important to define what the requirements are up front, before starting the work, as this will make the subsequent parts of the process easier. Time spent on this part of the design and development process will save time in the long run. There is no point in getting to a finished product, then discovering that there was a specific product requirement for a certain market and that, without modifying the design, the organization will not be able to sell the product in that market.

Design and development outputs (Clause 7.3.3)

Design outputs show that the design inputs have been translated into the product or service. Organizations often develop a matrix to show how the design inputs have been achieved through the design and traced to the outputs. This will form the record of the design outputs that is required by ISO 13485.

The design and development outputs provide information to the organization that will be used to produce the medical device, including the information for the materials and services to be purchased, and the environment and processes required to manufacture the device.

Examples of design outputs include:

- the device or service that is to be supplied to the customer. This includes the installation and servicing procedures and materials that are needed to install or maintain the device;
- the documentation that will be used by the manufacturer to produce the product or service. For example, specifications for raw materials, component parts and sub-assemblies, drawings and parts lists, process and materials specifications, packaging and labelling specifications, and quality assurance procedures (including acceptance criteria) relating to how the device is to be released for sale;
- in addition to the specific documentation related to the device or service, further outputs may include manufacturing and inspection and testing procedures, working environment requirements for the device, and identification and traceability requirements – these may include how a measurement related to the device is traceable to an accepted standard;
- records to demonstrate that each design was developed and verified in accordance with the design and development planning;
- the documentation that has been submitted to the regulatory authorities where the product or service will be placed on the market;
- the training materials for the customer, so that it can be ensured that the device is used appropriately.

There must be records of the design output. These will often form part of the design history file or design dossier. The records do not have to be physically in the file; there may be links to the system where they are stored electronically. It is important, however, that, if the system is being certified to ISO 13485, the information can be easily shown to the assessor in whatever way it has been stored.

Design and development review (Clause 7.3.4)

Review of the progress of the development (or redevelopment) of the medical device is important as a business process, as well as a requirement of ISO 13485.

The reviews must be planned to take place at various stages in the product's development; the stages at which they should occur should be defined in the design and development plan and then take place at the defined times. There must be records of the reviews, which should record the conclusions. The main aim of these reviews is to determine whether the product being developed is meeting the design inputs and that it is on track to doing what it is supposed to do.

The reviews should consider whether the device is on track to be safe and effective. Often linked to the reviews, the risk analysis for the device will be revisited to ensure that the risks remain as expected for the relevant stage of the development and that no new risks have been introduced that cannot be resolved.

When the reviews take place will be determined by the maturity and complexity of the medical device that is being developed. Often the organization will define in the documented design and development system when the reviews will take place in relation to their process. The reviews go under many names: stage reviews or milestone reviews, for example. There may be a different name for each review, for example: a design input review after the feasibility of the design has been established; then, a raw materials review, when the materials that are critical to the product have been designed, and at which point they are fixed and come under design change management. This may be followed by a design verification review, where it will be confirmed that the product can move to the design validation stage, and the performance evaluation can be started for an in vitro diagnostic medical device or a clinical evaluation can be started for a medical device. Finally, there may be a pre-launch review before the medical device is placed on the market. The process will continue once the medical device has been placed on the market, after which the project may be formally closed. The monitoring of the product will continue throughout the life cycle of the medical device, through the post-market surveillance and the post-production review of experience of the medical device.

Different organizations have different approaches to the conduct of the reviews and who should attend the reviews. They may even have two levels of reviews – one with the project team (these may be the regular team meetings) and then a higher-level review with the top management of the organization.

The top-level review is where the go/no go decision is made about whether the medical device can be moved to the next stage of the

process. Senior management are present, because this is a business decision as well as a decision about the performance safety and effectiveness of the product; it is also important to include peer review. This is where staff who have an understanding of the technology and science of the product, but who have not been involved in the product development in detail, review the progress of the project and the technical aspects of the device. For a smaller organization, having expert individuals available to do this type of review may be difficult, but it will add value to the process if there is a person who can fulfil this role. This is a role that can be fulfilled by a person external to the organization. Having an independent review is a requirement of some regulatory bodies; it is a best practice for any organization, as, within the project, the people involved may get too close to the work that has been completed, and a fresh view is always beneficial.

Typical questions that may be asked at the reviews are as follows.

- Does the design satisfy the requirements specified for the product? This relates to whether the design inputs are being met. At the reviews in the early stages of a project, this will be determining if the project is on track to achieve the design inputs.
- Are the inputs adequate to perform the design and development tasks?
- Are product design and processing capabilities compatible? Can the product or service be manufactured or made available to the customer?
- Have safety considerations been addressed?
- What is the potential impact of the product on the environment?
- Does the design meet functional and operational requirements, for example, performance and dependability objectives? Will the performance evaluation or clinical evaluation be acceptable? This will be determined as the information builds on the performance of the medical device during the design and development process.
- Have appropriate materials been selected? It is important to determine this in the early stages of the product, before the design is finalized. It should also be considered if the supply of these materials will be adequate for the quality of the product that is going to be produced.
- Have appropriate facilities been selected? It is important that an appropriate manufacturing facility is available for the device.
- Is there adequate compatibility of materials, components and/or service elements?
- Is the design satisfactory for all anticipated environmental and load conditions?
- Are components or service elements standardized and do they enable reliability, availability and maintainability?
- Is there a provision in tolerances, and/or configuration, for interchangeability and replacement?

- Are plans for implementing the design technically feasible (e.g. purchasing, production, installation, inspection and testing)? It is important for considering these activities that the appropriate personnel are present at the design reviews. It may not be appropriate for this expert input to be given by other functions on their behalf.
- If computer software has been used in design computations, modelling or analyses, has the software been appropriately validated, authorized, verified and placed under configuration control?
- Have the inputs to such software and the outputs been appropriately verified and documented?
- Are the assumptions made during the design and development processes valid?
- Are the results of model or prototype testing considered?
- Have risk management activities been carried out and, if so, are they adequate?
- Is the labelling adequate? Without consideration of the appropriate labelling it may not be possible to sell the medical device in certain countries.
- Will the design reasonably accomplish the medical use intended? This is directly linked to having the appropriate inputs for the device and confirming that these can be met as the project develops.
- Have the regulatory requirements been considered for the countries in which the device will be sold? Have these requirements changed while the device has been developed? It has been known for devices to reach the end of their development before the project team realizes that they cannot be sold in a specific market because the market requirements cannot be met for that country.
- Is the packaging adequate, particularly for sterile devices?
- Is the sterilization process adequate for the type of device, and compatible with the device?
- Is the device compatible with the sterilization method?
- How are changes and their impacts controlled during the design and development process?
- Are problems being identified and corrected?
- Is the product meeting verification and validation goals?
- What is the progress of the planned design and development process?
- Are there opportunities for design and development process improvement?

These are typical of the topics that can be covered. Not all of the questions are appropriate for the design reviews for all medical devices, but some of the questions will apply for all reviews.

For any of the topics that are covered there should be a link to the risk assessment process and the risk analysis for the medical device; organizations often tie the review of the risk assessment to the design

reviews – in particular, the design input review, the review before the design validation and the review before placing the medical device on the market. This is because the risks should be reduced as the design and the development progresses, but it is also important that any new risks identified are included in the risk assessment; the design reviews are a way of managing this process.

The design process is a business process. Painful decisions may need to be made at design reviews. Sometimes these decisions are left until too late in the process; it may be recognized only at a late stage that the project is not viable. If there are concerns about any aspects of a project, it is important to discuss these promptly at the appropriate level in the organization, so that they are recognized at an early stage in the process. If not, they could affect the viability of the project.

Design and development verification (Clause 7.3.5)

Verification of the design is an important part of the design and development process, as this is where it is confirmed whether the design outputs meet the requirements of the design inputs.

This is often carried out in the organization, although studies may be done externally. It is a requirement of ISO 13485 that the design and development verification is carried out according to planned arrangements. This means that the activities to be carried out as part of the design and development verification are to be defined; they will have to be documented, with the expected criteria defined, before the design and development verification can begin. There must also be records of the results. If changes have to be made to the design or the processes related to the design, following the review of the design and development verification, records should be kept of the actions that are taken.

The types of activities that would be considered as part of the design and development verification include:

- tests that can be carried out on a bench or as analysis in the laboratory. These are tests to ensure that the product fulfils the design inputs. For an in vitro diagnostic medical device these tests would cover aspects such as defining the temperatures at which the assay will perform and the limits at which it will give the results required by the design inputs. This information can then be used in the instructions for use as limitations for the assay;
- alternative calculations. If calculations are used, it must be ensured that they are appropriate for the design;
- comparison with proven design;

- inspections and document reviews (e.g. specifications, drawings, plans, reports) to ensure that the product is within the defined requirements.

Design and development validation (Clause 7.3.6)

Design and development validation is where the product is used as it would be used by a potential customer. For example, an in vitro diagnostic medical device will be reviewed to ensure that when the medical device is used by customers it will be safe and effective in their hands.

An important part of the design and development validation is that the medical device is used or assessed with all the labelling and instructions for use that will be provided with it, as well as with any accessories that are to be used with it, by customers. It should be performed under the actual or simulated conditions as near as possible to how the device will be used by customers.

The design and development validation is intended to test how the medical device will perform in customers' hands without any intervention from the manufacturer or provider of the service. As part of design validation, the organization has to perform a clinical evaluation for a medical device and a performance evaluation for an in vitro diagnostic medical device, if this is required by regulatory requirements for the markets in which the device is to be sold.

Clinical evaluations can include various ways of ensuring that the medical device performs as intended, including a critical analysis of the relevant scientific literature as to how the medical device will perform, historical evidence relating to similar designs and their performance, and a clinical trial or performance evaluation.

The GHTF published guidance and also has draft guidance for clinical evaluations and performance evaluations that is currently undergoing review. The GHTF documents include guidance for medical devices and in vitro diagnostic medical devices.

For medical devices these include:

- SG5/N2R8:2007, Clinical Evaluation;
- GHTF/SG5/N3:2010, Clinical Investigations;
- SG5/N1R8:2007, Clinical Evidence – Key Definitions and Concepts.

For performance evaluations for in vitro diagnostic medical devices these include:

- GHTF/SG5/N8:2012, SG5 (PD)/N8R3 Clinical Performance Studies for In Vitro Diagnostic Medical Devices;
- GHTF/SG5/N6:2012, SG5 (PD)/N6R3 Clinical Evidence for IVD Medical Devices – Key Definitions and Concepts;
- GHTF/SG5/N7:2012, SG5 (PD)/N7R4 Clinical Evidence for IVD Medical Devices – Scientific Validity Determination and Performance Evaluation.

Design and development validation usually takes place after the design and development verification has been completed successfully or any issues that have been identified have been resolved. Some organizations take a risk and complete their design verification and validation in parallel.

Again, as for design and development verification, it is a requirement of ISO 13485 that the design and development validation is carried out according to planned arrangements and records of the results are kept. As before, if there are changes that have to be made to the design or the processes related to the design, following the review of the design and development validation, records should be kept of the actions that are taken.

It is important to ensure that the medical device used for any clinical evaluation or performance evaluation is prepared appropriately. The device should be prepared to the final method and in a manufacturing environment. This means that:

- the methods used to manufacture and test the medical device to be used in the performance or clinical evaluation should be the final documentation and should be approved, at least in draft. Organizations would then normally make only minor changes to the documentation after the evaluation, if required. If any major changes are required, the impact on the medical device has to be considered and, if appropriate, the evaluation repeated;
- the reagents and materials that are used to manufacture the medical device for evaluation should be to the final formulation and should be received according to any quality control processes that will be in place where the medical device is to be sold to customers;
- the environment in which the device for evaluation is prepared should be where the medical device will be manufactured when it is being sold to customers. This evaluation will be on the equipment in the final manufacturing facility; the equipment and environment should be validated and calibrated to the final specifications to ensure the product is of the expected quality;

- the instructions for use and the labelling to be used by the personnel carrying out the evaluation should also be the final draft version. The evaluation is an evaluation of the instructions as much as it is an evaluation of the product;
- when the batches are prepared for evaluation, the organization usually uses this as an opportunity to complete the process validation of the manufacturing processes.

By the time the evaluation has been completed, the organization should know whether the medical device is ready to be placed on the market, when all the internal aspects of the design and development process have been completed.

Control of design and development changes (Clause 7.3.7)

Design and development changes can relate to changes that are made to the medical device during the design and development process or after the medical device has been placed on the market. This can seem confusing to organizations, but it reflects the fact that the design and development process continues through the complete life cycle of the product until it is no longer on the market, through to when the last of the devices has completed its lifetime.

There are many reasons why the design of a medical device may need to be modified or changed. Some examples are:

- changes may be identified during the reviews as part of the design and development process. These may relate to any changes to the design inputs and outputs and whether these can be achieved. When changes are made during the design and development process, it is important to assess those changes to check whether they affect the design inputs, including any impact they may have on regulatory requirements. There may also be changes to regulatory requirements. For example, when the EU Medical Devices Directive (MDD) was changed, the change to the requirements would have been considered by any organization that was developing a device at the time, to ensure that their device took account of the changes to the requirements. This point will also be important in the near future as the EU directives for medical devices are changed over the next few years;
- omissions or errors (e.g. in calculations, material selection) that should have been identified during the design phase may have been identified afterwards;
- work difficulties in manufacturing, installation and/or servicing may have surfaced after the design and development phases;
- there may be change requests from engineering relating to the environment in the manufacturing facility or to the equipment being

used. It may be that the equipment is being replaced with an updated version, for example, moulding equipment or filling equipment;
- changes may be required in response to risk management activities and the linkages through the risk management system to other systems in the quality management system. For example, a corrective or preventive action, customer complaints, or design changes made to a similar product manufactured by the organization;
- changes may be required because a change to a supplied material is requested by the supplier;
- changes may be needed because of safety considerations related to the product. This may be due to a medical device having to be recalled or customers being notified about the product, with changes required for future batches of the product that are to be released;
- improvements to the function or performance of the product may be required. These may be classed as a redevelopment of the product if the changes are extensive. There may also be changes that are requested by customers.

When a change that is to be made is reviewed, it is important to consider the impact that the change could have on other aspects of the product. In addition, it is also important to consider whether a series of small changes that are to be made to a product could combine to have a much larger impact. Every organization should have a mechanism for reviewing cumulative changes in their change management system. This may be part of annual product reviews or part of regular reviews of the risk management field for the product. The extent of how and when cumulative change is reviewed will usually depend on the risk level of the medical device.

The following questions are helpful when considering the potential impact of a proposed change on other aspects of the medical device.

- Does the product still meet the product requirements and the specification that have been defined in both the manufacturing and the quality control release testing for the medical device?
- Does the intended use of the medical device need to be changed?
- Does the risk assessment need to be changed and should the risk management file be reviewed?
- Does the proposed change have an impact on any other components or materials that are used in the product?
- Does the product labelling need to be reviewed to determine if it needs to be changed?
- Does the change have to be notified to any of the regulatory authorities of the countries in which the product is placed on the market, and are these changes that have to be approved? (This could have an impact on the time it takes to implement any change.)

- Is there a need for further interface design (e.g. physical contact with other components in a product or system)?
- Does the change result in any problems in manufacture, installation or use of the medical device?
- Does the change have an impact on the verification or validation of the design?

Organizations may have slightly different systems for managing the changes before the medical device is placed on the market. After this point, when the medical device is actually on the market and being sold to customers, the approach to managing the change will depend on the extent of the change and whether the change is to become a redevelopment.

The key element of the process for the control of design and development changes is that any change that is to be made has to be considered, however large or small it is.

Changes made when the product is on the market are normally managed through a change management system. These systems will often have two phases. The first phase assesses the impact of the change; the second phase ensures that all the actions that have been identified as required are co-ordinated and completed.

The first stage is the planning stage. As part of this stage the change should be notified to all functions and activities that could be affected by the change, or to personnel who manage the changes to the medical device with regard to external activities. These functions could include:

- research and development, or the technical function that manages product that is already on the market;
- manufacturing, including primary or secondary manufacturing (including product labelling and storage);
- planning;
- the quality function considering incoming, in-process and final release;
- regulatory;
- marketing.

Each of these functions, as appropriate to the change, should review the change to consider both the impact to the product and to the activities that they carry out to the product or service that will need to be amended before the change can be implemented.

When all the relevant functions have identified the actions that they will be required to perform to implement the change and signed off to confirm that the change can progress, the change may then be

overviewed by a specific manager (usually from the quality and regulatory function) to confirm that the activities to implement the change can begin.

If the change is a complex change, where several functions have activities, it is important that there is one person responsible – not for completing all the actions, but as a champion for the change. This person co-ordinates the change so that it is progressed in a timely way and ensures that all the activities are completed to the same timescale. When all the preliminary activities have been completed the change can be implemented.

Organizations often use software for this type of process, especially if it is a larger-sized organization. Software has the advantage of providing documented evidence that all the aspects of the change have been considered for their impact on the medical device. Off-the-shelf systems can be purchased or the organization may prefer to develop its own system. It is important to note, however, that if software is used it has to be validated, and if it is interfacing with other software systems in the organization (even if it is purchased software) the impact of the interface has to be considered.

During the design and development phase, the control of the changes may be a simplified process with fewer functions having to consider the impact of the change. However, it is important to remember that the design inputs should be considered and the impact on design outputs that have already been completed, as well as the impact it could have on the manufacturing or delivery of the product or service, as well as on the customer.

For any change that is made – either during the design and development phase or afterwards, when the product is being supplied to customers – it will be necessary to consider whether verification and validation have to be redone, either fully or in part.

Sometimes a change that is to be made to a product on the market may be so extensive that it is classed as a redevelopment of the product. Within its system for managing change, an organization should have a process by which it defines when a change being made to a product is a redevelopment, and so is to be managed through the design and development process, rather than a less significant change that can be managed through the change management process. This will often relate to whether the catalogue number of the product is going to change.

In summary, the design and development processes ensure that the medical device is designed to meet the customer and regulatory requirements; they are important processes in the organization's quality management system.

Purchasing (Clause 7.4)

The requirements for purchasing of materials or services that meet the requirements of the organization are important to the supply of the product or service and include the identification, evaluation and management of suppliers.

Purchasing process (Clause 7.4.1)

The organization must have documented requirements in place, which ensure that the product that is purchased meets the specified purchase requirements. In order to do this the organization must have systems that define these requirements. These will relate to the product or service that is being manufactured or delivered. The amount of control that an organization will apply to a supplier will depend on the impact that the material or service will have on the final product or service that that organization is supplying.

Selection, evaluation and re-evaluation of suppliers

Supplier management is part of the purchasing process and includes the selection, evaluation and monitoring (re-evaluation) of suppliers.

The amount of control that needs to be applied to the suppliers will depend on the risk and nature of the product or service that is being supplied. For new product or services, or a change to a product or service, this would need to be considered during the design and development process or the change management process. The control required by an organization for the supply of a finished medical device will be very different from the control required for the supply of a catalogue item such as a simple chemical.

Why is supplier management important?

The management of suppliers and the materials or services received from suppliers can affect the quality of the product and service supplied by the organization to its customers. Without good management of suppliers and the supply of appropriate materials or services, an organization will not be able to deliver its product or service. Supplier management and purchasing controls are emerging topics of interest and there are examples of supplied items resulting in unintended consequences, some very serious. The ultimate responsibility is with the manufacturer and it cannot be delegated.

Supplier management is of increasing importance and a systems approach to supplier quality can help reduce unintended consequences. It should

be remembered that suppliers are an extension of an organization's business. In the medical device industry there is much use of subcontractors that supply critical components or complete product and, in recent years, there have been issues that have resulted in needing greater control over these subcontractors. There have been high-profile examples of supplier issues relating to counterfeit electronic components and contamination of heparin, which have had a serious impact on medical device suppliers. Regulatory expectations of purchasing controls and acceptance have increased as a result of these issues.

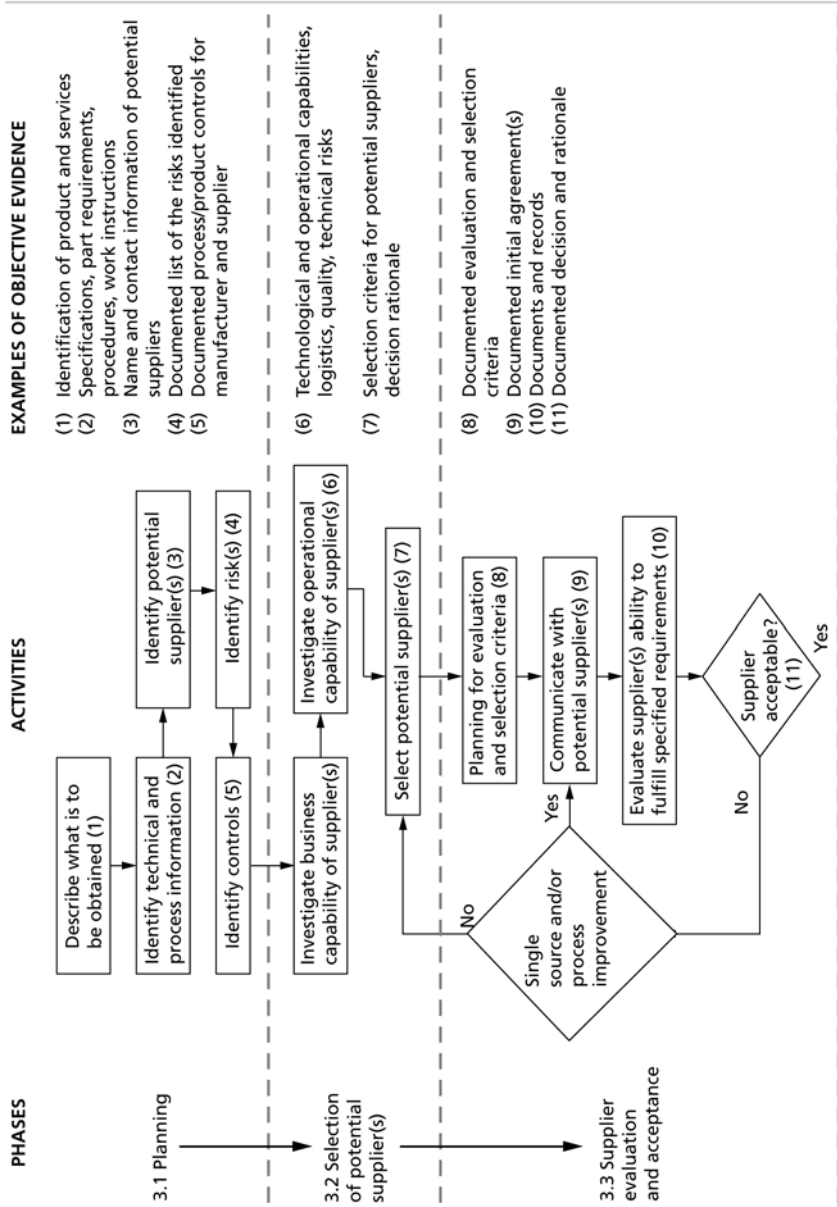
The GHTF published the guidance GHTF/SG3/N17:2008, Quality Management System – Medical Devices –Guidance on the Control of Products and Services Obtained from Suppliers. The guidance describes the 'process of establishing controls for products and services obtained from suppliers[, which] typically comprises six phases…':

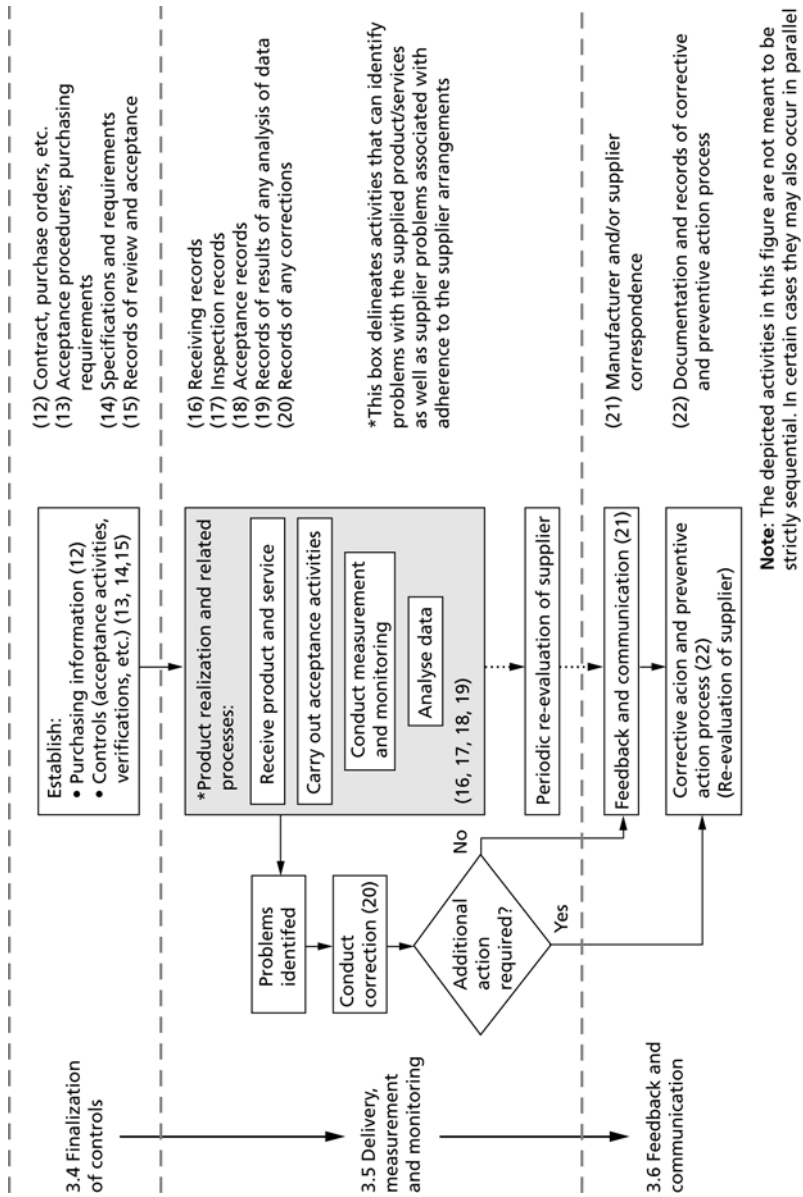
- 'Planning
- Selection of potential supplier(s)
- Supplier evaluation and acceptance
- Finalization of controls
- Delivery, measurement and monitoring
- Feedback and communication, including Corrective Action and Preventive Action process.'

[The Global Harmonization Task Force (GHTF) Study Group 3 (2008)]

The first four stages of this process defined in the GHTF guidance often take place in parallel and would be part of the design and development process.

The GHTF guidance includes a process flow for the process, detailing more information related to the six phases of working with suppliers throughout the lifetime of a medical device. This is shown in Figure 8.


PHASES
ACTIVITIES
EXAMPLES OF OBJECTIVE EVIDENCE
3.1 Planning
3.2 Selection of potential supplier(s)
3.3 Supplier evaluation and acceptance
Describe what is to be obtained (1)
Identify technical and process information (2)
Identify potential supplier(s) (3)
Identify controls (5)
Identify risk(s) (4)
Investigate business capability of supplier(s)
Investigate operational capability of supplier(s) (6)
Select potential supplier(s) (7)
Planning for evaluation and selection criteria (8)
Communicate with potential supplier(s) (9)
Evaluate supplier(s) ability to fulfill specified requirements (10)
Supplier acceptable? (11)
Single source and/or process improvement
No
Yes
No
Yes
(1) Identification of product and services
(2) Specifications, part requirements, procedures, work instructions
(3) Name and contact information of potential suppliers
(4) Documented list of the risks identified
(5) Documented process/product controls for manufacturer and supplier
(6) Technological and operational capabilities, logistics, quality, technical risks
(7) Selection criteria for potential suppliers, decision rationale
(8) Documented evaluation and selection criteria
(9) Documented initial agreement(s)
(10) Documents and records
(11) Documented decision and rationale



[source: Global Harmonization Task Force (GHTF) Study Group 3 (2008)]

Figure 8 – Process flow for managing suppliers

'Planning' – interface with other aspects of a quality management system

The planning phase is where the product or service that is required from the supplier(s) is identified. This shows the direction for establishing the extent of controls for the product and services to be obtained from the supplier. Product and services may include:

- off-the-shelf product;
- parts or components;
- services;
- finished medical devices;
- consultants.

The technical information and process information has to be identified. It is important that the appropriate personnel are involved and that the specifications are defined, as well as the requirements, so that these can be communicated to the potential supplier. When identifying potential suppliers it is important to consider existing suppliers. It is also important to consider the product or service risks, including:

- the complexity of the manufacture;
- whether it is to be custom-built;
- the criticality of the part;
- whether the supplier currently manufactures for the medical device industry.

The business risks should also be considered, including:

- the financial viability of the supplier;
- continuity of supply;
- risks associated with a single source supplier.

Once the risks have been identified, the organization will need to consider how to control them. Examples of controls are supplier audits, testing/verification, process validation, batch or lot sizes and change management.

'Selection of potential supplier(s)'

In selecting potential suppliers manufacturers should consider various factors related to the potential supplier, which include business capability and operational capability.

Potential suppliers should then be selected according to the predefined criteria and the results of the capability investigations. A key consideration for potential suppliers is whether they already produce supplies for medical devices. If they do not, the organization might need

to explain to them how the materials or service that they might be supplying could affect the medical device or the use of the medical device.

Aspects of supplier operational capability to consider include:

- ability to supply – timely delivery, response times;
- supplier's past performance;
- technological capability;
- adequacy of manufacturing processes and equipment;
- engineering resources.

'Supplier evaluation and acceptance'

When planning for supplier evaluation and selection, the criteria should be defined for how the supplier's competencies/capabilities should be evaluated. The factors to be considered should include:

- the technology used;
- whether the item is an off-the-shelf product;
- a comparison of the product or service to specifications;
- the history of working with the supplier, if it is an existing supplier to the organization;
- whether it has certification to relevant standards, such as ISO 13485 or ISO 9001.

There should be good communication and exchange of information with potential suppliers. This should include communication of specified criteria for the item to be purchased.

The ability of potential suppliers to meet the selection criteria should be assessed; this could be through various methods, including assessment by a questionnaire or by completing an audit. It will not be possible for an organization to audit all of its suppliers, so this is where risk management should be used. The methods and rigour of the evaluation should be proportionate to the risks associated with the product or service that is to be supplied.

At the end of this phase the information to select a suitable supplier from the potential suppliers will be available. Draft agreements (or contracts) should also be available; these should contain information describing the controls that will be applied routinely to the service or to the acceptance of the part.

'Finalization of controls'

This is the final phase before the medical device is placed on the market. It is about making sure that all the controls are in place, to ensure appropriate control of the process and the materials or service supplied. Controls should be mutually agreed by the manufacturer and supplier; they will include the acceptance and verification activities, supplier agreements, the processes for handling any complaints related to the product or service that are received, and the interface for product risk management. They will also include how the change management, management of nonconformities and product recall processes will be managed.

At the end of this phase everything should be in place for routine manufacture, including contracts, purchase orders, interface agreements, incoming goods procedures, purchasing requirements, specifications and requirements, and records of review and acceptance.

Some organizations choose to have a quality agreement between the supplier and their own internal quality function. This supports the contract between the two organizations; more importantly, it gives a better understanding of the interfaces and responsibilities at the working level of the quality functions in both the supplier and the manufacturer organizations.

'Delivery, measurement and monitoring'

This phase relates to the activities that are to be completed throughout the time period when materials or services continue to be received from the supplier. These are the activities completed once the product/service is received by the manufacturer as input to the manufacture of its product. The manufacturer establishes checkpoints to monitor the supplier's performance, to ensure customer requirements and regulatory requirements are met.

The manufacturer organization needs to establish a system for measuring and monitoring its suppliers. Again, this should be risk-based in relation to the medical device for which the supplier's product or service is to be used. Different organizations have a different scale of approach to monitoring suppliers; this can vary from a simple review of the information to a scorecard-based approach. Examples of the parameters that can be monitored are:

- delivery performance;
- inspection or testing/review of certificates of conformity or analysis;
- results of continuing audits;
- maintaining certification;
- re-evaluations of the product or service supplied;

- complaints/recalls related to the part or service received.

Another aspect that is rather more subjective is the interface with the supplier, dealing with 'soft' qualitative aspects rather than tangible measures. This would include the effectiveness of the communication between the supplier and the organization, and how it responds when there are problems.

'Feedback and communication, including Corrective Action and Preventive Action process'

Feedback can be either positive or negative; communication is the continuing dialogue between the supplier and the manufacturer in developing the working relationship, especially for critically important suppliers. Communication is essential to the continuing partnership between the supplier and the manufacturer.

The corrective action and preventive action (CAPA) process is an important part of the communication activity. This process will be necessary if nonconforming product is received from the supplier, or if issues occur with the medical device that relate back to the material or service that was supplied to the organization. Activities can be delegated but the manufacturer still has overall responsibility, including effectiveness checks. If the supplier is not able to fulfil the CAPA activities, the manufacturer has to make sure actions are put in place to correct the problems.

Notification of changes is another aspect that is part of the continuing communication between the organization and the supplier. The type of changes that have to be notified by the supplier should be agreed as part of the finalization of controls; the organization has to evaluate any change proposed by the supplier to determine if it could affect the medical device. If the change is significant and could have an impact on the medical device, then this needs to link back into the planning stage of the supplier control/design control process.

The supplier control process is a key process that supports an organization's business and ability to supply the medical device to its customers.

Purchasing information (Clause 7.4.2)

This covers the information that the organization has defined shall be communicated to the supplier. These requirements are normally in a contract or agreement with the supplier and may be part of a detailed technical specification of the product or service to be supplied.

The types of topics that may be covered in an agreement are:

- regulatory requirements – any specific standards that need to be applied to the material or service to be supplied;
- technical information relating to the material or service;
- if there is a change to the processes used by the supplier: the circumstances under which these need to be notified;
- how the material is to be tested by the supplier, and the type of detail of the results of that testing to be supplied by the supplier to the organization;
- whether, for the testing, specific equipment should be used. For example, it may be possible to use various types of analytical test equipment, so the organization may need to specify the type.

For example, if the service to be supplied is the pest control for a facility, the specification may state what types of pest control are to be used – for example, bait boxes for mice, insectocutors for insects – and how frequently these need to be checked, as well as specifying the layout of the equipment within the facility.

For a material this may be a detailed specification of the properties of the material, including the criteria that are to be met.

Verification of purchased product (Clause 7.4.3)

The organization must put into place a system to accept materials and services that are purchased. It will also need to define the type of inspection, testing or checking that is to take place, to ensure that this is commensurate with the criticality of the product or service that is being purchased, and to ensure that it meets the organization's needs.

There must be records of any inspection or testing that takes place. If these activities take place at the supplier's site or any other place that is not the organization's facility, then the organization must define how the inspection or testing is to be completed and the results that are to be achieved. This needs to be included in the purchasing documentation that is given to the supplier.

Organizations have different approaches to how they ensure that product or services meet their requirements, which will depend on the criticality of the material. Risk management tools are useful in deciding the extent of activity that is to be completed by the organization. For example, the material being received from the supplier is a standard chemical for which the analysis is well documented; this type of material could be received on a certificate of conformity. However, if specific analytical criteria are needed for the use of the material, a certificate of analysis with the required information should be supplied for every batch that is received.

It may be that the material is critical and is being made to a specific specification. In this situation it may be necessary to test it in the manufacturing process, using a trial batch of the component for the medical device before the first main batch of product is accepted.

It is also important to ensure that the supplier is informed of any testing that the organization is using to determine whether the product is acceptable. If this testing has not been mutually agreed and the product supplied does not meet the requirements, the supplier may not accept that the material is nonconforming and may not agree to credit for the material.

One of the difficulties is that organizations have to decide what needs to be reviewed for verification of the manufactured product. How does the organization determine whether the material or service could affect the quality of the product or service to be supplied to the organization's customers? Is the bottle that materials are stored in important – could that affect the quality? This can only be decided by the organization; usually the decision should be linked back to the design and development of the medical device and whether the organization considers that the bottle (for example) could have an impact. It may be that the materials are stored in a plastic bottle and the type of plastic could react with the component used in the manufacture of the finished medical device.

Summary

In summary, having robust systems for purchasing and supplier management in place will ensure that the organization will have the materials and services that it needs to supply its customers with product that meets the customer requirements and regulatory requirements.

Production and service provision (Clause 7.5)

Production and service provision includes:

- control of production and service provision – general requirements;
- control of production and service provision – specific requirements;
- particular requirements for sterile medical devices;
- validation of processes for production and service provision;
- identification and traceability;
- customer property;
- preservation of product;
- control of monitoring and measuring devices.

An organization is expected to plan and carry out its production, or how it provides its service, in a controlled way. In ISO 13485 this is called

'controlled conditions that are applicable to their activities'. When applying these controlled conditions to a process, the organization needs to consider the impact of quality and regulatory requirements, and the impact to the medical device.

Control of production and service provision (Clause 7.5.1) — General requirements (Clause 7.5.1.1)

The general requirements for production and service provision cover how an organization should carry out production or provide the service. This links back to the requirements in Clause 6.3, which relate to the infrastructure required to support production in relation to the building, equipment and supporting services to be used.

In order for the production and service provision to be achieved under controlled conditions, the organization must consider any customer requirements or regulatory requirements that relate to the product or service. The level of control will relate to the criticality of the product or service in relation to the level of training that is required for the personnel using the processes and the requirements for the product.

The following aspects must be covered:

- there should be information available that describes the characteristics of the product;
- the organization needs to ensure that the information required for the processes is available. This will include the procedures, documented requirements and work instructions. Organizations approach this in different ways. The documented procedure or requirements may become the record, as the information relating to the activities is recorded. There is much discussion about whether the procedures need to be in front of the user during the process. This again relates to the risk. If it is a process that is used daily by the operator then it may not be necessary to have the procedure in front of them, but they should know where it is kept so that they can refer to it if necessary. Procedures can also be available in different ways – they may be laminated and displayed in the user area or they may be available only through the electronic document control system;
- if standard/reference materials are being used, the procedures related to the use of these materials must be available. There may be specific storage conditions for these reference materials, in which case access must be possible in the area of use. The reference materials also need to be in a state that is appropriate for use. For example, reagents are used when testing an in vitro diagnostic medical device; it needs to be ensured that these are within the

appropriate temperature range. It may also mean that incubators need to be at the required temperature for the assay;
- the equipment needs to be an appropriate design for the process for which it is to be used. Any equipment that is required for the process must be ready for use. The equipment should be within calibration (if that is necessary) and the maintenance completed. The equipment may need to be set up before being used for the process. For example, it may need to heat up or it may need to be cooler than room temperature. The same point applies for the environment;
- an important area of product and service provision where there have to be adequate controls for medical devices is where the product is being packed and labelled. It is a significant problem if a medical device is incorrectly labelled or it is not packed properly. This could result in the recall of the product from the customer or having to contact the customer to correct the problem with the product.

A key element of control is segregation during packing and labelling operations. In order to do this the organization has to make sure that there is adequate space to prevent a mix-up; if this cannot be achieved, only one product should be labelled and packed in an area at any one time.

Aspects that need to be considered during packing and labelling are:

- identification of the line where the labelling or packing is taking place. This can be with a board giving the product and batch number;
- reconciliation: making sure that the number of labels or items that were brought to the area for packing or labelling have been accounted for. One of the difficulties with this is knowing the number of labels that have been brought in to the area. Can the supplier be relied on to know the number of labels that are on a roll, or should they be re-counted before they are brought into the area for use?
- the storage of the labelling is also important. This needs to be controlled with restricted access. Labelling is an important part of the product and it must be stored in such a way that it cannot be used for product for which it is not intended. Note: when labelling is discussed, this means both the labels placed on the containers and the instructions for use (also called ‘package insert’ or ‘directions for use’);
- it is sensible to avoid packing similar materials in the same area even if there can be adequate segregation. This prevents a mix-up when the materials are brought to the area;
- when the labels are printed as part of the process there should be checks to ensure that the printing is clear and that every label is

printed. Vision systems are often used to do this. They check that the lot number and expiry date have been printed and that the label has been placed on the container;

- at the beginning and the end of the activities taking place there should be a review of the area, known as line clearances. This is to make sure that there are no materials from the previous activity left behind before the work starts, and to make sure all the materials have been removed at the end of the activity. There should be a process for how line clearances are carried out;
- records of each batch that is manufactured should be available. For certain product (say, an instrument or a machine), a batch may be a single medical device. Within the records there should be sufficient information to allow traceability to the materials and equipment used. These records are often referred to by different names, which will depend on the specific organization and customer and regulatory requirements, for example, manufacturing batch record, lot record or device history record (this is the term used in the QS regulation used by the FDA). Some organizations choose to align their terminology to reflect their main markets.

If it is not possible to include all the information in one batch record and they are stored separately, there needs to be clear traceability between all of the records for the complete medical device. There should also be traceability to other documents, such as standard operating procedures, if it is not possible to include all the information in the batch record. There should be a link to the specification of the product from the batch record – this will come from the stage when the device was designed and developed, as part of the design output.

The organization will need to decide how the information is to be recorded to form the batch record, which should be in a format that facilitates easy recording of the information. If this is not the situation, it will lead to errors in the documentation and it will probably not be completed properly. The documentation should be in the language of the personnel that are going to complete the information, so they will understand the requirements. For example, if the organization is based in the United States but the language used by most of the workforce is Spanish, then the documentation should be in Spanish.

All the relevant information should be recorded. Examples of the information that should be included are:

- a unique batch number for each batch. This may be a serial number for an instrument that is used throughout the processing activities. However, if the final medical device contains several components, there may be a lot number for each component and these are then brought together in the finished device, which will have its own lot number;

- the date the work started and when it has been completed. In addition, if the work is completed over several days, the dates when the key activities are completed should be included in the record. Some processes can take place over much extended periods, for example, a continuous moulding process or the manufacture of a monoclonal antibody;
- sterilization records, if they are appropriate to the medical device. These must be included;
- the quantity of the product that is being manufactured, together with the quantity of raw materials, material components and intermediate product, with details of the lot numbers. This information is important if there are any subsequent issues with the product being manufactured; knowing the exact details of the materials included can assist the investigation;
- traceability to the equipment that has been used. This information is required so that there is evidence that the equipment was calibrated when the process was carried out;
- signatures for the points where key activities are completed. This could be at the end of a sub-part of the processes, where testing or inspection takes place. In some circumstances the activity may be signed off by two people, if the stage is really critical and there is no easy way of checking that the activity has been completed. Often line clearances are checked by a second person, or they check the first label that has been printed before they are placed on the containers. The organization should avoid having second signatures in too many parts of the process. This safeguard should be used only where it is really critical, because when there is a second signature the first signatory may not take full responsibility; there is a risk that they will rely on the second signature. Many organizations have removed second signatures from some parts of the process for this reason and have only left them for key activities in the process;
- where any part of the process has not been followed or the defined requirements have not been achieved. Information about the deviations or nonconformities should be included in the records. There should be traceability to the point where the deviation or nonconformity has been approved to confirm that the output of the process is acceptable. (Control of nonconforming product is explained further in Chapter 8.)

The processes should now be in place to ensure that manufacture or service provision can be carried out in a controlled way.

Control of production and service provision — Specific requirements (Clause 7.5.1.2)

ISO 13485 includes requirements relating to the cleanliness of product and contamination control, requirements for installation and servicing

activities, and specific requirements for sterile devices that should be met if they apply to the product or service.

Cleanliness of product and contamination control (Clause 7.5.1.2.1)

An organization has to define if there are specific requirements for the cleanliness of its product, and to document these requirements.

There are various situations where these requirements may need to be defined, including for items that are to be cleaned before they are sterilized. There may also be product that has been contaminated during use and has been returned to the manufacturer for reprocessing; this may include sterilization, so it needs to be cleaned before it is handled by the organization completing the reprocessing. There are also situations where an agent that has been used during the manufacture has to be removed before the next stage of processing, such as cleaning agents, including mould release agents and lubricating oils. For all these processes there should be a documented method for how these activities are to be carried out. There is additional information relating to cleaning procedures in ISO 12891-1.

Installation activities (Clause 7.5.1.2.2)

When a medical device is installed by putting it into service in the location where it will be used, this has to be completed in a consistent manner to ensure that the medical device works as it should. To ensure this there must be documented requirements for the installation process.

When an organization installs a device, it is the responsibility of the organization to have in place documented requirements that the personnel who are completing the installation can use. These requirements should include the acceptance requirements for the installation and verifying that it has been completed as required.

The types of activity that are covered by verification are: connecting an instrument to the services required for its use, and the installation of instrumentation for use with in vitro diagnostic assays. This is different from the implantation of an active implantable medical device such as a pacemaker, which is a surgical procedure.

For any of the tests that may be carried out as part of the installation or the commissioning, records must be kept and the installer should also ensure the correct operation of the medical device. If there are special regulatory requirements or performance parameters, there should be instructions provided to the user to allow them to complete these activities correctly.

In some circumstances, the user and the organization installing the medical device may have agreed that the medical device can be installed by a distributor or an agent. When this happens, the manufacturer of the device has to provide documented instructions to explain to the organization that is installing the equipment how to do so. In these circumstances, it is important that the agent is approved by the organization that is supplying the device. An assessor reviewing this process in the supplying organization would expect to see this recorded in its quality management system records.

Servicing activities (Clause 7.5.1.2.3)

Often a medical device will require servicing at regular intervals to ensure that its performance is maintained during its lifetime. This includes routine preventive maintenance, but can include the repair of the medical device if this is required. These servicing activities may be provided by the organization under warranty or through a specific service agreement.

Some organizations will maintain such a programme throughout the life of the medical device. The organization is expected to maintain instructions about the tasks that should be completed as part of the servicing, and a record of servicing that has been completed by them.

Some examples of the aspects that could be covered by servicing activities are:

- responsibilities. It should be clear who is responsible for the activities when distributors and users are involved, as well as the organization supplying the medical device. There may be parts of the servicing that have to be completed by the user – these would normally be the simpler activities that are to be completed at more frequent intervals, and then the service agent will complete the more complex part of the servicing (for example) at an annual service;
- agreements with the customers;
- planning. The organization needs to ensure that the servicing activities are planned – this may be on a rolling schedule so that the technicians performing the servicing are able to plan their jobs over the subsequent period;
- procedures and records of the activities;
- training. The personnel completing the servicing need to have been appropriately trained; it is the organization's responsibility to ensure that they are competent to carry out the tasks, even if these are staff of an agent or a distributor;
- feedback. Information determined as part of the servicing activities should be an input into the feedback and improvement process, as part of customer feedback;

- maintenance and calibration. Any equipment that is used as part of the servicing has to be maintained and calibrated in the same way as other equipment used by the organization;
- complaints or issues. A system should be defined for managing any complaints or issues that may arise during the servicing.

Particular requirements for sterile medical devices (Clause 7.5.1.3)

In ISO 13485 there are particular requirements for sterile medical devices, due to the critical nature of the sterilization process and the impact on the safety of the medical device if the process is not completed correctly. These include the requirement that records of the process parameters are to be kept for each batch of products sterilized; there also has to be traceability to the batch of medical devices that was being sterilized during the sterilization run.

Various international standards are relevant for the sterilization process.

Validation of processes for production and service provision (Clause 7.5.2)

For medical devices, ensuring that processes are capable of producing the required product consistently is important, both for the business and for its ability to supply product to meet customer requirements.

Within the medical device industry there is a wide range of technologies and applications, ranging from simple hand tools to complex, computer-controlled surgical machines, from implantable screws to artificial organs, and from blood glucose test strips to diagnostic imaging systems and laboratory test equipment. These devices are manufactured by organizations of varied size, structure, volume of production, manufacturing processes and management methods. These factors, especially production volume and number of manufacturing steps per unit (e.g. soldering or welding steps), significantly influence how process validation is actually applied. Due to this diversity in the industry, the methods of implementation of process validation should take a practical approach to process validation principles. Manufacturers can (and should) consider technology-specific guidance on applying process validation to their particular situation.

In ISO 13485 there are requirements for validation that must be met. Process validation is part of the integrated requirements of a quality management system. It is conducted in the context of a system that includes design and development control, quality assurance, process control, and corrective and preventive action.

The term 'process validation' is used in the medical device industry to indicate that a process has been subjected to such scrutiny that the result of the process (a product, a service or other outcome) can practically be guaranteed. This is very important if the predetermined requirements of the product can only be assured by destructive testing. Some examples of destructive testing are: sterilization, clean room conditions, aseptic filling, heat treating, injection moulding, electroplating or polishing, glueing, bonding or welding assemblies. Also, processing deficiencies may only become apparent after an intermediate component is further processed or the finished product is in use.

Why is process validation important?

Process validation is important because it assures that a product can be manufactured consistently, using processes that are capable of manufacturing the product.

There are many reasons why processes are validated. These include:

- for regulatory/legal requirements;
- to enhance quality;
- to eliminate scrap (waste);
- to reduce costs;
- to increase customer satisfaction;
- for process control;
- for consistency of product;
- to improve overall quality.

Validation of a process entails demonstrating that a process will consistently produce a product that complies with the predetermined design and development requirements, when it is operated within specified limits.

The GHTF published guidance: Quality Management Systems – Process Validation Guidance [GHTF/SG3/N99-10:2004 (Edition 2)].This process validation guidance is intended to assist manufacturers in understanding the quality management system requirements concerning process validation and has general applicability to manufacturing (including servicing and installation) processes for medical devices. The guidance provides general suggestions on the ways in which manufacturers may prepare for and carry out process validations.

Process validation terminology

Process validation can be defined as establishing by objective evidence that a process consistently produces a result or product meeting its predetermined requirements.

The terminology that is used for the stages of process validation is 'installation qualification', 'operational qualification' and 'performanceEquipment that is used for monitoring and measuring qualification'. The following are the definitions of these commonly used terms:

- installation qualification (IQ):
  establishing by objective evidence that all key aspects of the process equipment and ancillary system installation adhere to the manufacturer's approved specification and that the recommendations of the supplier of the equipment are suitably considered;
- operational qualification (OQ):
  establishing by objective evidence process control limits and action levels that result in a product which meets all predetermined requirements;
- performance qualification (PQ):
  establishing by objective evidence that the process, under anticipated conditions, consistently produces a product which meets all predetermined requirements.

Process validation and the quality management system

Process validation can be shown in relation to the quality management system in the following way (see Figure 9).

Design verification and validation versus process validation

There is often confusion between design verification, design validation and process validation. Process validation is a separate design validation that focuses on process design. Process validation looks at the capability of the processes of the manufacture of the product; design validation relates to the design of the device and that it will meet user needs.

Design verification, as described by ISO 13485 in Clause 7.3.5, is where it is established that the design outputs meet the design inputs. This is usually performed by the design and development function as part of the product development process and does not examine the processes employed to manufacture the product.

Design validation, as described by ISO 13485 in Clause 7.3.6, is where it is established that the device functions as intended when completed and in the user's hands. It is usually in the form of clinical studies (and by literature reviews) for medical devices, or in the form of performance evaluations for in vitro diagnostic medical devices.

Process validation, as described by ISO 13485 in Clause 7.5.2, is where it is established that the process output achieves planned results. These

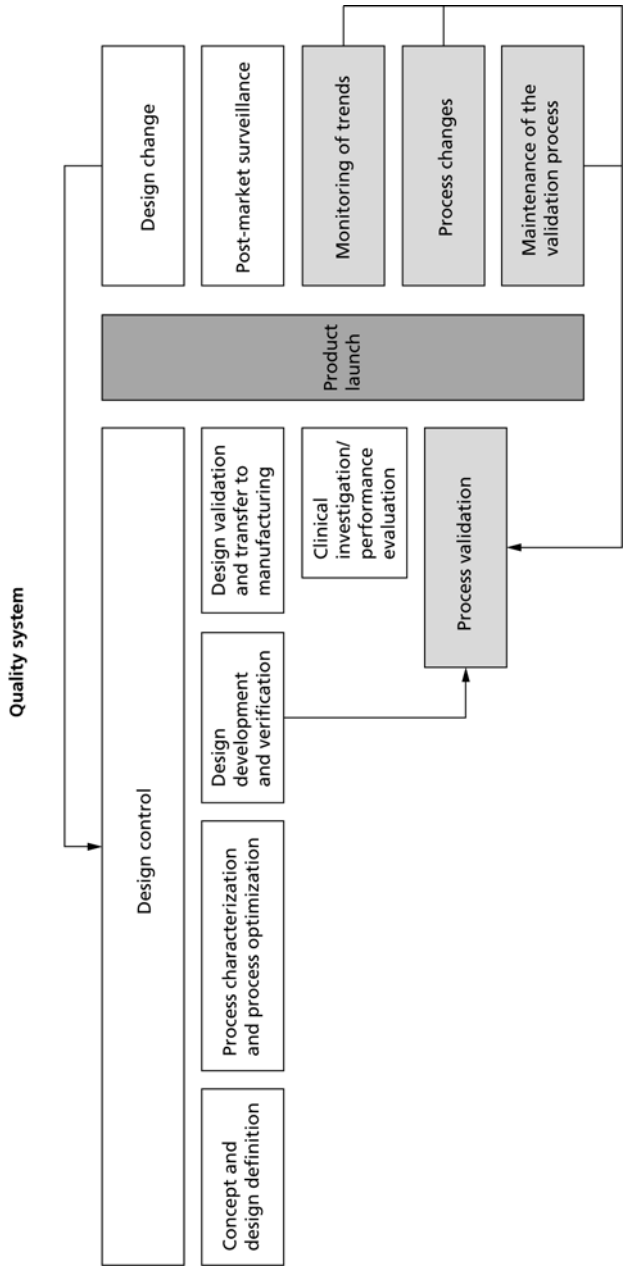


Figure 9 – Process validation in relation to the quality management system

validations are usually performed on manufacturing processes, using trained personnel and manufacturing documentation in the manufacturing environment.

What should the approach to process validation be?

The approach to process validation (as shown in Figure 10) will include:

- forming a multifunctional team to plan and oversee the validation activities;
- planning an approach and defining requirements;
- identifying and describing processes;
- specifying process parameters and desired output;
- deciding on verification and/or validation;
- creating a validation master plan;
- selecting tools and methods for the validation;
- creating validation protocols;
- performing the IQ, OQ and PQ stages and documenting results;
- determining continuous process controls.

Validation versus verification

ISO 13485, Clause 7.5.2.1 states: 'The organization shall validate any processes…where the resulting output cannot be verified by subsequent monitoring or measurement. This includes any processes where deficiencies become apparent only after the product is in use or the service has been delivered'.

Trying to determine whether a process can be verified or whether it needs to be validated is often a difficult decision for an organization.

Verification can be defined as 'the confirmation by examination and provision of objective evidence that the specified requirements have been fulfilled' (source: GHTF/SG3/N99-10:2004).

Even though a process can be verified, an organization may decide to validate that process, as it would be a benefit to the business to know that the process is capable of delivering the product that it is required to deliver in a consistent way, day-in day-out.

There are many reasons why an organization will validate a process. These may include:

- process output cannot be verified by 100 per cent inspection and testing. For a process to be fully verified this may mean that all the

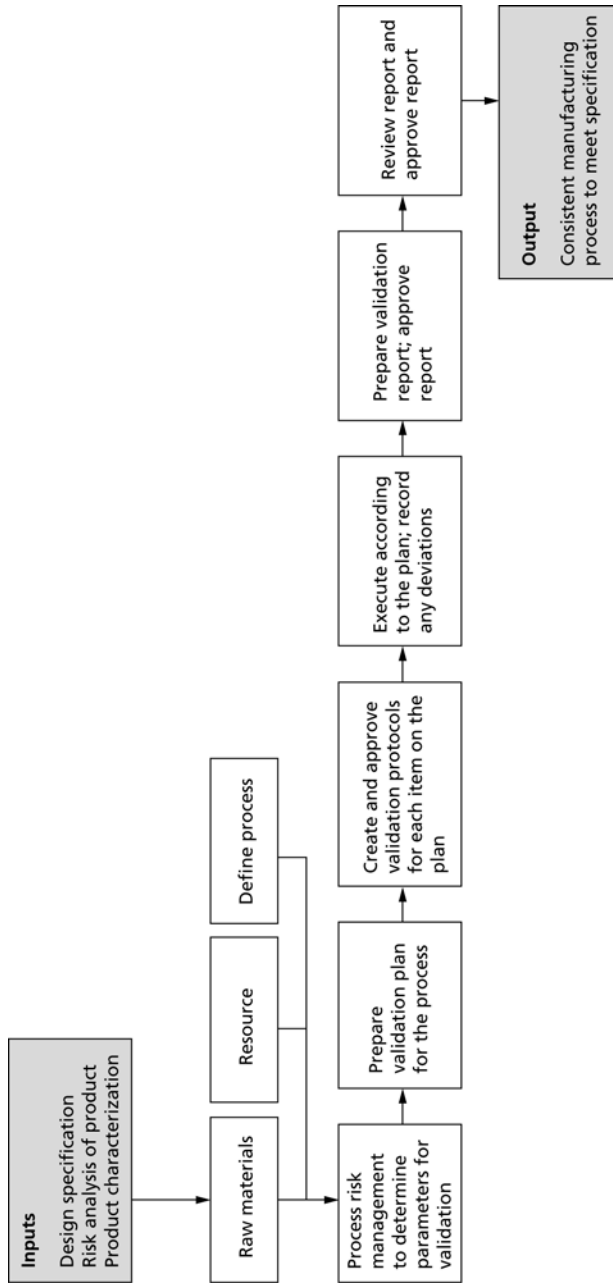


Figure 10 – The approach to process validation

product is destroyed as 100 per cent testing would be required. So process output can only be verified by destructive testing. For example:
  - sterilization;
  - clean room conditions;
  - aseptic filling;
  - heat treating;
  - injection moulding;
- some manufacturers validate many processes in order to maintain high quality without endless testing.

When an organization validates a process it has to demonstrate the ability of the process to achieve the planned results. This means that a protocol or plan has to be prepared for the validation, which must be approved before the validation is started. Within this protocol/plan there must be defined criteria that the process must meet for the completed validation to be approved and be acceptable. These criteria may include:

  - the approval of equipment and qualification of personnel;
  - the use of specific methods and procedures;
  - requirements for records;
  - revalidation.

What should be considered before starting process validation?

If an organization is to carry out process validation in a way that will support the business, there are aspects that need to be considered before becoming too involved in the task of process validation. These include:

- a single-track approach to process validation is seldom sufficient or appropriate. It will depend on the type and characteristics of the process;
- validation must be undertaken within the overall scope of the quality management system, and with attention to specific aspects appropriate to the technology under study;
- detailed protocols for performing the validations are essential, to ensure a comprehensive study with meaningful and valid results;
- detailed reports will be needed, reviewing the results from carrying out the protocols;
- during the design and development/engineering development phase:
  - the medical device should be carefully defined (inputs):
- characteristics (physical, material, chemical, performance);
- user interface and accessories;
  - design outputs must be documented, for example:
- component part dimensions;
- material composition and formulations;
- part drawings and part lists/bills of materials;
- power requirements;

- surface finish or hardness;
- sterility requirements;
- manufacturers will translate expectations into product and process specifications:
  - all relevant aspects that affect safety and effectiveness should be considered:
- performance, reliability, stability;
- establish acceptable limits for each characteristic;
  - in FDA language, the translation of these specifications from design and development into working documentation used in the actual manufacturing is referred to as 'Design transfer' [QS regulation, 21 CFR 820.30(h)];
  - clear and accurate translation of the design into the manufacturing documentation is crucial.

Validation master plan

A validation master plan is a useful tool to define the approach that will be taken to validation for a site or product range, as well as for individual processes. For complex or large systems (e.g. organization-sized), a validation master plan can be used to define which processes require validation and what validations will be performed (IQ, OQ, PQ or software).

A validation master plan will often 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. It will define whether a process is to be validated or verified. The appendices are often presented as a spreadsheet, giving the priorities for the time period, and also listing which processes/equipment require revalidation or requalification.

Various types of validation can be used: prospective, retrospective and concurrent.

Prospective validation is performed after the product is fully developed and before manufacturing the device. The acceptance criteria are defined before the process runs are completed. This is the method of choice. It addresses issues in the early stages of new product development or when a change in manufacturing process will have a significant impact on product characteristics.

Retrospective validation is used when the product may already have been on the market without sufficient pre-market validation. It is performed on existing processes where sufficient data is available to demonstrate that the process is controlled. The process inputs and outputs (product

characteristics) should be defined. The adequacy of the process can be known to some extent by examination of accumulated test records; records of manufacturing and production lot data can also be used to evaluate the adequacy of the process. Quantifiable results can be statistically analysed for target stability and variance; the data can be used to determine the variables that need validating.

Concurrent validation is a subset of prospective validation, where the intention is to distribute the product that has been manufactured prior to the completion of the validation. This would be defined in the validation plan. Concurrent validation can be performed when product attributes and specifications can be verified through non-destructive testing.

Historical data can be used, but the limitations of the use of historical data need to be understood. A complete validation cannot be based on historical data; however, the data can be used to determine what requires further prospective validation. Legacy systems often have large amounts of historical data, which can be used as a basis to remediate an earlier validation and in conjunction with performing prospective validations.

Risk management can be used as part of the process validation. Risk analysis tools can be used to define process criticality and establish risk-based confidence levels [failure mode and effects analysis (FMEA) is often used]. Key variables can include time, temperature and pressure. Risk management cannot be used to justify why a process does not need to be validated, but it does enable the organization to determine the extent of the validation required, including helping to define the criteria that are important for validation.

Validation protocols

Detailed protocols for performing the validations are essential, to ensure a comprehensive study with robust and valid results. Process validation protocols should include:

- identification of the processes to be validated;
- identification of the device (or family of devices) to be manufactured using this process;
- objective and measurable criteria for successful validation;
- length and duration of the validation study;
- equipment, shifts and operators to be used in the study;
- identification of facilities needed for the equipment;
- identification of operators and operator qualifications;
- complete description of the process;
- relevant specifications that relate to the product, materials and components;

- special controls or conditions placed on the process;
- process parameters to be monitored;
- methods for controlling and monitoring parameters;
- product characteristics to be measured;
- method for measurement of product characteristics;
- any subjective criteria to be used to evaluate the product;
- definition of 'acceptance' and 'nonconformity';
- statistical methods to be used for data analysis;
- maintenance aspects;
- criteria for revalidation.

Maintaining a state of validation

Once validation has been completed and the report signed off it is important to ensure that the validation is maintained. This can be done by monitoring the process's trends to ensure that it is still within the established parameters.

If revalidation is required, the organization should determine whether a change has been made to the process. The questions that should always be asked are: 'If there is a change to a process, could it have an impact on the quality of the product? Is there a change to the product?'

Examples when revalidation would be required include when:

- significant changes in the process occur that are likely to affect quality;
- changes occur that affect the validation status;
- a negative trend in quality indicators occurs;
- significant changes in product design occur that affect the process;
- a process/equipment is transferred from the facility;
- equipment is relocated within a facility;
- a change occurs in the application of the process.

Revalidation may not need to be as extensive as the original validation activities. A new piece of identical equipment will require an IQ (however, the OQ and PQ may not have to be repeated in their entirety). There should always be a link to risk management.

While the completion of process validation is a regulatory requirement, the organization may decide to validate a process to improve overall quality, eliminate scrap (waste), reduce costs, improve customer satisfaction, or for other reasons. When combined with properly controlled design and development activities, a validated process may result in a reduced time to market for new product.

Non-product software validation

In ISO 13485, Clause 7.5.2.1 there is a requirement that non-product software is to be validated. There should be documented procedures for validating any software used for production and service operations that could affect the product's ability to conform to specified requirements. The software must be validated before use and there should be records of the results of validation.

Most organizations will use non-product software. This could include the systems that are being used for stock control, including the control of nonconforming product or the status of product that has been released for sale. Spreadsheets or databases are often used; if they are used for calculating results there needs to be a validation, which may be by comparison with a manual calculation.

If off-the-shelf software is used, there will also need to be some consideration and documentation that shows that the software works as expected and has been installed correctly.

In summary, process validation is a topic in its own right; this section has given an overview of the importance of process validation when used for the manufacturing of medical devices.

Identification and traceability (Clause 7.5.3)

Traceability and identification are linked because, without identification of the materials and equipment that are used to provide a product or service, it is not possible to have traceability.

- Identification (Clause 7.5.3.1)

ISO 13485 requires documented procedures for identification through every stage of product realization, from receipt of materials by the organization all the way through to the finished device and to the customer.

It is important to identify all the materials used in manufacturing the medical device and used in the finished medical device for several reasons:

  - it is a means of controlling the materials used throughout production;
  - it allows traceability;
  - if, for any reason, there is a problem with a component during manufacturing or in the finished medical device, being able to trace the materials used to make the device, or installed in the device, means that this information can be used in investigating the cause of the issue. At times an organization may feel that

the effort to ensure traceability seems too great; but when it is needed for an investigation the value of the information is demonstrated.

When a medical device is returned to an organization, it must be possible to distinguish it from any medical devices manufactured in the same batch that still remain in the organization. These medical devices in stock must not be combined with the device that is returned, if the returned device is nonconforming, until it can be shown that it still meets requirements.

There are several reasons for this, including:

- the device may have been returned because there has been a complaint by a customer;
- the device may have been returned because of an incorrect order, but until it is clear that transporting the device to and from the customer has had no impact on it, it cannot be put back into stock for resale to another customer;
- equipment may have been used with the returned medical device, which means that it could be contaminated; it must not be put back into stock until it is known to be safe.

It is important that the way in which the raw material, component or finished device is identified does not have a negative effect on the item. Components can be identified in various ways, for example, by:

- marking the item;
- tagging the item using a label;
- having a physical location for the item.

It is also important that the means of identification cannot be lost, so if a container is marked it must be in such a way that it cannot easily be removed, e.g. making sure waterproof ink is used or making sure that a label sticks and does not fall off the item if, for example, it is stored in a freezer. However, it is equally important that, if items are kept in a labelled container, the label is removed before a different batch of component is stored in that container. If this does not happen systematically there is a risk that an item will be stored in a container that has been labelled with two different batches: the identification has been lost and also the traceability.

It is usual to mark the identification of the finished device clearly. Some regulatory requirements specify that the lot or serial number of a device is to be clear to the customer. This is only sensible, because if there is a complaint or an enquiry then an organization can investigate. Sometimes, an organization receives a complaint, but the customer does

not know the lot or serial number of the product they are complaining about; and then it is very difficult for the organization to investigate the issue adequately.

The extent to which a component is identified will depend on various factors, including where it fits in the process. These include:

  - the type of medical device;
  - the impact of the failure of a material or component on the finished medical device;
  - regulatory requirements;
  - if traceability is required to the end user or patient;
  - the raw materials involved.

- Traceability (Clause 7.5.3.2)

Traceability is impossible without identification of the item. ISO 13485 requires organizations to have a documented procedure for traceability; many organizations have a combined procedure for both traceability and identification. Where traceability is required, the organization has to have a record of the unique identification of the item. The record of traceability will need to be maintained for the lifetime of the device, normally through the batch records or the spreadsheets that support the lot identification. Often this will be part of the manufacturing system used by an organization.

Traceability should be two-way. If required, there should be traceability throughout the process, from the receipt of raw materials as manufacturing input through to the finished device and to the customer. This is important if there is an issue with a component in a device that could subsequently affect the performance or safety of the device. It must be possible to trace the batches in which that component has been used, so that the customer can be contacted to enable recall or correction of the device. It is also beneficial to have traceability from the finished device back through the manufacturing process to the receipt of raw materials, so that the appropriate investigation of a complaint can take place.

In some circumstances an organization may not be able to trace the batches that contain a specific lot of material. However, they may have a process that enables them to trace manufacture of batches (for example) to a time period. If there is an issue, the organization may then have to recall or correct all the batches within that period if it cannot identify the specific batch.

- Particular (traceability) requirements for active implantable medical devices and implantable medical devices (Clause 7.5.3.2.2)

There are specific requirements in ISO 13485 for active implantable medical devices and implantable medical devices. This is because it may

not be possible to inspect the device while it is in use. Due to the risks associated with these devices, organizations are required to have records of all the components and materials used in the devices and of the environmental conditions that were in place during their manufacture. This is normally achieved by giving each device a unique identifier.

In addition, records of traceability have to be maintained by the organization, and by distributors or agents for the medical device or service, where applicable. These records should be available for inspection and should include records of the shipping or package consignee. In certain situations this may mean that records need to be kept of the personnel who have serviced a medical device.

Status identification (Clause 7.5.3.3)

There are requirements in ISO 13485 to identify the status of product; status identification should be in place throughout the manufacture of the medical device, while it is being stored, and during installation and servicing. The aim of this status identification is to ensure that only product that has passed all the required testing and/or inspection is supplied to the customer.

As with traceability, there are various ways in which this can be indicated for the item. It can be identified by either physical means or electronically. This can be by marking the location with the status of the item, or by determining that the item in that location has a specific status in the manufacturing system. These systems will often prevent product moving to the next stage of the process unless it is at an appropriate status.

The status has to indicate whether the product has been inspected and tested. This should indicate if the product is:

- rejected, as the product did not meet the requirements of the specification;
- accepted, as it meets fully the requirements of the specification;
- accepted, but only with a concession because some of the requirements of the specification were not met. The concession will be to accept the nonconformities if they have no impact on the effectiveness or the safety of the medical device;
- held, awaiting further information as to whether the product is acceptable for use.

There is no specific requirement in ISO 13485 for organizations physically to separate product awaiting approval, nonconforming product or rejected product. However, organizations often do this, as it gives more control and prevents inadvertent use of materials that are not known to be acceptable for use.

Again, as for product identification, it is important that the way in which the status of raw materials, components or finished devices is marked does not have a negative effect on the medical device.

Customer property (Clause 7.5.4)

Customer property is where the manufacturing organization is responsible for property or assets that remain in the ownership of its customer.

Customer property is a clause in the standard that many organizations think may not apply to them, but it should be carefully considered by every organization. They might not have physical product that is owned by their customer, but information is a form of customer property.

Some examples of customer property are:

- where an organization is carrying out contract sterilization. The customer still owns the medical device that is to be sterilized;
- patients' records, where the information is supplied to support a clinical evaluation;
- intellectual property, where the organization has a licence to use that process under an agreement. This could include drawings and specifications;
- if contract manufacturing is being performed, for example, packing of a product or filling a container with a component;
- storage of a product for a customer, where the customer still owns the product;
- services that are provided by an organization, for example, the shipping of material on behalf of a customer.

Where an organization is 'looking after' the property of its customer, it is the organization's responsibility to safeguard that property; it has to apply all the requirements, as appropriate, to ensure that the property is safeguarded. This means that the material or information should be treated in the same way as the organization would treat its own product or services. If a circumstance arises where the customer property is lost or damaged, or if something happens to the product that makes it unsuitable for use, then there must be a process in place to ensure that the customer is informed about what has happened. The timescale for this process and who the communication will be between is likely to be defined in a contract between the organization and its customer.

Organizations often include a statement in their quality manual about how they would manage customer property, even if, at that time, they are not carrying out this activity. This means that it is within the scope of their quality management system if they are in a situation where they do need to carry out this activity.

Records must be maintained for the activities relating to managing customer property.

Preservation of product (Clause 7.5.5)

For many medical devices it is essential to ensure that they are stored and handled correctly, to ensure that performance is maintained.

Preservation of product covers many aspects, including storage at the defined temperature, making sure the product remains sterile and protection of fragile product.

ISO 13485 requires that an organization have either a documented procedure or documented work instructions to ensure that the conformity of the product (including the materials used to make the product) is preserved during the activities that take place during manufacture, during delivery of the product to the customer and throughout the lifetime of the product.

In order to be able to do this the organization has to understand the requirements specific to the product, for example:

- the temperature range at which the product should be stored;
- how the product should be protected if it is fragile.

Any special storage conditions must be controlled and recorded. This means that the organization must know that the area where the product is stored is capable of maintaining that temperature range throughout, whether it is a refrigerator, a freezer or a walk-in freezer. It has to have been qualified to confirm that it maintains the temperature range throughout the storage area. Often organizations do not consider the need to qualify their storage areas. Even if an area is a room temperature storage area, if the materials have to be stored within a specific temperature range (for example, 15°C to 30°C) the area would need to be monitored to show that this is achieved consistently. For example, a warehouse area often becomes too cold in winter; heating may be required that starts up when the temperature in the area drops near to freezing; conversely, the area may need cooling if it is too warm in summer. Some organizations build a specific storage area within their warehouse that can be more easily controlled than the larger warehouse, so that the temperature-specific materials can be stored in that area.

Methods should be defined for how the product should be handled. Examples of appropriate methods include providing equipment such as straps, protective clothing and gloves, and specifying the way the product should be transported, for example, on a pallet and in protective packing cases for instrumentation, to protect from damage by vibration, shock and corrosion.

For some regulations it may be necessary to carry out transportation studies to define the requirements for transporting the product. These studies will be completed during the design and development process.

Control of monitoring and measuring devices (Clause 7.6)

The purpose of controlling measuring equipment is to ensure that measurements that could affect the medical device are taken consistently. It is important from the perspective of the user and the manufacturer to provide evidence of the conformity of the product in meeting the defined requirements.

For example, for an in vitro diagnostic medical device an assay is often run within a specified temperature range. It is important that the measuring equipment is calibrated in both the manufacturer's laboratory and the customer's laboratory, and traceable to national standards, so that there is a link to ensure that the assay has the intended performance in the customer's laboratory.

Equipment that is used for monitoring and measuring is often used throughout the processes of an organization and would include equipment used in production and storage, for example, freezers and refrigerators, where the temperature controllers/monitors will need to be calibrated. Some equipment in a facility may not be used in relation to the product and service or may only be used to provide an indication. These must be clearly marked so that they are only used for their intended purpose and never used where a calibrated measurement is required. An example of this would be the balance in the mail room. This equipment would be outside the scope of the programme for calibrating equipment.

In ISO 13485, Clause 7.6 there are requirements relating to measuring equipment and the systems that support that equipment. The requirements in this clause refer specifically to measuring and monitoring equipment (devices), including test software. The aim is to give an organization confidence that the product it is producing, or the service it is undertaking, will meet customer and regulatory requirements. It is important that the uncertainty of any measurement is known; it may be appropriate to use statistical methods to do this.

The organization must have a documented procedure that ensures that the processes for the control of monitoring and measuring are carried out consistently. The procedure should include details of:

- the type of equipment;

- a specific identifier for the equipment (often the asset number of the equipment);
- where the equipment is located;
- the frequency of the calibration checks that are to be carried out;
- how the calibration is to be completed;
- and the acceptance criteria for the measurement. These acceptance criteria would need to be related to the requirements of the product with which they are being used.

Records of the results of calibration and verification must be kept.

To ensure that valid results are always achieved from the equipment, the following points are important:

- the equipment must be calibrated or verified at an interval that has been defined by the organization to be appropriate, or before use, if the organization requires this. Equipment may need to be calibrated before use if the measurement to be made is critical. Another reason may be that measurement with that particular equipment is not made very frequently, so it needs to be ensured that there has been no change since it was last used. Organizations sometimes choose to calibrate their measuring equipment before and after a manufacturing process is undergoing process validation, to be sure that there will be no issues related to measurement during the process validation. Equipment should also be calibrated before it is taken out of use or decommissioned; this is important because it has to be shown that the equipment has remained in calibration for the process for which it has been used up to the time of decommissioning;
- for the calibration, the measurement should take place using equipment that can give traceability to national standards. For many organizations this may mean that the equipment has to be sent to an outside organization. For items of equipment such as balances, a supplier may visit on site to calibrate balances, using weights that are traceable to national standards. If a supplier provides this service it should be accredited by a national organization, for example, the United Kingdom Accreditation Service (UKAS) in the UK. If there is no national standard for a particular type of measurement, the rationale for the calibration should be documented;
- it may be necessary to adjust or readjust the equipment to ensure that the results remain valid;
- it should always be possible to determine the status of calibration, to ensure that when the equipment is being used it is not past the date when it was due for recalibration. This needs to be easily identifiable to the user of the equipment; this is normally done with a sticker on the equipment that details when the equipment was last calibrated and when it is next due for calibration. It is also normal practice that

each piece of equipment has an identification number (often its asset number to align with other processes in the organization);
- it may not always be possible to place a label on a piece of equipment; in this situation there must be a system in place that enables a user to check each time the equipment is used that its calibration is within date. This can be achieved by using the asset number of the equipment; personnel using the equipment may also be asked to record that they have checked that the equipment is in calibration;
- if the equipment is adjustable, there needs to be a system to ensure that it cannot be adjusted by the user in such a way that it would invalidate any measurement made using it;
- measuring equipment must be protected from damage when it is being stored, when maintenance is being carried out on it, and when it is being used. There may be a reference piece of calibration equipment that is used to calibrate other pieces of equipment used in the manufacturing process, for example, a reference thermometer or a reference weight. These should have defined storage conditions so as to prevent damage. If a calibrated weight is dropped it should be recalibrated.

If a piece of equipment is found to be out of calibration there must be traceability to the process for which it has been used. This ensures that the impact of using equipment that is out of calibration on relevant processes can be considered. The impact can be assessed in various ways; usually, it is done through the nonconformity process for nonconforming product, and documented.

Often software applications are used to support the calibration of equipment. The type of software may vary from a simple spreadsheet calculation that is used to record the results of check weighing when measuring equipment is being calibrated, to more complex systems. These include the systems that may be used to schedule the calibration of equipment if no manual record is kept of the activities. These systems should be validated (see ISO 13485, Clause 7.5.2). This ensures that the results which are determined using the software, or the planning of calibration, will be appropriate and as defined.

Summary

In summary, the activities included in product realization – planning, customer-related processes, design and development, purchasing, production and service provision, and control of monitoring and measuring devices – are the core of any organization supplying its customers with a product or service. Clause 7 may appear to be the only part of the quality management system that relates to the manufacture and supply of a service or product, but, in fact, the processes in Clause 7

are supported by the requirements in the other clauses of ISO 13485. This takes us to the next chapter and Clause 8, which addresses the ways in which the processes of the quality management system can be maintained and improved.

Chapter 8 – Measurement, analysis and improvement: meeting the requirements of Clause 8 of ISO 13485

This chapter discusses the issues to consider when implementing the requirements of Clause 8 of ISO 13485.

Measurement, analysis and improvement include all the elements that comprise the part of the Plan–Do–Check–Act (PDCA) cycle that relates to analysing the information related to the quality management system, and identifying what improvements can be made.

It includes:

- general requirements;
- monitoring and measurement;
- control of nonconforming product;
- analysis of data;
- improvement.

General requirements (Clause 8.1)

The general requirements set the scene for the activities in the organization to demonstrate that:

- the product or service meets the requirements that have been defined for it and is conforming to those requirements;
- the quality management system is being followed and remains effective, and how this is achieved is planned and implemented. This should include defining the methods that will be used to demonstrate this, and when and where they will be used.

For all medical devices, there should be inspection and testing methods that demonstrate how the product or service is conforming to the requirements that have been defined for it. These methods will have been defined as part of the design and development process. There will also be tests and inspection criteria for the in-process activities related to the product, as well as for the final product. The methods will include

the criteria for each test or inspection as well as the equipment to be used, if required. There should also be measurement of the processes that are used to manufacture the product or supply the service, as well as of those in the quality management system.

The independence and integrity of the personnel who are completing the inspection or testing is important, to ensure that their work is not compromised and that there are no conflicts of interest with suppliers or manufacturing personnel. There is often discussion about the organizational reporting relationship between those doing the quality control inspection and testing and Operations (Production) personnel. This is not defined in the standard but it is important that independence can be demonstrated.

The organization will need to consider carefully which parameters to measure and monitor; the information gathered must be of value and benefit to the organization. There must not be too many parameters to measure and monitor properly. It often happens in organizations that the number of parameters increases, as someone thinks that it would be a good idea to monitor this parameter, and then someone else thinks it would be beneficial to monitor another parameter. Before the organization realizes it, it is monitoring many parameters that are not being reviewed, because it has become too much of a task, which means that there is no benefit to the organization.

Different systems can be used for monitoring. They are often colour-coded and presented in tabular format. A traffic light format is one example of this, where metrics are coded red, yellow or green to indicate how well they are meeting the defined criteria.

Statistical techniques can be helpful in many situations where data is being collected; they can be used throughout the quality management system and in management of the product and services. Some examples where statistical techniques can be used are:

- when completing an investigation to find root causes and analyses of problems;
- any use of risk analysis;
- during the design and development process, in relation to the product and to the processes that will be used to manufacture the product;
- during the verification and validation of processes and the characterization of those processes before validation or verification;
- establishing limits for processes;
- monitoring a process. For example, a simple chart shows action and warning limits for a parameter that is being measured during a process. In true statistical process control, the process will be adjusted when a measurement is recognized as showing a trend towards moving from the warning limit to the action limit. A very simple

example of this is monitoring of the amount filled into a container, where there may be a run of several thousand bottles being filled; weights will be taken at fixed intervals and recorded, with adjustments made if necessary.

There is also a variety of statistical methods that can be used. Some examples are:

- experimental design, which can be used to determine the potential variables that can have a significant influence on a process and product performance, as a way of understanding the interrelationship and the effect on each other;
- a wide range of graphical methods, which can be used in many circumstances – histograms, Pareto charts, scatter plots, and cause and effect diagrams. Often a pictorial representation of data can aid in the interpretation of that data, as it gives many people a better understanding of it;
- as mentioned above, statistical control charts, which can be used for controlling and monitoring processes and all types of product or services resulting from those processes;
- regression analysis, which provides a quantitative model for the behaviour of a process or a product when the conditions of the operation of the process or the design of the process are changed;
- analysis of variance;
- methods of sampling throughout a process by continuous monitoring, e.g. temperature or pressure;
- statistical methods used in inspection or testing.

When statistical methods are used, it is essential to ensure that the methods remain appropriate for the data that is being collected. It will be important to have a rationale for the choice of the statistical applications that are used; this will need to be documented, as they may be reviewed as part of the regulatory requirements relating to the medical device. If more complex statistical methods are being used, they should be reviewed by personnel who have appropriate knowledge/training in statistics. Often organizations employ statisticians or have an external expert who they can go to for advice. It is important to have access to this type of expertise, because the conclusions that are drawn from the statistics could influence the safety or performance of the medical device.

Monitoring and measurement (Clause 8.2)

Feedback (Clause 8.2.1)

Obtaining feedback is a key part of monitoring and measurement, so that the performance of the product or service can be assessed, as well as

that of the quality management system. There are many sources of feedback, which include sources internal to the organization, and also external sources.

The methods for obtaining the information must be defined and the organization should have a procedure for the feedback system. The aim of this feedback is to give early warning of quality problems that may arise, so that they are detected early, investigated to identify the cause, and corrections made, if required, and included in the corrective and preventive action process. In addition to having information that is fed into the corrective and preventive action system, the measurements of performance should give information about whether the quality management system is being maintained to meet customer and regulatory requirements.

Regulations often have requirements for monitoring product in the post-production phase; ISO 13485 recognizes that these requirements are to be met and that they form part of the organization's feedback system. It will be up to the organization to define the requirements relating to the regulations where the product or service is being sold.
Post-production means the part of the life cycle of the product or service after the design has been completed and the medical device is being supplied to customers. It is an analysis of the activities that take place until the product or service ceases to be used. Again, this will relate to the lifetime of the device, which may be a very long period, for example, a medical device such as a replacement hip may be in place for many years.

Post-market surveillance/post-production review

Post-market surveillance is an important activity for all medical devices. There is guidance from the GHTF for post-market surveillance (GHTF/SG2/N47R4:2005).

There are many sources for obtaining customer-related information, which should be of both a positive and a negative nature. Examples of sources are:

- positive information:
  - customer and user surveys. There are many customers and users of medical devices. There is the patient who will be the recipient of a medical device such as a pacemaker or a hip implant, or the user of a more simple device, such as a tongue depressor. The extent to which surveys can be used will depend on how easy it is to obtain information from the user; in some cases a general survey is more appropriate;
  - published literature about where the device has been used;

  - customer requirements or information related to contracts with customers;
  - service information and service delivery data;
- negative information:
  - customer complaints;
  - advisory notices;
  - vigilance issues;
  - a call-out for repair or maintenance that is outside planned servicing or preventive maintenance.

In addition to feedback from external sources, there should also be information from internal sources, for example, regarding nonconforming product, quality control testing or inspection.

All these sources will demonstrate whether customer and regulatory requirements have been met. They will link back to an understanding of customer-related requirements throughout product realization, including input to the design and development or redevelopment of medical devices.

The risk management file may need to be reviewed in response to feedback received. It may need updating if:

- a new hazard has been identified;
- there is a new mode of control, or a change to a mode of control is required; or
- there is new or additional design verification or validation, or
- process validation data confirms that risks are not being managed.

The goals of post-market surveillance for Europe, taken from NB-MED/2.12/Rec1, are listed below and shown in Figure 11:

- detection of manufacturing problems
- product quality improvement
- confirmation (or otherwise) of risk analysis
- knowledge of long-term performance/reliability and/or chronic complications
- knowledge of changing performance trends
- knowledge of performance in different user populations
- feedback on indications of use
- feedback on instructions for use
- feedback on training needed for users
- feedback on use with other devices
- feedback on customer satisfaction
- identification of vigilance reports
- knowledge of ways in which the device is misused
- feedback on continuing market viability

[Co-ordination of Notified Bodies Medical Devices (NB-MED) on Council Directives 90/385/EEC, 93/42/EEC and 98/79/EC (2000)]

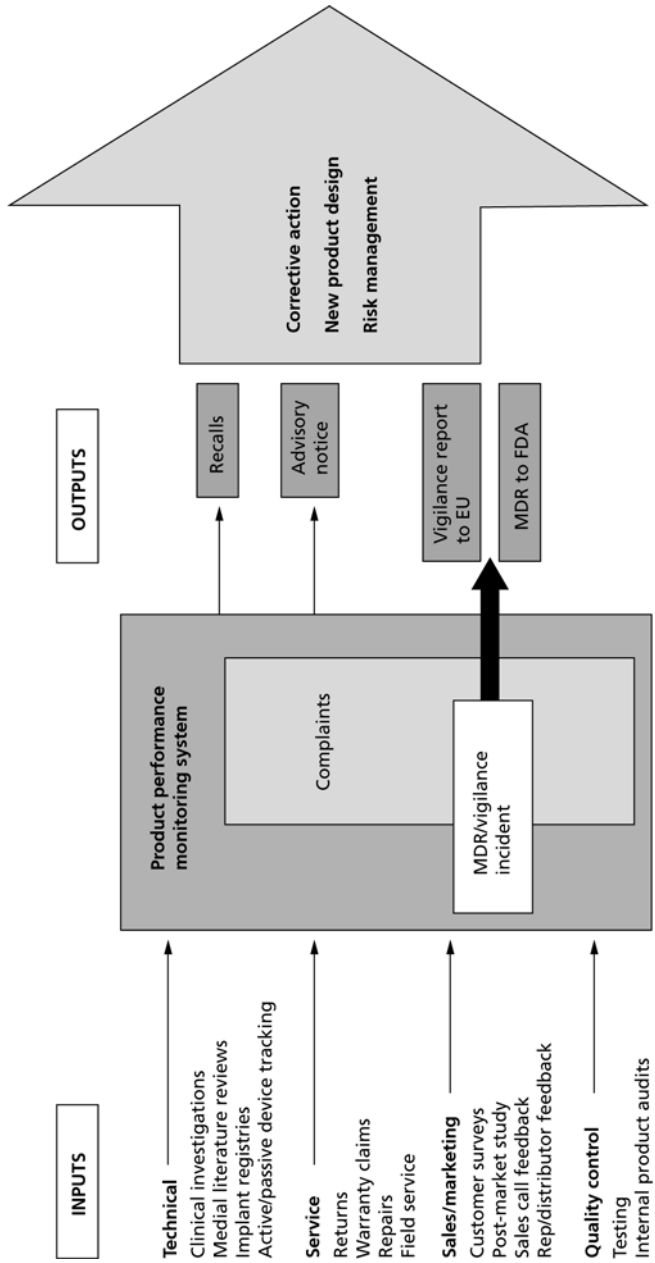


Figure 11 – Process of post-market surveillance

There are many reasons why an organization should be undertaking post-market surveillance.

- It is a regulatory requirement.
- Pre-market studies for medical devices are often of limited size, so they cannot detect or characterize events that occur at a low rate.
- There is a need for long-term follow-up, especially where the device may have a long lifetime in the recipient, as there may be issues of durability/biocompatibility, etc.
- An error in the use of the device may have been identified, or the device is being used 'off label' (outside the scope of its intended use) and there may need to be specific warnings about this.
- The device may be being used in community practice or home care where this is not appropriate.
- There may be concerns for selected patient groups.
- There may be device/device or device/drug interactions that had not been recognized initially.

Several activities should be considered to demonstrate post-market surveillance. Organizations may complete post-market surveillance on groups of product or individual product. Often they will have a procedure that defines the approach to be taken and the topics to be considered, which could include:

- the summary of a customer complaint;
- requirements for 'proactive' elements included in the system;
- clear references or linkages to the device;
- linking post-market surveillance to the risk management report.

In summary, post-market surveillance/post-production reviews are key processes that an organization must have as part of its quality management system, to ensure that the medical device remains safe and effective.

Internal audit (Clause 8.2.2)

Internal audit is a fundamental cornerstone of any quality management system. This is the process by which an organization can determine if the processes that it has defined are being followed, and where improvements can be identified.

The quality management system needs to be implemented and in use before internal audits are conducted. To conform to ISO 13485, an internal audit programme must be operational, helping the organization to investigate any quality problems and to verify that solutions are effectively implemented. Periodic audits also maintain the level of quality awareness of personnel and develop improved internal communications.

An audit is the 'systematic, independent and documented process for obtaining **audit evidence**…and evaluating it objectively to determine the extent to which the **audit criteria**…are fulfilled'. This definition is taken from ISO 19011:2011, Clause 3.1. ISO 19011:2011 is the Guidelines for auditing management systems; it is a helpful framework for an organization that is setting up an internal audit programme, as well as for carrying out audits of suppliers. In addition, it includes information about third-party audits for when an organization is audited by a certification body. If the organization is going to be certified to ISO 13485, ISO 19011:2011 describes the process for how the assessment for certification will be carried out.

Internal audits are expected to cover all areas and all workforce shifts. Some functions and systems may be audited more frequently than others; this will be based on previous results, increasing audit frequency for changed or high-risk areas. This is a risk-based approach to auditing.

Various aspects of the internal audit process must be included in a documented procedure. These include:

- details of the people in the organization who are responsible for the various aspects of the internal audit system;
- how audits are planned;
- how an audit is reported (including what information should be included); and
- who is responsible for keeping records of the audits.

The process should also define how the issues identified in the audit are resolved and corrected.

ISO 19011 includes information on:

- auditing principles;
- Managing an audit programme, including objectives of the programme, and establishing, implementing and monitoring the programme;
- performing internal and external audits;
- the competence and evaluation of auditors.

The annexes in ISO 19011:2011 include guidance and examples of the knowledge and skills that are required of auditors, and 'Additional guidance for auditors for planning and conducting audits' (ISO 19011:2011, Annex B).

For an organization that is putting an internal audit system in place, ISO 19011:2011 provides very good guidance to be used in establishing and maintaining an internal audit process. It is also useful for supplier audits, if these are being carried out by the organization.

Benefits of auditing

Internal audits are used as a means of evaluating an organization's quality management system. There are various reasons why an organization carries out internal audits:

- to verify conformity to requirements;
- to increase awareness and understanding of requirements;
- to provide a measurement of the quality management system's effectiveness to top management;
- to reduce the risk of management system failure;
- to identify improvement opportunities;
- to bring improvement to the processes;
- to support regulatory compliance, if the audits are performed regularly. It is a requirement of ISO 13485, but this should not be the only reason for having internal audits;
- to provide a self-check;
- to monitor and measure the quality management system;
- to promote continuous improvement of the quality management system, as the audits should look for positive improvement points as well as areas where the system requirements are not being met.

In the same way that ISO 13485 uses an overall process approach, the process approach can be used when auditing. This means that the interrelationship between the processes will be assessed. This is important, because the links between the processes are where the quality management system may show its weaknesses. Personnel will complete the tasks that they are responsible for, diligently, but the interface between their activity and the activity completed by another member of the organization is where problems may be identified in internal audits. If process audits have not been carried out, these issues may never be recognized.

Audit programme

The planning of audits should be flexible, so that changes can be made to the planned audits if a change in situation arises. These may be internal issues, for example, if there have been a number of complaints relating to a product, or if specific customer requirements are identified during the year, then the audit programme may have to be amended to take account of these issues.

Internal audits must be carried out at planned intervals, with the aim of determining that the quality management system requirements are being met. The approach taken by many organizations is to divide up the processes that make up the quality management system and then audit these processes individually or as groups, an activity that would be spread

over a year. The expectation is that all elements will be audited during a year. How often the various elements are audited will depend on the risks associated with the processes.

This is the audit programme, which is often called the audit schedule. It is good practice to consult the managers of the functions and the owners of the processes when preparing an audit schedule, before obtaining management approval for the schedule.

Quite often organizations have a schedule that will run for a calendar year, which is approved at the start of the year. The audit programme needs to take into account the status and importance of the processes that are being audited, in addition to the results of the previous audits. This means that if there is a particular area of concern (for example, a specific manufacturing process or how quality records are being completed), this activity or process will be repeated more frequently in the audit programme. For example, the manufacturing process might be audited twice in the calendar year, six months apart.

Another good way of approaching audits is to follow processes through to the review of a larger process. An audit could follow through the process of ordering, from identifying the requirements, purchasing the item, receiving the item and accepting it at Incoming Quality Control, to it being available for manufacturing. This allows the auditor to look at the interfaces between the various functions and activities. Often the issues in the processes arise with following the requirements of the quality management system at the interfaces between the various activities, because, in general, personnel know their own processes and follow them, but the issues may arise where they are interfacing with another activity in the overall process.

Audits may be conducted by a single auditor or a team of auditors. This will depend on the size of the organization and the approach taken to auditing. If the whole organization is audited at one time, this will require more than one auditor in the audit team; otherwise, the independence of the auditor will not be maintained unless the audits are conducted by an external consultant. Internal audits can be subcontracted either in part or in full.

The audit

The following aspects need to be defined for the audit:

- criteria – these are the references against which any nonconformity identified during the audit will be defined. This could be the internal procedures of the organization, ISO 13485 or a contract with a customer;

- scope – this defines the extent and the boundaries of the audit, for example, the building where the activities being audited are taking place or the process that is being audited;
- methods – this will define how the information is sampled, for example, by reviewing records or by observing the process;
- frequency –how often a particular activity is audited. This would normally be defined in the audit programme;
- objective – this should be explained to the owners of the process that is being audited, defining what will be accomplished during the audit. An example would be 'evaluation of the effectiveness of the quality management system in meeting the requirements of ISO 13485 and the organization's procedures. It may also be to identify areas of potential improvement of the quality management system'.

Records of audits must be kept; these will include the audit programme as well as the record of the audit. There are different approaches to audit reports. Some organizations use checklists; others will have a standard template that they use for recording the audit. There are benefits to the different approaches; the best approach will depend on the size of the organization and the experience of the auditors. There should be a link between the reports and the investigations and corrective action taken for any nonconformity that is identified.

Attributes of internal auditors

Confidence of an organization in its internal audit process will depend on the competence of the auditors carrying out the audits.

Auditors need to have the appropriate personal attributes to carry out audits, and also the appropriate knowledge and skills relating to the activities that they are auditing.

Auditors must have the personal attributes needed to conduct audits in accordance with the principles of auditing. These include being ethical, open-minded, diplomatic, observant, perceptive, tenacious, decisive and self-reliant.

The auditor's appropriate knowledge and skills will be gained through their education, their workplace experience, the training they have had to become an auditor and their experience of auditing. A good way of learning how to audit, in addition to completing a training course, is to observe other auditors or to be on the 'receiving end' of an audit as the process owner or part of a team whose process is being audited. This means that all areas can be audited by independent auditors. It is also important that auditors continue to develop their skills though continual professional development and by auditing regularly.

Organizations have different approaches to selecting their internal auditors. There may be one person in the organization who is a full-time auditor, or there may be part-time auditors, from across all functions of the organization, who carry out internal audits in addition to their job role. The latter has advantages, as it means personnel throughout the organization have an understanding of the audit process and the requirements of standards such as ISO 13485. It is important to ensure that any part-time auditors audit regularly, so that they maintain their auditing skills.

The audit programme would usually define the auditor who is going to carry out a specific audit. The selection of auditors is important, as they must be independent of the activity that is being audited and must not audit their own work. This can be challenging for a small organization.

Internal auditors need to have training in the standards and regulations that are used by the organization. These would include ISO 13485 but may also include the EU directives for medical devices, the QS regulation relating to the sale of medical devices in the United States and, possibly, ISO 14971, if this is used for risk management in the organization. When standards and regulations change, internal auditors must be trained on the changes.

Follow-up following audits

The aim of internal audits is to confirm that the requirements defined in the organization's quality manual and other documented procedures have been met, and that the defined processes also meet the requirements of ISO 13485 and remain effectively implemented and maintained. Over time processes can change and can move away from the requirements, so an essential aspect is to ensure that conformity with the requirements is maintained. If the internal audit finds that conformity has not been maintained, ISO 13485 requires the management of the responsible area to ensure that actions are taken to resolve the nonconformities. These actions must be timely and must ensure that the cause is identified. When defining the action to be taken it is important to make sure that the cause is really understood and that the action relates to the cause. If this is not done appropriately the organization runs the risk of repeating the original nonconformity. As part of the follow-up of any correction or corrective action that takes place there should be verification that the actions have been completed as they were defined. The team being audited would normally complete the verification, which would be checked at the next internal audit.

Correction is where the product or the service is affected – this may not be necessary for all nonconformities that are found in an internal audit, but it should always be considered. The correction may be simple, such as

amending a record appropriately with additional information; or it may be necessary to rework a product to correct the nonconformity.

Corrective action is where the cause is identified and an action plan is implemented, which will ensure that the issue does not recur.

Organizations often put the actions from internal audits into their corrective and preventive action system, so that they are managed by the same process as nonconformities that are identified from other sources. Some organizations choose to manage the actions from internal audits in a separate system from other nonconformities, depending on their regulatory authorities. The FDA, under the QS regulation, does not normally review internal audits, although it may look at the corrective actions from audits.

The outputs of internal audits are a key input to management review. They give management an understanding of how the quality management system is functioning at all levels in the organization.

At times it may be necessary to have special audits, which are instigated for a variety of reasons. These include: when the quality management system has to meet specific requirements as part of a contract with a customer, if significant changes are being made to the system, or when there are product issues that need to be assessed in relation to the systems around that product.

Measuring and monitoring of processes (Clause 8.2.3)

Systems for measuring processes must be established by the organization. It is important for the organization to know that the processes making up the system are performing as expected. In order to do this, the organization has to establish what should be monitored for each process. There should not be too many parameters to be monitored, as this could take up a lot of time and resource without adding much value. The parameters that are monitored must show that the process is achieving the results expected from the process – that is, the planned results. If the results of the monitoring are not as expected then an investigation, a correction and corrective action should be put in place to make sure that the expected results are achieved. There should be a clear interface with the corrective action system.

Some examples of circumstances where the expected results may not be achieved are:

- when internal audits are not completed as defined in the schedule;
- when the complaint-handling process is not being followed;

- in document control – where there may be issues in ensuring that all types of documents are controlled. Sometimes procedures are developed by an area that then do not follow the organization's document control process;
- in the design control process;
- during process validation – organizations sometimes struggle with the process for legacy product that have been on the market for some time.

Monitoring and measurement of product (Clause 8.2.4)

With medical devices, the product or service that is being supplied to customers, and its entire manufacturing process, will have parameters that can be measured. For these parameters there will be criteria established, both for the finished medical device and for the in-process testing and receipt of incoming materials. These requirements have to be documented.

The organization must monitor and measure the defined parameters for the medical device, to ensure that the product or service has met the defined requirements before it is released to customers.

In-process testing is testing that is performed on raw materials when they are received, or testing that is performed during manufacturing. It is often used for controlling the processes or for identifying nonconforming product at an early stage. The amount of in-process testing that is performed will be a balance between the time and resource needed for that testing and the risk of the product being nonconforming. As a medical device goes through the manufacturing process the value of the medical device increases. This is a decision based on the amount of testing that an organization has to do, taking into account the way its business is structured and the risk to the product. The amount of testing may also be balanced by the amount of validation that has taken place on the processes that are being used.

If a medical device is assembled at the customer's premises, the final inspection and testing may take place after installation has been completed.

The customer requirements, and the claims that are to be made for the product, must be considered when measuring the product or service before release. The organization needs to ensure that these requirements and claims will be met when the customer uses the product. Examples of the points to consider include:

- any claims that are made in the instructions for use, and the acceptance criteria that are to be used. For example, for an in vitro diagnostic assay, the criteria used in the manufacturer's testing of the

product to be used for the assay will be more rigorous than those that are stated for the product in the instructions for use;
- any product characteristics that will determine the types of measurement that can be made, the appropriate means of measurement to be used, the accuracy required and the skills needed to use the product;
- any equipment, software and tools that will be required when the product is to be tested; these need to be of the same type that the customer will use;
- the customer-established points for observation or verification of selected product characteristics;
- any requirements for inspections or testing that are to be observed or performed by regulatory authorities. For example, high-risk in vitro diagnostic product: every batch has to be released by the notified body, for a CE-marked product to be sold in the EU. This is also the practice for other high-risk medical devices in other regulated markets;
- the qualification of people, materials, product, processes and the quality management system, and the need to have sufficient independence. This links back to the responsibility and authority requirements in Clause 5.5 of ISO 13485;
- the final inspection/testing, which will confirm that verification activities have been completed and accepted during the manufacturing process;
- how the results of product measurements are to be recorded, for example, a standard worksheet that will include the criteria of the tests or measurements that are to be performed.

The records are an important part of monitoring and measuring. They provide evidence that the performance of the medical device meets the defined requirements when it is released for sale by the organization. The records should address the following points:

- the documented procedure that is used for the testing or inspection should identify the inspection/test procedure(s) and revision level to be used, and should be a controlled document;
- the records must include the results and demonstrate that they meet the predefined criteria;
- the records should identify any test equipment used and, if this is measuring equipment, evidence that it was within calibration. This may be by traceability to the calibration records that are held separately;
- records should be signed and dated by the person responsible for the inspection or test. It is usual for the records to be reviewed and countersigned by an independent person (they may be from a different function or the same function – the main issue is that the reviewer must be independent of the person doing the testing or inspection);

- the lot or serial number of the product being inspected or tested, the number of samples that were tested from the batch and how the samples were selected must be in the record. The selection process may be defined in a procedure;
- there must be records of the disposition of any product failing inspection or testing, the reasons for failure and, if appropriate, traceability to the record of any investigation or corrective action.

Control of nonconforming product (Clause 8.3)

Nonconforming product needs to be identified and controlled to prevent its unintended use or delivery. The process controls and responsibilities for the control of nonconforming product in the organization must be defined in a documented procedure.

The personnel throughout the organization should understand the process for nonconforming product and have the authority to identify and report in the system anything that has been shown to be nonconforming. This should be completed in a timely way. The timing is important because the nonconformity that has been identified could have an impact on the processing or delivery of the medical device further down the manufacturing or delivery process. It may be appropriate for the technician or operator to report the issue to their supervisor, who will decide whether to proceed with the process; this will depend on the organization's process for managing the control of nonconforming product or the processes used to manufacture them. If the medical device continues to be manufactured (while waiting for a supervisor's decision) and then has to be scrapped, this adds extra cost. If the decision can be made straightaway then the cost to the business will be less. Sometimes a business may proceed with a process while recognizing the risk, but at least this is a considered decision.

There is much discussion as to what is timely. This will depend on the philosophy of the organization and its approach to the control of nonconforming product. With high-value and high-risk medical devices, as soon as nonconforming product or potentially nonconforming product has been identified, the manufacturing process will be stopped until the issue has been reviewed and the disposition of the material determined.

The definition of disposition in the context of the control of nonconforming product is to determine:

- if the material can still be used in the manufacturing process as it is;
- if it can be modified (reworked) so that there is no impact to the finished medical device; or
- if it has to be scrapped (thrown away and not used in the manufacturing process or service delivery).

When developing the procedure for the control of nonconforming product, the organization needs to consider what the process should cover and when processes that are not completed as intended can affect the final medical device that is to be delivered to the customer. The process should cover more than just the point that the final medical device is not meeting the defined requirements; it should take account of any activities throughout the organization that could have an impact on the medical device.

Some examples of nonconformity are:

- personnel identify during testing of the finished medical device that it does not meet the requirements defined in the testing specification;
- a defined process is not being followed in manufacturing;
- incoming material does not meet the specified requirements;
- a certificate of analysis for a material is not received from a supplier;
- there is a calibration failure for equipment being used during manufacturing;
- the temperature of the manufacturing area does not remain in the defined range;
- calculation checks and quality records are not completed as defined;
- retraining has not been completed;
- the preventive maintenance process is not being followed;
- the complaint-handling process is not being followed.

There are various ways to manage situations when a product does not meet the defined requirements when manufactured, or the service does not meet the defined requirements when delivered by a process. This relates to the disposition of the product and can include:

- performing activities to remove the nonconformity that has been identified. This often involves reworking the medical device or component. This is discussed further in a subsequent part of this section;
- authorizing a nonconforming product's use, release or acceptance by concession;
- scrapping the product or taking action to ensure that it cannot be used in finished product. Sometimes this may mean that the product has to be destroyed, which has cost implications.

The following elements need to be included in the process for the control of nonconforming product:

- the personnel responsible for making the decision relating to the disposition of the nonconforming product. This may vary depending on the impact of the medical device. If the product is found to be nonconforming during testing of the finished medical device, the decision about disposition would probably be made by personnel

who are more senior in the organization, so that the quality and regulatory impact can be considered with the widest knowledge in the organization;
- how the product is identified and controlled, so that it is not used inadvertently.

Physical control of nonconforming product

This has been discussed previously in relation to storage (see 7.5.4/7.5.5) . The issue is that the organization must make sure that any product that may be nonconforming cannot be used unknowingly in the manufacturing process or during service delivery. This can be approached in different ways. The most secure way is physically to separate the nonconforming or potentially nonconforming material (until the disposition has been made) in a separate area/location with a physical barrier, and locked away. The location will depend on the size of the organization's facility – it may have just one area or it may have several areas in various functions, for example, in receiving, in manufacturing, or in the finished goods area. For smaller organizations it may not be possible to do this, so they will have one area where the nonconforming product is kept.

The organization may choose physically to label any material that is nonconforming, to show its status as nonconforming and whether it is approved for use or not.

Another approach is to have an electronic system that controls the use of materials and intermediate components; the system ensures that, unless the material is 'approved', it cannot be used in the manufacturing process. The organization will then rely on this system to ensure that nonconforming product cannot be used. It is essential to have 100 per cent certainty that personnel cannot get round the system in any way, for example, transacting one batch of material when they have picked a different batch off the shelf.

Organizations may choose to have a combination of these systems – using the electronic system when the nonconformity is being investigated, and physically putting the material in a secure location when the material is confirmed as nonconforming. They may often use a different status for this type of material in their electronic system or physical labelling system.

An important aspect of the physical control of nonconforming product is what happens to a medical device that is returned from the customer following its use, for example, surgical instruments that are being returned for sterilization and then reuse. It may be that the medical device is being returned because it was not what the customer ordered. Before it can be put back into stock, the organization must ensure that

nothing happened while it was being returned from the customer, or stored by the customer, that could affect its performance. It may be that the medical device is being returned following a customer complaint, and is to be used in the complaint investigation.

For all of these situations the organization needs to have a system in place to ensure that returned product is controlled as nonconforming product, usually physically separated from product in the factory that may be of the same batch, until it is known that the product meets the expected requirements. Organizations often have a separate area where material for complaint investigation is stored.

Rework

Product that is found to be nonconforming may need to be reworked, if the reason for the nonconformity can be corrected. This is an acceptable practice, for example, it may be that the medical device needs to be relabelled because there is an error on the label. It is important that any of the activities that are part of the rework process do not affect the performance of the medical device that is being reworked. For example, if the device is sterile and the package has to be broken to change the labelling, then the device would have to be re-sterilized if this does not affect the performance of the product (the impact on performance of the second sterilization would need to be determined and the conclusion documented).

How the medical device or the component of the medical device is to be reworked has to be documented. This should be described in a work instruction that is approved before the rework activity begins, and should include any activities that are required to ensure that the performance and requirements of the product meet the original specification.

This approval should be by the same functions that would have approved the process in the first place, so if it was approved by Quality Assurance, Research and Development and Manufacturing the approval of the rework to take place would be by the same functions. It will also be expected that the reworked component or medical device is to be tested or checked to ensure that it meets the same requirements as it would have done if it had not required rework.

Acceptance of nonconforming product by concession

Acceptance of nonconforming product by concession can only be approved if the regulatory requirements are met. The identity of the person authorizing the concession must be recorded. It must be ensured that either the personnel who understand the regulatory requirements sign off concessions or the person signing ensures they are consulted.

Analysis of data (Clause 8.4)

The intention of this clause of the standard is to ensure that the organization collects and analyses data as part of the quality management system, both from the inside (e.g. production or quality control) and from external sources, which include complaint handling and more active ways of post-market surveillance. It supports demonstration of the suitability and effectiveness of the quality management system. In many cases, a selection of the analysed data might be used to promote awareness about quality and motivate staff to further improve quality and efficiency.

Data from these sources has to be analysed; this analysis should be integrated, with a documented procedure for the approach to be taken for data analysis throughout the organization.

The types of data that can be collected for evaluating the effectiveness of the quality management system include:

- data that shows whether a product has met its requirements. This could be data from in-process components or the finished medical device;
- data that shows whether the customer requirements relating to the product have been met. This can be from a positive perspective, for example, a product is delivered on time and in the way the customer required. This is in addition to reviewing customer complaints;
- process effectiveness data – this may be the monitoring of not only the manufacturing processes, but also all the processes included in the quality management system, for example, internal audits. This monitoring should also include identifying preventive actions;
- information relating to suppliers' performance;
- improvement objectives and quality plans.

This could mean that the data is reviewed to look for common threads across the various systems, to identify any common issues. For example, data from nonconformities of the manufactured product could be related to customer complaints; or data from nonconformities related to processes could be reviewed with data from internal audits.

There are many ways in which the data can be analysed, as discussed at the start of this chapter.

The analysis of the data, including information from internal audits and other management information, will provide input to a management review. Top management will use this management review to make an informed conclusion about the (continuing) effectiveness of the quality management system, as well as to ensure its continuing suitability.

Improvement (Clause 8.5)

The focus for improvement in ISO 13485 is about identifying activities that 'identify and implement any changes necessary to ensure and maintain the continued suitability and effectiveness of the quality management system' (ISO 13485:2003, Clause 8.5.1). Where issues occur, it is important that they are identified by systems that are in place to ensure that they are corrected, so that the quality management system continues to remain effective.

There is a range of sources that can be used to measure and monitor the quality management system and identify areas for improvement. These include:

- quality objectives and quality policy;
- corrective and preventive action;
- customer complaints and enquiries;
- measurement of internal processes; and
- following the review of the inputs to management review.

General (requirements) (Clause 8.5.1)

There are specific references in this clause to activities relating to customer complaints, adverse events and advisory notices, as well as to maintaining the quality management system.

Customer complaints

Customer complaints, enquiries or any claims about the product or service within the warranty period are an indication of the external performance of the product or service. They give indicators about where correction, corrective action or preventive action is required in the product or the service provided to customers.

The process for management of customer complaints is an important part of the quality management system and should ensure that any complaint received by the organization is evaluated. Customer complaints can be received from many sources and may be received by anyone working for the organization; it is essential that they are then sent to the appropriate part of the organization so that they can be evaluated and included in the complaint system. The other aspect that organizations have to consider is to ensure that they receive all of the complaints communicated through their supply chain, distributors, agents or affiliates. This is an important regulatory requirement for medical devices that is often included in the regulations, although the specific requirements may differ between different regulators.

In some organizations, internal complaints can also be considered as customer complaints. This may be particularly relevant in large, multinational organizations where sites supply other sites, or even in organizations that have just two sites that supply to each other. In these circumstances the organization should have systems in place to manage inter-site complaints.

When evaluating complaints and determining whether an investigation is required (and the extent of that investigation), the organization should consider whether:

- the product or the service is still meeting the claims that were made for it, and conforming to the specification to which it was released;
- the product or service meets the specifications that were defined for it, but, in the customer's hands, it is not working in the way it should do or in the way in which the customer would like it to.

Typically, the procedure for management of complaints would include:

- establishing responsibility for operating the system, by defining who in the organization will receive and investigate the complaint, and who will be the contact for the customer. The organization should formally designate a person or persons, normally by their role or position, to collect and co-ordinate all written and oral customer complaints about medical devices. It could be that the quality function is responsible for investigating the complaint, or it may be the manufacturing team that produced the product or service, or the technical department. It may be that different functions have different tasks in the process;
- evaluating the complaint to determine whether the product or service still meets specifications. This is often done by inspecting or testing the product returned from the customer, perhaps in parallel with product from the same batch that has been retained as a sample of that batch. In certain circumstances it may not be possible to evaluate a returned sample of the product, so only the sample that has been retained would be inspected or tested;
- creating records and statistical summaries to monitor the trends in complaints for individual product or services, or groups of product or services, to enable the major causes of complaints to be determined. This type of information would also often be an input to management review;
- taking any corrective action that is required. In certain circumstances it may be determined that corrective action or preventive action is not required; there would have to be a record of the reason why this was not necessary, which would have to be authorized. It would need to be defined in the procedure who has the authority to agree that a corrective or preventive action is not necessary; normally, this is a supervisor or the quality manager;

- segregating any returned material – this is important. Often organizations will store this product in a quarantine area. The process for disposing of customer returns and faulty stock should also be defined. It may be that the product that has been returned has to be decontaminated;
- filing of customer correspondence and other relevant records. The time period for retaining the complaint investigation records needs to be defined. There may be specific regulatory requirements relating to the retention of complaint records;
- defining a complaint and an enquiry in the organization's procedure, so that there is a consistent approach to any issue that is communicated by the customer – this would be a helpful point to include in the procedure. It should be remembered that a complaint does not have to be received in written form, even if this is the usual method – a complaint can be received orally.

Typically, the information expected in a complaint investigation includes:

- the name of the medical device;
- the date the complaint was received;
- the reference number given to the complaint;
- the name and address of the complainant;
- the details of the complaint and any samples or product that were returned as part of the investigation;
- the date when the investigation was completed;
- the results of the investigation and the names of the individuals who performed the investigation;
- details of any corrections that were made as a result of the complaint;
- details of any corrective actions taken;
- if no correction or corrective action was required, details of the justification for no action being taken for inclusion in the complaint report;
- the reply that was sent to the complainant;
- closure of the complaint.

A point that is often discussed is whether the person who has made the complaint has confirmed that the follow-up action is acceptable. In addition, there is often discussion about at what point the complaint should be closed. Often, if the complaint is found to be justified (that is, the product or service was not meeting the specification), then a replacement product or service will be supplied to the customer. There may be a further investigation to determine why the issue occurred, which could result in corrective action. Should the customer be told that the corrective action has been completed, considering that this may be some time after a replacement product was supplied? In most cases it is probably appropriate to inform the customer. Complaints are seen as a negative event between an organization and its customer; however, if

the complaint is resolved in a timely way, with good communication between the organization and the customer, this can help to build a strong relationship.

When the cause of the complaint has been identified, there should be a link from the complaint system back to the risk management file for the product or service, to determine if anything in the file should be changed as a result of the complaint. The same process should be followed for issues identified from internal nonconformities and any changes that have to be made to the product or service. When a complaint has been justified, the organization should also determine whether the issue was identified in the risk assessment; if it was already identified there, this could provide useful information about the corrective action.

Adverse events

ISO 13485 states that, if the national or regional regulations require the reporting of adverse events, the organization should have a documented procedure for the process for when and how these notifications should take place. Adverse events are given various names by different regulators. The terms 'illness' and 'injury' are frequently defined by national and regional regulations; the definitions of these terms may vary between regulatory authorities, so it is important that this is recognized in the procedure. For example, the reporting of adverse events is called 'vigilance' in the EU and the requirements are defined in the Medical Devices guidance document, MEDDEV 2.12, which is currently at version 8 (as of January 2013); it is called 'medical event reporting' in the United States and the requirements are defined in Medical Devices: Reports of Corrections and Removals, 21 CFR part 806. It is essential for organizations to have a process in place to ensure that they are using the most current version of the requirements.

The record of the complaint investigation must have enough information to demonstrate that the complaint was properly reviewed, to determine whether:

- there was an actual failure to meet the specifications that have been defined for the medical device, both for release for sale by the organization and as defined in the instructions for use;
- the medical device was being used to treat or diagnose a patient;
- a death, injury or illness occurred;
- there was any relationship between the medical device and the reported incident or adverse event, if this information was required.

Medical knowledge may be required, if the organization needs to determine whether an event was serious. Many medical device manufacturers employ a qualified medical practitioner; for smaller

organizations where this is not practical they will retain the services of a doctor or clinician, who can be consulted when an issue occurs.

Advisory notices

ISO 13485 has requirements relating to advisory notices. The ISO 13485 definition of an advisory notice is:

[a] notice issued by the organization, subsequent to delivery of the medical device, to provide supplementary information and/or to advise what action should be taken in

- the use of a medical device,
- the modification of a medical device,
- the return of the medical device to the organization that supplied it, or
- the destruction of a medical device

(ISO 13485:2003, Clause 3.3)

There is also a note, which states that the 'Issue of an advisory notice might be required to comply with national or regional regulations'.

'Advisory notice' is, again, a generic term that is used in ISO 13485; different regulatory authorities have different names for advisory notices, for example, in the EU they are called Field Safety Corrective Actions.

It is important for an organization to have documented in its quality management system how it manages advisory notices to comply with the regulations in the various areas of the world where its product are sold, as the requirements and the terminology used in the different regulations differs. It is a requirement of ISO 13485 that there is a documented procedure for advisory notices. The advisory notice should cover the following aspects:

- a description of the medical device and model designation;
- the serial numbers or other identification (for instance, batch or lot numbers) of the medical devices concerned;
- the reason for the issue of the notice;
- any advice regarding possible hazards;
- any consequent actions to be taken.

The procedure for advisory notices should include the following:

- how the advisory notice is prepared, approved and issued;
- the arrangements for managing how the procedure is to be activated; it should ensure that this is possible even if the key personnel are not available. There needs to be a system for deploying the deputies of the key personnel;

- the level of management that is authorized to initiate corrective action, and the method of determining the affected product. This is important, because, although the complaint may be from a specific batch of a medical device, the organization will need to determine whether other batches, or other similar medical devices, are affected;
- the system for determining the disposition of returned product (e.g. rework, repackage, scrap);
- the communication system to be used to contact all customers who have the affected medical device. This should include reporting to local or national authorities, as required, about where the affected medical device has been distributed. There should be a process in place to ensure that it can be determined quickly where the medical device has been distributed;
- the points of contact and the methods of communication between the organization and national or regional regulatory authorities;
- if the medical device is returned to the organization, the monitoring of the progress of agreed corrective actions;
- if appropriate, the reconciling of the quantities of product physically returned to the organization or scrapped locally or corrected locally. It can often be difficult to obtain information from distributors or local branches of the organization in other countries to confirm that product has been destroyed locally. The organization needs to consider how it will manage this, because, if an advisory notice is required, it will be important that it is understood by the distributors of the local branches of the organization in other countries. The organization should have a contract or inter-site agreement so that the responsibilities are understood with regard to advisory notices.

The organization must be able to make sure that the procedure can be put into practice at any time, so there needs to be provision for the process to be used at weekends and during public holidays. The procedure should define who is responsible for managing the process and making the decision related to advisory notices, with arrangements for how these personnel can be contacted or have nominated deputies to cover for them, at any time.

There should be clear linkages in the quality management system between the receipt and investigation of a complaint, or an issue identified from an internal nonconformity, and the process of assessing that issue to determine whether it needs to result in an advisory notice. This may also require input from a doctor or clinician to ensure that the medical implications of the issue are evaluated in the same way as for adverse events.

It may be that an organization does not use the procedures because it has no issues that require an advisory notice. In this situation the organization should 'test' the process by putting a mock issue through the system to determine whether it can be used; ideally, this should be

done annually. This should include testing that there is full traceability about where the medical device has been sent to and used; this is particularly important for implantable medical devices.

Corrective action and preventive action (Clauses 8.5.2 and 8.5.3)

ISO 13485 requires that actions be taken to prevent the recurrence of nonconformities. This is corrective action. Preventive action is when actions are taken to prevent the potential occurrence of a nonconformity.

A clear distinction should be made between cases where a nonconforming situation is found, and correction and/or corrective action to prevent recurrence is required, and cases where no nonconformity is found, but where preventive action could prevent nonconformities from happening at all.

According to ISO 9000:2005, Quality management systems — Fundamentals and vocabulary, the definitions are:

- correction – 'action to eliminate a detected nonconformity…' (ISO 9000:2005, Clause 3.6.6). The correction is the immediate remedy to a nonconformity;
- corrective action – 'action to eliminate the cause of a detected nonconformity…or other undesirable situation' (ISO 9000:2005, Clause 3.6.5). The corrective action, which follows the root cause analysis (e.g. using the '5 Whys' method), is the sum of measures that will ensure the same nonconforming situation does not recur;
- preventive action – 'action to eliminate the cause of a potential nonconformity…or other undesirable potential situation' (ISO 9000:2005, Clause 3.6.4).

The main difference between corrective and preventive action is that corrective action puts in place actions to prevent the recurrence of something that has happened, whereas preventive action puts in place actions to prevent something that could happen.

For both corrective and preventive action the extent of the action that is taken needs to be related to the risk from the issue.

ISO 13485 requires that there is a documented procedure for both corrective and preventive action. The procedure should clearly establish who is responsible for taking corrective and preventive action, when and where corrective and preventive actions are required, and how the effectiveness of any corrective and preventive action will be verified.

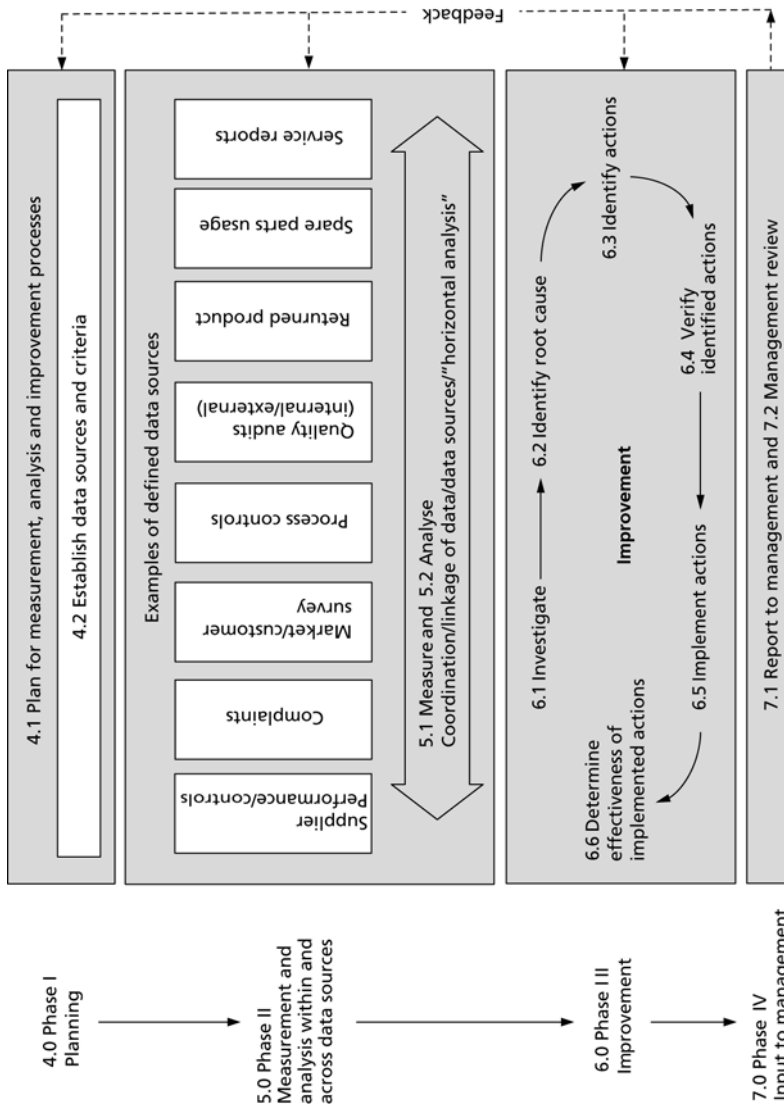
It is also important that, where there is a corrective action, any information related to the identified issue is communicated throughout the organization to the personnel who are responsible for quality.

Following the documented procedure for corrective action, and recording the results of the action taken, will allow quick identification of any findings in one area. This can potentially help the remaining areas to avoid a similar problem (and reduce the number of reported nonconformities in ISO 13485 certification assessments). Preventive actions are a different part of the improvement system, which work in a similar way to ensure a nonconforming situation does not occur, but they are based on rationale and other input, which do not stem from an existing nonconformity.

The GHTF published a document on corrective and preventive action entitled Quality management system –Medical Devices – Guidance on corrective action and preventive action and related QMS processes (GHTF/SG3/N18:2010). The guidance includes a diagram of how analysis and measurement lead to the improvement activities of corrective and preventive action.

Figure 12 shows a review of processes for measurement, analysis and improvement.

Organizations often have one system that is abbreviated to the CAPA (corrective action and preventive action) system, with one procedure covering both corrective and preventive action. The acronym ‘CAPA’ could be used incorrectly, as the concept of corrective action and preventive action could be interpreted incorrectly to assume that a preventive action is required for every corrective action. It has to be realized that, although the same approach can be used for both corrective and preventive action, they have different inputs and the definitions are different. Some organizations also confuse the relationship between corrective and preventive action and the term ‘correction’.



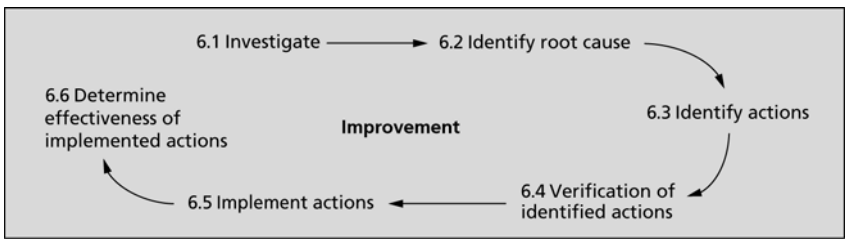
[source: The Global Harmonization Task Force (GHTF) Study Group 3 (2010), Figure 1]

Figure 12 – Review of processes for measurement, analysis and improvement

Some organizations put very complex systems in place, usually based on databases that manage corrective and preventive action, but a simpler approach may be possible for smaller organizations. The important point is that the inputs to the system that is used should be from all parts of the quality management system; they should not just be product related, which is often the focus.

There are requirements in ISO 13485 for procedures for both corrective and preventive action. Organizations often combine these into one procedure covering both topics. The key elements that should be included in any system and that are needed to fulfil the requirements of ISO 13485 are discussed below.

The phases of a CAPA system can be shown from the 'Improvement' part of Figure 12 (Figure 13).



[source: The Global Harmonization Task Force (GHTF) Study Group 3 (2010), Figure 3]

Figure 13 – Phases of a CAPA system

Corrective action

There are many inputs to corrective action that come from all aspects of the activities in the organization, demonstrating linkages within the quality management system. When the action has been completed to prevent the identified issue from recurring, there are clear linkages back in to the quality management system to which it is related. These linkages may be to more than one aspect of the quality management system.

The extent to which corrective action is performed for any issue that is identified will depend on the size of the issue, the risk related to the issue and the impact that it can have on the quality of the product or

service that the organization is supplying or manufacturing. This is where an organization can use its system for managing risk to assess the amount of activity needed, including the depth of the investigation. Risk management will also help an organization to determine the priority, where there are several issues that need investigation, and corrective action to determine the extent of the investigations and actions that are required. An input to risk management would be the impact that the nonconformity requiring corrective action could have on the safety and effectiveness of the medical device.

It is important that an organization implements corrective action in a timely way.

Examples of inputs to corrective action are:

- issues identified in internal audits;
- issues identified from product found to be nonconforming;
- where a procedure cannot be followed;
- inspection and test records;
- validation study results;
- observations during process monitoring;
- field, service or customer complaints;
- regulatory authority or customer observations;
- observations and reports by personnel. Issues that are identified by anyone in the organization should be inputs to corrective action. This may be via nonconformities;
- supplier problems, which may be identified within the organization or by the supplier; wherever the issue is identified it should be included in the corrective action system to ensure that action is put in place to prevent it recurring;
- management review results;
- information from customers following surveys on new or modified product. There should be a linkage from the corrective action system to the new product development system;
- published literature, both related to the product of the organization and similar product from other organizations. Here there would be a linkage to the post-market surveillance system;
- published reports of failures of similar product.

Preventive action

Many organizations do not understand the difference between corrective and preventive action. Preventive action is where actions are being taken to prevent an issue from occurring, so the definition includes the words ‘to eliminate the cause of a potential **nonconformity**’.

This means that an organization has to analyse records and other sources of information in order to determine where preventive action is required.

Examples of inputs to preventive action are:

- the analysis of trends. This may be from a manufacturing environment where a measurement can be taken from the outputs of a part of a process; this information can be used in statistical process control, on a chart with warning and action limits. If action is taken between the warning and action limits this is preventive action; for example, this means measuring the amount of liquid being poured into a bottle so that it does not go below the minimum allowed fill volume, and so will not have to be disposed of or reworked;
- difficulties with suppliers;
- sources of information for initiating preventive actions, including:
  - purchased product rejected on receipt;
  - evidence that previous decisions affecting product conformity were false;
  - product requiring rework;
  - in-process problems, e.g. wastage levels;
  - final inspection failures;
  - customer feedback;
  - warranty claims;
  - process measurements;
  - statistical process control documents;
  - service reports.

Review of actions and their effectiveness

For both corrective and preventive action it is important that these actions are completed in a timely way and that the actions that are taken are shown to be effective.

There are different ways in which effectiveness checks can be approached; it will depend on the type of issue. If the issue for which the corrective action has been put into place relates to the manufacture of the product, several batches may need to be manufactured before it can be confirmed that the action that was taken was effective. This may take some time, especially if it is a manufacturing process that is not undertaken frequently. For this reason organizations may regard the phase of checking the effectiveness to be separate to the actual completion of the corrective action, as time may need to be left to ensure that the action is effective.

A useful way of considering how effectiveness will be assessed for any corrective or preventive action that has been taken is to define an effectiveness check plan when the corrective or preventive action plan is being defined.

Data to support the effectiveness of an action that has been taken would be gathered over a period of time; one of the main aims is to ensure that taking the corrective or preventive action has not resulted in new issues or areas of concern.

Examples of questions that could be considered during the implementation of the corrective or preventive action, and when the action is finally signed off as being effective, are:

- Was the cause of the problem appropriately identified?
- Has all the product that was affected, or could have been affected, been included in the corrective or preventive action?
- Have all the actions that were taken been verified?

Links to management review

There should be clear linkages from the corrective and preventive actions back to management review. With an overview of the issues that are inputs to corrective and preventive action management, and whether these actions have been effectively implemented, top management of the organization can have a real indication of the health of the quality management system for which it is responsible.

Summary

In summary, with the requirements of Clause 8 in place in the quality management system, all the building blocks of the processes for the ISO 13485 quality management system are in place. The next step in the process is to have the system reviewed and certified by a registrar.

Chapter 9 – Achieving and continuing to maintain ISO 13485 certification

This chapter reviews the issues to consider in achieving and maintaining ISO 13485 certification.

The focus of this chapter is on:

- preparing for certification to ISO 13485;
- after the certificate is received – maintaining certification;
- the future of ISO 13485, and the changes that are being made to ISO 13485.

Preparing for certification to ISO 13485

Formal certification is achieved only through external (third-party) assessment by a certification body. Certification can only be achieved after correct preparation for the initial audit, which is a two-stage process:

1. the Stage 1 assessment, which is a review of the documentation of the organization's quality management system, as well as a review of the management review and internal audit process;
2. Stage 2 follows, as a complete, in-depth audit of all applicable areas of the standard, to review the implementation and effectiveness of the quality management system (more is said on these two stages below).

The benefits of certification include expanded access to world markets, the improved ability to bid for contracts and use of the standard as a market differentiator. The display of the certification mark (e.g. a symbol granted by the certification body, which is usually a combination of the registrar's logo and ISO 13485), and the evidence of independent audits by professional, independent certification bodies designated by an accreditation agency, can help to promote much greater trust in the organization's ability to provide a consistently high-quality product or service.

These benefits clearly outweigh the barriers to certification, such as the difficulty in identifying and creating new processes for the quality management system, development of the necessary documented procedures and instructions, and resistance by some employees to change (and process measurements), that are found in most organizations.

Factors to consider when selecting a certification body

When looking for a certification body to certify an organization's ISO 13485 system, it is important to check how that certification body is itself accredited. It may also be necessary to consider where the medical device is registered; for example, the ISO 13485 certification may have to be given by a specific registrar, for Canada. In the EU, for higher-risk devices, there are benefits to choosing an organization that can act as the ISO certification body and also that is a notified body for that type of medical device.

Being ready for certification

For an organization to be ready for certification it must have fully implemented an ISO 13485 quality management system and be using that system. When the quality management system is being assessed for certification the certification body is considering two aspects:

1. Are all the requirements included in the quality management system? This will be confirmed by the review of the system as it is documented and by review of the internal audits and management reviews that have taken place. This is often called a Stage 1 assessment or Document Review. Stage 1 assessments are normally conducted as a one-day, on-site review, although in certain circumstances they may take place by reviewing the documentation remotely;
2. the second stage of the certification process is to confirm the effectiveness of the processes that have been put in place to meet the requirements of the standard. During this assessment the organization must demonstrate the continual improvement of the quality management system. This is Stage 2 of the assessment. This will normally require more than one day, even for the smallest organization, as it has to be ensured that all the requirements of the quality management system have been implemented effectively.

An organization needs to be sure that it is ready to demonstrate both these aspects. Often organizations try to complete the process too quickly and do not have sufficient evidence of the working of the quality management system to be able to demonstrate its effectiveness.

The number of days that the assessment takes depends on the number of employees in the organization. If only one part of the organization is within the scope of the ISO 13485 quality management system, the number of employees who support this part of the organization will be used as the basis for calculating the number of days that will be required for the review. This time period is calculated using a document published by the International Accreditation Forum (IAF): IAF Mandatory Document for the Application of ISO/IEC 17021 in Medical Device Quality Management Systems (ISO 13485), Issue 1, Version 2. The current version is IAF MD 9:2011, which was applied from 15 July 2012.

Organizations can encounter several pitfalls, which include the following:

- there is insufficient awareness throughout the organization of the ISO 13485 quality management system and how it relates to individuals' roles, for example, how the quality policy relates to the activities in an individual's job role;
- management has not been sufficiently involved to demonstrate that it is taking its management responsibility seriously. It is important that management can show how it has led the organization in implementing and maintaining the ISO 13485 quality management system;
- management reviews cannot demonstrate top management's involvement in the quality management system, or cannot fully demonstrate it. This includes maintaining the effectiveness of the quality management system once it has been implemented;
- there has been insufficient training throughout the organization to understand what is required to implement and maintain an ISO 13485 quality management system;
- the requirements, especially those in Clause 6 and Clause 7, have not been related to the product that the organization is manufacturing or to the services that it is delivering;
- internal audits that have been performed have not covered the complete quality management system;
- the appropriate metrics and measures have not been put in place for the analysis of data and the feedback loop to demonstrate maintenance of the quality management system's effectiveness;
- the quality management system has become too complex and lacks flexibility. It does not necessarily have to be complex to meet the requirements of ISO 13485.

After the certificate is received – maintaining certification

When an organization achieves certification to ISO 13485 it is a major achievement that is cause for celebration. This, though, is just the start of the process.

When the celebrations are over it is important for everyone in the organization to realize that maintaining the effectiveness of the quality management system is just as important as implementing the system. This is not the end of the process but the beginning of the continuing process of maintaining the quality management system, as part of the continual improvement process. This includes understanding that it is a continuous process that everyone is committed to and involved in, to ensure that the requirements of the quality management system continue to be met.

A gap analysis is often performed as part of implementing an ISO 13485 quality management system. It is useful to maintain this gap analysis and revisit it from time to time, to ensure that the organization's quality management system has not moved away from the requirements of ISO 13485. The gap analysis will also be a useful tool if regulatory requirements or the requirements of ISO 13485 are changed, as it will provide a basis for completing a gap analysis against the new or revised requirements.

The future of ISO 13485

This section outlines recent developments in resolving harmonization issues (EN ISO 13485:2012), and describes the topics that are being reviewed for further updates of the standard.

EN ISO 13485:2012

As discussed in Chapter 2, EN ISO 13485:2012 has been issued, which addresses concerns about the harmonization of various European standards to EU directives.

During 2011, the European Commission raised an objection to the harmonization status, and the implied presumption of conformity, of a number of European standards, including EN ISO 13485:2003. Additionally, Sweden raised a formal objection in February 2011 to the European Commission on the link between adhering to the standard and complying with the directives. Changes were made to restore confidence and bring back the presumption of conformity indicated by the harmonized status of the standard.

EN ISO 13485:2012 was published in February 2012. On 31 August 2012, the standard was harmonized as expected to three medical devices directives: Council Directive 90/385/EEC [the Active Implantable Medical Devices Directive (AIMD)], Council Directive 93/42/EEC [the Medical Devices Directive (MDD)] and Directive 98/79/EC [the In Vitro Diagnostic Medical Devices Directive (IVDD)]. EN ISO 13485:2012 is applicable to manufacturers placing medical devices that have the CE mark on the

market. The changes are in the Foreword and Annexes ZA, ZB and ZC only; these annexes add further details on the link between the standard and the three medical devices directives mentioned above. In the rest of the world ISO 13485:2003 remains the applicable standard. There has been no change to the requirements (normative text); the clauses/requirements of the standard are exactly the same as the 2003 version.

Depending on the organization's circumstances, certification bodies may issue certificates to EN ISO 13485:2003 and/or to EN ISO 13485:2012.

ISO 13485:2003 under review

ISO 13485:2003 is under review by ISO/Technical Committee (TC) 210, Working Group (WG)1 and GHTF Study Group 3. A number of meetings have been held since starting the review in 2010. The purpose of the revision is to improve the clarity and compatibility of the standard with current regulatory requirements and expectations.

In April 2011, a Justification Study and a new work item proposal (NWIP) were agreed and the results were reviewed in October 2011. The areas for consideration included:

- the publication of Directive 2007/47/EC:
  - clinical data;
  - post-market surveillance;
  - software as a medical device, including requirements for validation;
- the Swedish Competent Authority formal objection to ISO 13485:2003;
- the European Commission objections to several EN standards and their harmonization statuses, etc., including the content and format of the Annexes ZA, ZB and ZC;
- the potential impact of any revision to ISO 9001, and the effect of the high–level structure for management system standards proposal by the ISO Technical Management Board;
- scope revision, with a reinforced focus on the quality management system not the product or product life cycle, and organization to include manufacturer, re-processor, distributor, etc.
- expanding risk management requirements;
- providing greater clarity;
- emerging markets;
- the requirements of other regulatory regimes and geographical areas;
- management responsibility, personnel competence, etc.

In all, 24 different topics/subject areas were highlighted.

ISO 13485, 3rd edition working draft (WD) 2 was compiled at a meeting of ISO/TC 210, WG1 held in October 2012. This WD has been issued for comment. The comments and other feedback will be reviewed at a meeting scheduled for early March 2013 in Japan. The intention is to issue a committee draft (CD) and start the ISO review process. The target date for the publication of the third edition of ISO 13485 is late 2014.

Some of the items that are expected to be included in the revisions are:

- risk management, post-market information, adverse event reporting and complaint handling;
- supply chain issues and outsourcing;
- process validation and software validation.

When any changes are made to the requirements of ISO 13485:2003 it will be important for the organization to assess how the changes affect its own quality management system. One of the ways to do this is to complete a gap analysis against the revised requirements. This has two benefits:

1. it considers the impact of any changes that have been made to the requirements;
2. it reviews the current quality management system against the revised requirements, to check that these requirements are maintained in the existing quality management system, as this is important to ensure that the organization meets regulatory requirements.

The FDA and ISO 13485

The FDA introduced a Medical Device ISO 13485:2003 Voluntary Audit Report Submission Pilot Program in 2012 for accepting ISO 13485 reports. It started on 5 June 2012. In the programme, the audit report is to be submitted to the FDA within 90 days from the last day of the most recent ISO 13485 audit. The report submitted will have to be consistent with Health Canada's Study Guide GD211: Guidance on the content of quality management system audit reports. This study guide is based on the work of Study Group 4 of the GHTF, and, in particular, on the technical content of GHTF document GHTF/SG4/N33R16:2007 Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers – Part 3: Regulatory Audit Reports. Details of the programme can be found on the FDA – Center for Devices and Radiological Health (CDRH) website.

Summary

The process of implementing and maintaining ISO 13485 can be demanding and time-consuming for those who are leading the project, or are part of the project team, but the rewards are worthwhile.

At the end of the process the organization will have a quality management system that will support the business process; it will have been independently certified and the organization will have a certificate to prove it. This will support the organization in meeting customer requirements and regulatory requirements.

The keys to success in implementing an ISO 13485 quality management system are having:

- a defined quality management system → saying it;
- selective documentation → writing it;
- conforming implementation → doing it;
- effective results → doing it well;
- records as evidence → proving it;
- internal audits → checking it.

Appendix – Background and origins of ISO 13485:2003

ISO 13485:1996 was published in 1996. It had been prepared by ISO/TC 210 WG1. This was aligned with the 1994 version of ISO 9001.

ISO 9001:2000 was published in December 2000, replacing the ISO 9001:1994 series. There was a three-year transition period before the 1994 versions [ISO 9001:1994, Quality systems — Model for quality assurance in design, development, production, installation and servicing (the complete management system), ISO 9002:1994, Quality systems — Model for quality assurance in production, installation and servicing (the exclusion of design and development), and ISO 9003:1994, Quality systems — Model for quality assurance in final inspection and test (the exclusion for design and development, and manufacturing)] were withdrawn for those organizations that were already certified to the standards.

The ISO 13485:1996 standard made reference to ISO 9001 throughout; it was not a stand-alone standard, but, rather, provided additional requirements for the medical device industry. There was also ISO 13488:1996; it was aligned to ISO 9002:1994, which focused on all the quality management system aspects with the exception of design and development.

During April 2000, ISO 13485:1996 and ISO 13488:1996 were adopted as European standards and replaced the then existing, sector-specific European standards (i.e. EN 46001, EN 46002, EN 46003). The European Commission redirected the harmonized references to the EU medical devices directives to the ISO series, away from the European Norms (ENs).

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 option of revising ISO 13485 and ISO 13488 to bring them in alignment with ISO 9001:2000 was considered but thought not to be appropriate, so the Technical Committee decided that ISO 13485 should become a stand-alone

standard. This meant that organizations did not have to have certification to ISO 9001 as well as to ISO 13485 and ISO 13488 in order to fulfil the regulatory requirements.

As stated in the Foreword to EN ISO 13485:2003:

> The text of the International Standard ISO 13485:2003 has been prepared by Technical Committee ISO/TC 210 "Quality management and corresponding general aspects for medical devices, Working Group 1". The transposition into a European Standard has been managed by the CEN Management Centre (CMC) with the assistance of the CEN/CENELEC Co-ordinating Working Group on quality supplements for medical devices.
>
> (EN ISO 13485:2003, Foreword)

As stated in the Foreword to ISO 13485:2003:

> [ISO 13485:2003] cancels and replaces the first edition (ISO 13485:1996).... It also cancels and replaces ISO 13488:1996. Those organizations which have used ISO 13488...may use this International Standard by excluding certain requirements in accordance with 1.2 [of ISO 13485:2003].
>
> (ISO 13485:2003, Foreword)

Annex A of ISO 13485:2003 details the correspondence between ISO 13485:1996 and ISO 13485:2003.

Although ISO 13485:2003 is a stand-alone standard, the 'clauses or subclauses that are quoted directly...from ISO 9001:2000 are in normal font' (ISO 13485:2003, Clause 0.3.1). Where additional requirements have been introduced, or the clause changed, in ISO 13485:2003, this is shown in italics; in electronic or colour-printed versions of the standard this is shown in blue italics.

Annex B of ISO 13485:2003 details the similarities and differences between the requirements of ISO 13485:2003 and ISO 9001:2000, and also gives a rationale for the changes that have been made for ISO 13485:2003. The reasons for the differences are provided in the table in the annex.

ISO 13485:2003 is published by various bodies; each body is identified by the letters placed before the main identifier 'ISO 13485:2003'. For example, in the UK the standard is published by the British Standards Institution (BSI); this could be denoted by the standard being identified as 'BS ISO 13485:2003'. However, as it is also a European standard (an EN), it is published as 'BS EN ISO 13485:2003'.

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Implementing an ISO 13485 Quality Management System for Medical Devices

Implementing an ISO 13485 Quality Management System for Medical Devices provides the reader with the appropriate background information and guidance for them to confidently implement a quality management system against the requirements of Medical Device Quality Management system requirements and then to subsequently maintain a quality system that remains certified to ISO 13485. It is practically based, using the author's experience of working for many years in the Medical Device industry and maintaining quality systems certified to ISO 13485.

The book provides background understanding relating to the interpretation of requirements of the standard and includes practical self-assessment, project planning and review guides in order for the reader to effectively benchmark their progress. It introduces the reader to the core processes and enhancements that are required in order to successfully implement to the degree whereby a Notified body, Regulator or major customer is satisfied that the system fulfils requirements.

The book features examples of good and best practice drawing on the author's experience of what is good and bad. In addition elements of world-wide regulatory requirements are featured within the book in order to understand the common denominators and the impact of world-wide regulations on the process.

About the author

Ann Goodall is currently working for BSI Healthcare as an IVD Technical Specialist in the IVD team as well as a Lead Assessor for **ISO 9001/13485** and delivers training on ISO 13485 Quality Management Systems.

Before joining BSI, she worked for over 30 years in the In Vitro Diagnostic industry after completing her Ph.D at St Mary's Hospital, London. This has included a variety of roles in small and large diagnostic companies including R&D, Quality Assurance and more recently five years in Supplier Quality Management working with international suppliers of finished products, to ensure appropriate product quality and quality system interface. Ann was an EDMA Member of Standardisation Quality and Risk Management Working Party for more than 15 years.

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BSI Group Headquarters
389 Chiswick High Road
London W4 4AL
www.bsigroup.com

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