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Medical devices — Quality management systems — Guidance on the application of ISO 13485:2003

Dispositifs médicaux — Systèmes de gestion de qualité — Lignes directrices pour l'application de l'ISO 13485:2003

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

In exceptional circumstances, when a technical committee has collected data of a different kind from that which is normally published as an International Standard ("state of the art", for example), it may decide by a simple majority vote of its participating members to publish a Technical Report. A Technical Report is entirely informative in nature and does not have to be reviewed until the data it provides are considered to be no longer valid or useful.

Attention is drawn to the possibility that some of the elements of this Technical Report may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

ISO/TR 14969 was prepared by Technical Committee ISO/TC 210, *Quality management and corresponding general aspects for medical devices*.

NOTE ISO/TC 210/WG1 is prepared to accept questions and comments related to the content of ISO 13485:2003 and/or ISO/TR 14969:2004. Please address all such questions and comments to the ISO/TC 210 secretariat at: *hwoehrle@aami.org*. These questions and comments will be considered for development of additional guidance in the application of ISO 13485:2003 either by revision of ISO/TR 14969 or the development of a “Frequently Asked Questions” document. You will not receive a response to your questions or comments, however, they will be considered for future use as noted above.

This first edition of ISO/TR 14969 cancels and replaces ISO 14969:1999, which has been technically revised.

Throughout this Technical Report, when the text of ISO 13485 is directly quoted, it appears enclosed in boxes prefaced by: “ISO 13485:2003, *Medical devices — Quality management systems — Requirements for regulatory purposes*”.

Introduction

0.1 General

0.1.1 This Technical Report 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 13485 specifies the quality management system requirements for medical devices for regulatory purposes (see Annex A). ISO 13485 accommodates the previous ISO 13488 by permissible exclusion as specified in ISO 13485:2003, 1.2.

When judging the applicability of the guidance in this Technical Report, one should consider the nature of the medical device(s) to which it will apply, the risk associated with the use of these medical devices, and the applicable regulatory requirements.

As used in this Technical Report, the term “regulatory requirement” includes any part of a law, ordinance, decree or national and/or regional regulation applicable to quality management systems for medical devices and related services.

This Technical Report provides some approaches that an organization can use to implement and maintain a quality management system which conforms with ISO 13485. Alternative approaches can be used if they also satisfy the requirements of ISO 13485.

0.1.2 The guidance given in this Technical Report is applicable to the design, development, production, installation and servicing of medical devices of all kinds. It describes concepts and methods that can be considered by organizations which are establishing and maintaining quality management systems.

An organization can voluntarily incorporate guidance from this Technical Report, wholly or in part, into its quality management system.

0.1.3 Guidance contained in this Technical Report can be useful as background information for those representing quality management system assessors, Conformity Assessment Bodies and regulatory enforcement bodies.

The guidance contained in this Technical Report is not to be used for identifying specific deficiencies of quality management systems, unless such guidance is voluntarily incorporated by the organization into the documentation describing and supporting the organization’s quality management system, or unless such guidance is specifically made part of the regulatory requirements relevant to the organization’s operation.

0.2 Process approach

ISO 13485 promotes the adoption of a process approach when developing, implementing and improving the effectiveness of a quality management system, with the objective of meeting customer and regulatory requirements, and providing medical devices that meet customer and regulatory requirements.

For an organization to function effectively, it has to identify and manage numerous linked activities. An activity using resources, and managed in order to enable the transformation of inputs into outputs, can be considered as a process. Often the output from one process directly forms the input to the next.

The application of a system of processes within an organization, together with the identification and interactions of these processes, and their management, can be referred to as the “process approach.”

An advantage of the process approach is the ongoing control which it provides over the linkage between the individual processes within the system of processes, as well as over their combination and interaction.

If used within a quality management system, such an approach emphasizes the importance of

— understanding and meeting requirements,

— considering processes in terms of added value,

— obtaining results of process performance and effectiveness, and

— improving processes based on objective measurement.

The model of a process-based quality management system shown in Figure 1 illustrates the process linkages presented in ISO 13485:2003, Clauses 4 to 8. This illustration shows that customers and regulatory authorities play a significant role in defining requirements as inputs. Monitoring of customer feedback requires the evaluation of information relating to whether the organization has met the customer requirements. The model shown in Figure 1 covers all the requirements of ISO 13485, but does not show processes at a detailed level.

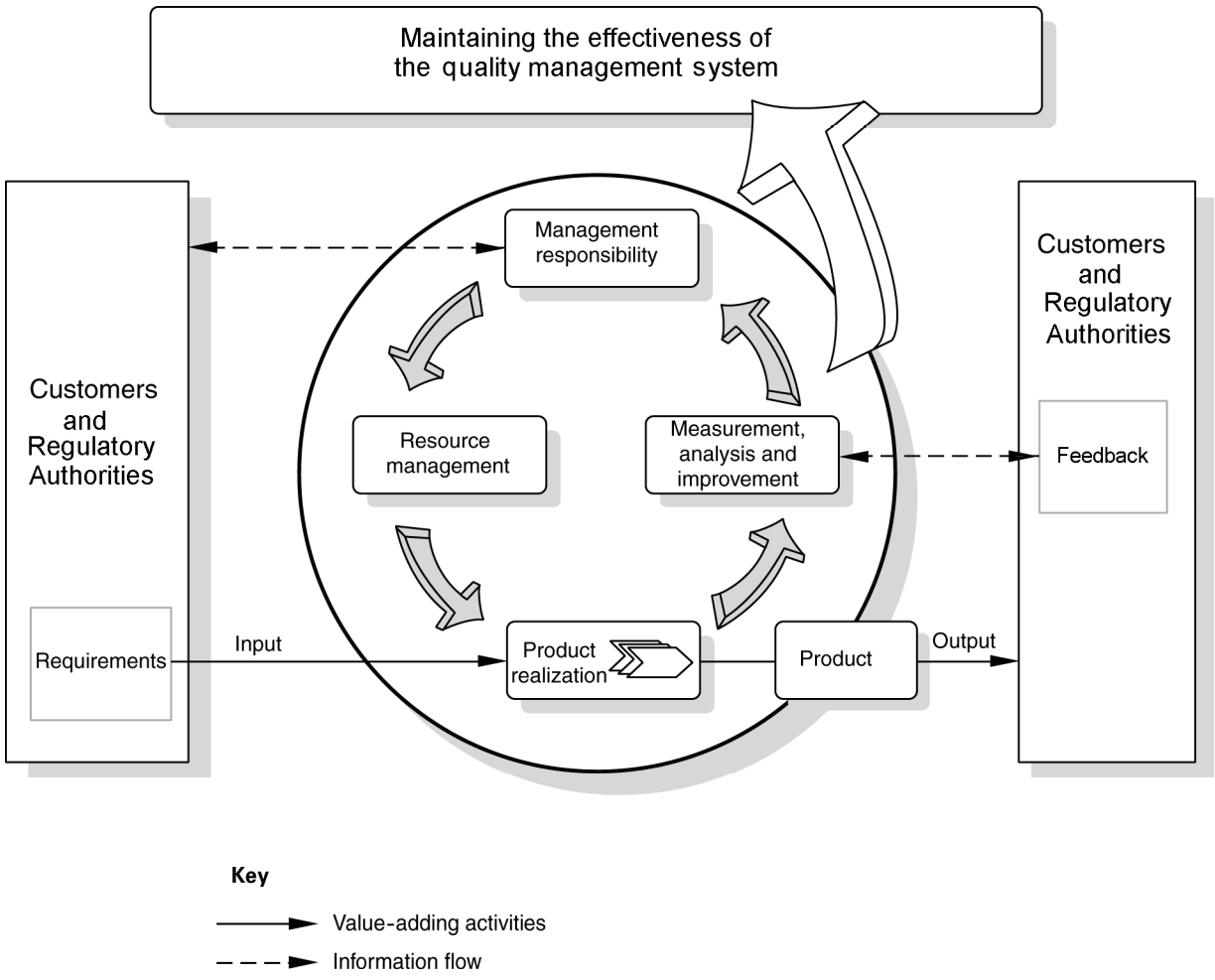

Figure 1 — Model of a process-based quality management system

In addition, the methodology known as “Plan-Do-Check-Act” (PDCA) can be applied to all processes. PDCA can be briefly 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 process performance.

0.3 Relationship with other standards, guidance documents and regulatory requirements

The relationship between ISO 13485, this Technical Report and the general standards for quality management systems (ISO 9001 and ISO 9004) is summarized as follows.

a) This Technical Report provides guidance on the application of ISO 13485.

b) ISO 13485 specifies requirements for quality management systems in order to achieve regulatory compliance in the medical devices industries. It follows the format, structure and process approach of ISO 9001. It differs from ISO 9001 in that it specifies additional requirements but does not include the explicit requirements for continual improvement and customer satisfaction.

c) ISO 9001 is an International Standard for quality management systems in general.

d) ISO 9004 gives guidance on a wider range of objectives of quality management systems than does this Technical Report, particularly for the continual improvement of an organization’s overall performance and efficiency, as well as its effectiveness. ISO 9004 is suitable as a guide for organizations whose top management wishes to move beyond the requirements of ISO 13485, in pursuit of continual performance improvement and customer satisfaction. However, it is not intended for certification or for contractual purposes.

ISO 13485 includes those generic quality management system requirements contained in ISO 9001 that are relevant to a regulated organization that designs and develops, produces, installs and/or services medical devices, or which designs and develops and provides related services. This Technical Report, however, does not set out to provide specific guidance with respect to these generic quality management system requirements which are common to both ISO 13485 and ISO 9001. Guidance on ISO 9001 can be found, for example, in the ISO brochure, *ISO 9001 for Small Businesses – What to do*, and in *ISO 9000 Introduction and Package module*.

Guidance provided in this Technical Report has taken into consideration requirements and guidance contained in documents from the following organizations:

— Global Harmonization Task Force (GHTF);

— International Organization for Standardization (ISO);

— European Committees for Standardization (CEN and CENELEC);

— national regulatory bodies.

Many of these documents are listed in the Bibliography.

0.4 Compatibility with other management systems

Conformance to ISO 13485 quality management system requirements does not automatically constitute conformity with national or regional regulatory requirements. It is the organization's responsibility to identify and establish compliance with relevant regulatory requirements.

Medical devices — Quality management systems — Guidance on the application of ISO 13485:2003

1 Scope

1.1 General

This Technical Report provides guidance for the application of the requirements for quality management systems contained in ISO 13485. It does not add to, or otherwise change, the requirements of ISO 13485. This Technical Report does not include requirements to be used as the basis of regulatory inspection or certification assessment activities.

NOTE The terms “should”, “can” and “might” within this Technical Report are used as follows. “Should” is used to indicate that, amongst several possibilities to meet a requirement in ISO 13485, one is recommended as being particularly suitable, without mentioning or excluding others, or that a certain course of action is preferred but not necessarily required. “Can” and “might” are used to indicate possibilities or options. These terms do not indicate requirements.

This guidance can be used to better understand the requirements of ISO 13485 and to illustrate some of the variety of methods and approaches available for meeting the requirements of ISO 13485.

1.2 Application

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

1.2 Application

All requirements of this International Standard are specific to organizations providing medical devices, regardless of the type or size of the organization.

If regulatory requirements permit exclusions of design and development controls (see 7.3), this can be used as a justification for their exclusion from the quality management system. These regulations can provide alternative arrangements that are to be addressed in the quality management system. It is the responsibility of the organization to ensure that claims of conformity with this International Standard reflect exclusion of design and development controls [see 4.2.2 a) and 7.3].

If any requirement(s) in Clause 7 of this International Standard is(are) not applicable due to the nature of the medical device(s) for which the quality management system is applied, the organization does not need to include such a requirement(s) in its quality management system [see 4.2.2 a)].

The processes required by this International Standard, which are applicable to the medical device(s), but which are not performed by the organization, are the responsibility of the organization and are accounted for in the organization’s quality management system [see 4.1 a)].

In this International Standard the terms “if appropriate” and “where appropriate” are used several times. When a requirement is qualified by either of these phrases, it is deemed to be “appropriate” unless the organization can document a justification otherwise. A requirement is considered “appropriate” if it is necessary in order for

— *the product to meet specified requirements, and/or*

— *the organization to carry out corrective action.*

1.2.1 General

Certain product realization requirements of ISO 13485 can legitimately be omitted in one of two ways: they can be “excluded”, or they might be “not applicable”. It is important to note, however, that any exclusion or non-applicability should be detailed and justified in the organization’s quality manual.

1.2.2 Exclusions

Some regulatory requirements permit organizations to place some medical devices on the market without having to demonstrate conformance with design and development controls (see ISO 13485:2003, 7.3). Organizations should determine the exclusion of 7.3 on a product-by-product, market-by-market basis.

Even if the organization is permitted by regulations to exclude the requirements of 7.3, it still has obligations to meet product realization requirements of ISO 13485:2003, 7.2, 7.4 and 7.5 and 7.6.

1.2.3 Non-applicability

ISO 13485 provides for the organization to omit from its quality management system those product realization requirements that are not applicable due to the nature of the medical device.

For example, an organization providing single-use, sterile medical devices does not need to include within its quality management system elements related to installation and servicing. Similarly, an organization providing non-sterile medical devices does not need to include the elements related to sterilization.

It is important for the organization to review carefully all the requirements of ISO 13485:2003, Clause 7, in order to identify those requirements that do apply to functions performed by the organization. Once those requirements are identified, the organization is obliged to comply with ISO 13485:2003, 7.1, and to perform the planning associated with identified product realization requirements.

EXAMPLE An organization intends

— to place its own label on a medical device designed and developed, produced, and serviced by suppliers outside its quality management system, and to market this medical device,

— to communicate with customers who have purchased the medical device, and

— to have systems in place for receiving customer complaints.

Even though the organization does not perform design and development activities itself, it cannot consider 7.3 to be non-applicable. It still has obligations to meet the requirements of 7.3, unless relevant regulations permit an exclusion. Once the organization identifies those requirements, it is obliged under 7.1 to plan for the quality management system processes needed to meet those requirements.

2 Normative references

The following referenced documents are indispensable for the application of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 9000:2000, *Quality management systems — Fundamentals and vocabulary*

ISO 13485:2003, *Medical devices — Quality management systems — Requirements for regulatory purposes*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 9000 and ISO 13485 apply.

NOTE The terms provided in Annex A should be regarded as generic, as definitions provided in national regulatory requirements can differ.

4 Quality management system

4.1 General requirements

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

4 Quality management system

4.1 General requirements

The organization shall establish, document, implement and maintain a quality management system and maintain its effectiveness in accordance with the requirements of this International Standard.

The organization shall

a) identify the processes needed for the quality management system and their application throughout the organization (see 1.2),

b) determine the sequence and interaction of these processes,

c) determine criteria and methods needed to ensure that both the operation and control of these processes are effective,

d) ensure the availability of resources and information necessary to support the operation and monitoring of these processes,

e) monitor, measure and analyse these processes, and

f) implement actions necessary to achieve planned results and maintain the effectiveness of these processes.

These processes shall be managed by the organization in accordance with the requirements of this International Standard.

Where an organization chooses to outsource any process that affects product conformity with requirements, the organization shall ensure control over such processes. Control of such outsourced processes shall be identified within the quality management system *(see 8.5.1)*.

NOTE Processes needed for the quality management system referred to above should include processes for management activities, provision of resources, product realization and measurement.

4.1.1 An element of managing an organization is the implementation and maintenance of an effective quality management system that is designed to enable an organization to provide medical devices that meet customer and regulatory requirements.

The organization can maintain the effectiveness of its established quality management system through a range of activities, such as

— internal audits,
— management review,
— corrective and preventive actions, and
— independent external assessments.

4.1.2 Maintaining the effectiveness of the quality management system in its ability to meet customer and regulatory requirements will typically involve the organization responding effectively to external factors, such as

— changes in regulatory requirements, including adverse event reporting, and

— customer feedback,

and internal changes, such as changes to

— key personnel,

— facilities,

— manufacturing processes and equipment, including related software,

— software related to the quality management system, and

— product, including software.

4.1.3 Examples of activities to maintain an effective quality management system include

— defining and promoting processes which lead to achieving regulatory compliance,

— acquiring and using process data and information on a continuing basis,

— determining and providing resources, including human and information system resources,

— directing necessary changes to the quality management system, and

— using suitable evaluation methods such as internal audits and management reviews.

For guidance on activities related to outsourced processes, see 7.4.1.

4.2 Documentation requirements

4.2.1 General

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

4.2 Documentation requirements

4.2.1 General

The quality management system documentation shall include

a) documented statements of a quality policy and quality objectives,

b) a quality manual,

c) documented procedures required by this International Standard,

d) documents needed by the organization to ensure the effective planning, operation and control of its processes,

e) records required by this International Standard (see 4.2.4), and

f) any other documentation specified by national or regional regulations.

Where this International Standard specifies that a requirement, procedure, activity or special arrangement be "documented", it shall, in addition, be implemented and maintained.

For each type or model of medical device, the organization shall establish and maintain a file either containing or identifying documents defining product specifications and quality management system requirements (see 4.2.3). These documents shall define the complete manufacturing process and, if applicable, installation and servicing.

NOTE *1* The extent of the quality management system documentation can differ from one organization to another due to

a) the size of the organization and type of activities,

b) the complexity of processes and their interactions, and

c) the competence of personnel.

NOTE *2* The documentation can be in any form or type of medium.

4.2.1.1 Documented quality management system procedures are required for applicable requirements of ISO 13485 and should be consistent with the organization's quality policy. It is important to recognize that the structure and level of detail required in these procedures should be tailored to the needs of the organization, which in turn are dependent on the methods used and the skills and qualifications of the organization's personnel performing the activities in question (see also 6.2.2).

Procedures or instructions may be presented in text, graphic or audio-visual form. Frequently a simple set of pictures can convey the requirements more accurately than a lengthy detailed description.

4.2.1.2 Documented procedures, including work instructions and flowcharts, should be stated simply, unambiguously and understandably, and should indicate methods to be used and criteria to be satisfied. These procedures typically define activities and describe

— what is to be done, and by whom,
— when, where and how it is to be done,
— what materials, equipment and documents are to be used,
— how an activity is to be monitored and measured, and
— what records are required.

4.2.1.3 Documentation should be evaluated with respect to the effectiveness of the quality management system against criteria, such as

— functionality,
— human interfaces,
— resources required,
— policies and objectives, and
— interfaces used by the organization's customers and suppliers.

4.2.1.4 The file for each type or model of medical device referred to in ISO 13485:2003, 4.2.1 is sometimes referred to by different terms (see Annex A, section B). This file can contain, or give reference to the location of, documentation relevant to the manufacture of that product. Examples of such documentation include

— specifications for raw materials, labelling, packaging materials, sub-assemblies and medical devices,
— parts lists,
— engineering drawings,
— software programs, including source code (if available),
— work instructions, including equipment operation,
— sterilization process details, if applicable,
— quality plans,
— manufacturing/inspection/test procedures, and
— acceptance criteria.

4.2.1.5 The documentation referred to in ISO 13485:2003, 4.2.1 forms part of the quality management system and should be subject to document and record control procedures (see 4.2.3 and 4.2.4).

4.2.2 Quality manual

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

4.2.2 Quality manual

The organization shall establish and maintain a quality manual that includes

a) the scope of the quality management system, including details of and justification for any exclusion and/or non-application (see 1.2),

b) the documented procedures established for the quality management system, or reference to them, and

c) a description of the interaction between the processes of the quality management system.

The quality manual shall outline the structure of the documentation used in the quality management system.

There is no specific guidance for this subclause of ISO 13485.

NOTE Additional information relating to quality manuals is available in ISO/TR 10013.

4.2.3 Control of documents

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

4.2.3 Control of documents

Documents required by the quality management system shall be controlled. Records are a special type of document and shall be controlled according to the requirements given in 4.2.4.

A documented procedure shall be established to define the controls needed

a) to review and approve documents for adequacy prior to issue,

b) to review and update as necessary and re-approve documents,

c) to ensure that changes and the current revision status of documents are identified,

d) to ensure that relevant versions of applicable documents are available at points of use,

e) to ensure that documents remain legible and readily identifiable,

f) to ensure that documents of external origin are identified and their distribution controlled, and

g) to prevent the unintended use of obsolete documents, and to apply suitable identification to them if they are retained for any purpose.

The organization shall ensure that changes to documents are reviewed and approved either by the original approving function or another designated function which has access to pertinent background information upon which to base its decisions.

The organization shall define the period for which at least one copy of obsolete controlled documents shall be retained. This period shall ensure that documents to which medical devices have been manufactured and

tested are available for at least the lifetime of the medical device as defined by the organization, but not less than the retention period of any resulting record (see 4.2.4), or as specified by relevant regulatory requirements.

4.2.3.1 The system established for the control of internal and external documents will, if appropriate

- assign responsibilities for preparation, approval and issue of documents,
- ensure prompt withdrawal of obsolete copies of controlled documents,
- define a method for recording the implementation date of a document change, and
- allow controlled and non-controlled documents to be distinguished.

The quality management system may also identify recipients of controlled copies of documents.

4.2.3.2 Documents may be reviewed at various times throughout the life of a document, for example, as a result of

- facilities, personnel or organizational changes,
- audit activities,
- acquisitions,
- new products, technologies or software,
- a requirement of the organization's quality management system for periodic review.

4.2.3.3 Document control procedures can be assisted by the adoption of a consistent structure for the documents within the quality management system. These procedures should clearly indicate what document control information should be included in each document. Consideration should be given to the inclusion of

- title and scope,
- document reference number,
- date of issue/date effective,
- revision status,
- review date or review frequency, as required by the quality management system,
- revision history,
- originator or author,
- person(s) approving it,
- person(s) issuing it,
- distribution,
- pagination, and
- computer file reference, if applicable.

4.2.3.4 The topic of electronic documents is complex and evolving. National or regional regulations and guidance documents might address requirements for the organization to establish documented procedures specifically for control of electronic records. This may include, but is not limited to, access, storage, reproducibility, readability, audit trails and electronic signatures, if appropriate.

4.2.3.5 Organizations are required by ISO 13485 to define the lifetime of each of their medical devices; considerations for establishing the lifetime of the medical device are to be found in 7.1.

Document retention time should take into consideration

- period of time the medical device is expected to be in the market place,
- legal considerations including liability,
- need or advisability of keeping documents indefinitely,
- retention time of related records, and
- spare parts availability.

4.2.3.6 The organization should retain at least one copy of obsolete controlled documents for at least the minimum period of time required by regulation. Obsolete documents should also be retained for as long as is necessary to understand the content of records which are related to the document (see 4.2.4).

ISO 13485 requires the organization "to apply suitable identification" to obsolete documents; such identification can be applied physically (as with a stamp) or electronically (as in a computerized database).

ISO 13485 recognizes that there might be specific regional or national regulatory requirements for the retention of documents made obsolete by changes in medical devices or the quality management system. The organization should determine whether any market that it supplies has such regulatory requirements and should establish a system to ensure that such obsolete documents are retained for an appropriate period.

4.2.4 Control of records

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

4.2.4 Control of records

Records shall be established and maintained to provide evidence of conformity to requirements and of the effective operation of the quality management system. Records shall remain legible, readily identifiable and retrievable. A documented procedure shall be established to define the controls needed for the identification, storage, protection, retrieval, retention time and disposition of records.

The organization shall retain the records for a period of time at least equivalent to the lifetime of the medical device as defined by the organization, but not less than two years from the date of product release by the organization or as specified by relevant regulatory requirements.

4.2.4.1 Records can be considered as falling into one of three categories, as follows:

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;

c) those that demonstrate the effective operation of the overall quality management system (system records).

It is clear that records in categories a) and b) are related directly to particular medical devices. Those in category a) should be kept for a time at least equivalent to the lifetime of the medical device after manufacture of the last product made to that design. Those records in category b) should be kept for a time at least equivalent to the lifetime of that particular batch of medical devices.

4.2.4.2 Some system records may also have a retention period related to the lifetime of a medical device; for example, calibration and training of individuals. For some other system records, it is less straightforward to relate them to the lifetime of a medical device; for example, management review, internal audit, infrastructure, evaluation of some suppliers and analysis of data. In these cases, the organization is required by ISO 13485 to identify an appropriate retention period. In defining this retention period, the organization should take into account the nature of the medical device, the risks associated with its use, the records involved and relevant regulatory requirements.

4.2.4.3 Records should be stored safely, protected from unauthorized access, and protected from alteration. These records should be properly identified, collected, indexed and filed, and should be readily accessible as and if needed. They may be stored or copied in any suitable form (e.g. hardcopy or electronic media). If records are retained on electronic media, consideration of the retention times and accessibility of the records should take into account the degradation of the electronic data and the availability of devices and software needed to access the records. Such copies of records should contain all the relevant information captured in the original records.

4.2.4.4 Hand-written entries should be made by indelible medium. Persons making authorized entries on records or verifying such entries should do so in clear legible writing, and should confirm the entry by adding their initials, signature or equivalent, and the date.

Good recording practices can include the following procedures, as appropriate:

— enter data and observations as they occur;
— do not pre-date or post-date records;
— do not use another person's initial, signature or equivalent;
— complete all fields or check-offs when using a form;
— refer to raw data when transferring data, and have the transcription verified by a second person;
— verify all entries for completeness and correctness;
— number pages to ensure completeness.

4.2.4.5 If an error is made or detected on a record, it should be corrected in such a manner that the original entry is not lost and the correction is initialed and dated. If appropriate, the reason for the correction should be recorded. Where electronic records systems are used in place of paper-based ones, these systems should, wherever possible, incorporate time-stamped, immutable, system-generated audit trails, for tracking changes. Such audit trails may include the identity of the authorized user, creations, deletions, modifications/ corrections, time and date, links and embedded comments.

4.2.4.6 The organizations may have alternative provisions for critical data entry of electronic records, for example,

— a second authorized person with logged name and identification, with time and date, can verify data entry via the keyboard, or
— systems with direct data capture can have the second check as a part of validated system functionality.

A system should be implemented that assures the integrity of electronic records and protects against unauthorized entries. The topic of electronic records is complex and evolving. National or regional regulations and guidance documents might address requirements for the organization to establish documented procedures specifically for control of electronic records. This might include, but not be limited to, access, storage, reproducibility, readability, audit trails and electronic signatures, if appropriate.

4.2.4.7 In addition to considering the lifetime of the device (see 7.1) in determining record retention time, legal considerations, including liability, and the need or advisability of keeping records indefinitely, should be considered.

5 Management responsibility

5.1 Management commitment

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

5 Management responsibility

5.1 Management commitment

Top management shall provide evidence of its commitment to the development and implementation of the quality management system and maintaining its effectiveness by

a) communicating to the organization the importance of meeting customer as well as statutory and regulatory requirements,

b) establishing the quality policy,

c) ensuring that quality objectives are established,

d) conducting management reviews, and

e) ensuring the availability of resources.

NOTE For the purposes of this International Standard, statutory requirements are limited to the safety and performance of the medical device only.

It is important to note the emphasis on “top management” throughout this subclause. This is intended to ensure that the quality management system is effective as a result of commitment on the part of management at the highest levels of the organization.

Top management’s commitment is best demonstrated by its actions.

Remembering that the quality management system is a set of interrelated processes, top management should ensure that processes operate as an effective network.

Consideration should be given to

— ensuring that the sequence and interaction of processes are designed to achieve the planned results effectively,
— ensuring that process inputs, activities and outputs are clearly defined and controlled,
— monitoring inputs and outputs to verify that individual processes are linked and operate effectively,
— identifying hazards and managing risks,
— conducting data analysis to facilitate necessary improvement of processes,
— identifying process owners and giving them responsibility and authority, and
— managing each process to achieve the process objectives.

5.2 Customer focus

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

5.2 Customer focus

Top management shall ensure that customer requirements are determined and are met (see 7.2.1 and 8.2.1).

This subclause is intended to emphasize the responsibility of top management to make certain that customer requirements are understood and that the necessary resources are made available to meet those requirements, regardless of who in the organization actually undertakes the interaction with the customer. The references to ISO 13485:2003, 7.2.1 and 8.2.1, are pointers to what this process will be expected to cover.

5.3 Quality policy

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

5.3 Quality policy

Top management shall ensure that the quality policy

a) is appropriate to the purpose of the organization,

b) includes a commitment to comply with requirements and to maintain the effectiveness of the quality management system,

c) provides a framework for establishing and reviewing quality objectives,

d) is communicated and understood within the organization, and

e) is reviewed for continuing suitability.

The quality policy establishes

- a commitment to quality and the continuing effectiveness of the quality management system to meet customer and regulatory requirements,
- the context for quality objectives, and
- the relationship of the organization's objectives to the customers' requirements.

It is important that the organization's quality policy be considered when preparing the overall organization policies related to its business operations (e.g. marketing, sales, finance) in order to ensure that all organization policies are consistent and supportive of each other.

The quality policy should communicate the organization's commitment to quality and its overall vision of what quality means to the organization's business and customers.

ISO 13485:2003, 4.2.1, requires the organization to state this quality policy in writing.

In order to demonstrate that the organization is committed to implementing its quality policy, it will need to identify clear, overall quality goals for the business that are directly relevant to the organization and its customers.

Top management's commitment to the quality policy should be visible, active and effectively communicated. For example, a publicly displayed copy of the quality policy signed by top management is one method to show that commitment to both employees and customers. Another method is to present and discuss the quality policy at organization meetings throughout the year. Top management's commitment is best communicated through its decisions and actions.

All employees need to understand the quality policy and how it affects them. Top management should ensure that the organization decides on the methods which will be used to achieve this understanding.

The quality policy also needs to be reviewed from time to time to determine if it accurately reflects the current quality related goals and objectives of the organization. This review is often carried out during the management review required in 5.6.

5.4 Planning

5.4.1 Quality objectives

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

5.4 Planning

5.4.1 Quality objectives

Top management shall ensure that quality objectives, including those needed to meet requirements for product [see 7.1 a)], are established at relevant functions and levels within the organization. The quality objectives shall be measurable and consistent with the quality policy.

In order to put the organization's quality policy into effect, top management needs to establish clearly defined quality objectives for which the organization can aim. The activities undertaken to reach these objectives do not need to be carried out personally by top management, but the responsibility is still theirs.

In setting quality objectives and any associated targets, timeframes for achieving the targets are usually established.

ISO 13485 calls for quality objectives not only for the quality management system but also for medical devices and related services [see 7.1 a)].

Quality objectives should be realistic and related to achievable and measurable outcomes, such as

— meeting the requirements (customer, regulatory and other) for medical devices and related services,
— reducing errors,
— reducing internal audit closure times,
— meeting planned schedules, and
— reducing customer complaint handling times.

Groups within the organization typically establish group objectives which follow from the overall organization objectives and relate to the specific activities of the group.

Quality objectives provide one of the inputs into quality management system planning (see 5.4.2).

5.4.2 Quality management system planning

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

5.4.2 Quality management system planning

Top management shall ensure that

a) the planning of the quality management system is carried out in order to meet the requirements given in 4.1, as well as the quality objectives, and

b) the integrity of the quality management system is maintained when changes to the quality management system are planned and implemented.

5.4.2.1 This subclause deals with planning related to the quality management system in general, in contrast to planning required in other sub-clauses related to individual elements of the quality management system.

In order that the quality management system can meet the requirements of ISO 13485:2003, 4.1, most of this planning will be at the initial stages of development and implementation of the quality management system. This planning can assist the organization to fulfil its quality objectives. Since quality objectives can, and indeed should, change over time, this planning is likely to be ongoing, and can assist the quality management system to continue to be effective during and after changes.

5.4.2.2 Typical inputs into quality management system planning include

— quality policy,
— quality objectives,
— regulatory requirements,
— quality management system standards, and
— changes required (e.g. as a result of management review and/or corrective and preventive action).

5.4.2.3 Typical outputs from quality management system planning that demonstrate meeting the requirements of ISO 13485:2003, 4.1, and the quality objectives include

— the quality manual and supporting documentation,
— gap analyses,
— actions plans, and
— results of action plans.

It should be noted that the term “quality plan” is more frequently used in conjunction with product realization planning (see 7.1) than in conjunction with quality management system planning.

5.5 Responsibility, authority and communication

5.5.1 Responsibility and authority

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

5.5 Responsibility, authority and communication

5.5.1 Responsibility and authority

Top management shall ensure that responsibilities and authorities are defined, documented and communicated within the organization.

Top management shall establish the interrelation of all personnel who manage, perform and verify work affecting quality, and shall ensure the independence and authority necessary to perform these tasks.

NOTE National or regional regulations might require the nomination of specific persons as responsible for activities related to monitoring experience from the post-production stage and reporting adverse events (see 8.2.1 and 8.5.1).

This requirement is usually achieved by means of documented position descriptions which include responsibilities and authorities, and organization charts which describe the interrelation of personnel. As this documentation forms part of the quality management system, it should be controlled (see 4.2.3). Responsibilities and authorities (including those for substitute personnel) may also be included in documented procedures. Some organizations “map” quality management system processes to show the linkages between processes and the responsibilities associated with activities to be performed.

For some activities (e.g. internal quality audits and design and development reviews), it is important that there be participation by individuals who have the required knowledge of, as well as organizational independence from, the subject being reviewed.

5.5.2 Management representative

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

5.5.2 Management representative

Top management shall appoint a member of management who, irrespective of other responsibilities, shall have responsibility and authority that includes

a) ensuring that processes needed for the quality management system are established, implemented and maintained,

b) reporting to top management on the performance of the quality management system and any need for improvement *(see 8.5)*, and

c) ensuring the promotion of awareness of regulatory and customer requirements throughout the organization.

NOTE The responsibility of a management representative can include liaison with external parties on matters relating to the quality management system.

Only one member of management is designated by top management as its management representative.

The functions of the management representative may be entirely related to quality management system activities or may be in conjunction with other functions and responsibilities within the organization.

If the management representative has other functions to perform, there should be no conflict of interest between the responsibilities for the other functions and those relating to the quality management system.

The management representative may delegate responsibilities for the quality management system to others in the organization.

5.5.3 Internal communication

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

5.5.3 Internal communication

Top management shall ensure that appropriate communication processes are established within the organization and that communication takes place regarding the effectiveness of the quality management system.

For a quality management system to work effectively, open and active communication is essential. Top management needs to establish the processes which encourage people within the organization to communicate at all levels.

Information related to the quality management system should be clear and understandable and adapted to the personnel meant to use it. Such information relates to top management's expectations regarding the quality management system performance, and information related to the implementation and effectiveness of the quality management system [e.g. results of internal quality audits (see 8.2.2), management reviews (see 5.6), external assessments and regulatory inspections].

Examples of communication methods include

— posting information on bulletin boards,

— holding meetings, or

— circulating information via e-mail or copies of documents.

Internal communication can be facilitated by personnel having familiarity with a variety of activities or functions within the organization. This familiarity can be enhanced, for example, by placing personnel from one function into another function as a part of their personal development.

5.6 Management review

5.6.1 General

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

5.6 Management review

5.6.1 General

Top management shall review the organization's quality management system, at planned intervals, to ensure its continuing suitability, adequacy and effectiveness. This review shall include assessing opportunities for improvement and the need for changes to the quality management system, including the quality policy and quality objectives.

Records from management reviews shall be maintained (see 4.2.4).

Top management should typically review the quality management system on a regular basis; an annual review could be acceptable for an established and effective quality management system. If changes are planned or being implemented, more frequent reviews are normally needed. Circumstances can arise that might require a change to the planned intervals for management reviews.

Top management and other participants in management reviews should be able to contribute and/or take action on any outcomes, if necessary (see 6.2.2).

The method of carrying out the review should suit the organization's business practices and could consist of

— formal face-to-face meetings with an agenda, minutes and formally identified action points,
— a variant of the above by teleconference or Internet links, or
— partial reviews at various levels within an organization, reporting to the top management who review the reports.

Management review records can be in any form which suits the organization, such as notes in a daybook, formal meeting minutes or notes, which can be produced, distributed and stored on paper or electronically. The identity of those taking part in the management review should be recorded.

Records of the management review should address all points of the review together with a description of any corrective or preventive action to be taken, the responsibility for such actions, the resources which might be needed to complete such actions and target dates for completion, if known.

5.6.2 Review input

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

5.6.2 Review input

The input to management review shall include information on

a) results of audits,

b) customer feedback,

c) process performance and product conformity,

d) status of preventive and corrective actions,

e) follow-up actions from previous management reviews,

f) changes that could affect the quality management system,

g) recommendations for improvement, and

h) new or revised regulatory requirements.

5.6.2.1 To ensure that the entire quality management system is covered, a consistent approach should be followed to ensure that the review covers the following:

— the continued suitability of the quality policy and objectives with respect to current needs;
— the functional effectiveness of the quality management system and its ability to meet objectives;
— analysis of process performance;
— quality problems and actions taken;
— customer feedback, including customer complaints;
— quality audit reports (both internal and external);
— areas for improvement/changes needed;
— outstanding actions from previous reviews;
— new or revised regulatory requirements.

5.6.2.2 Individual problems should be dealt with as they occur, without waiting for the next management review. The management review is intended to see if the same problems re-occur, if the action taken is appropriate, and if the customer and regulatory requirements are being met. However, the attention given to individual problems should be complemented by a review of the entirety of the quality management system in order to see if it is effective in meeting the organization's quality objectives.

Management reviews should not be devoted to repeatedly discussing relatively insignificant problems. Rather, the management review will be more useful if it carefully considers reports to obtain a clear overview and does not just review a list of small details. Top management should analyse and decide on significant trends.

5.6.2.3 The analysis of data as required by ISO 13485:2003, 8.4, should also be included in the management review. Other inputs which could be considered include

— training needs,
— supplier problems, and
— equipment needs, working environment and maintenance.

By identifying these issues, and depending on the outcome of the review, the organization can develop and revise its quality, strategic and business plans for future activities.

5.6.2.4 For example, as improvements are achieved and problems eliminated, the organization can review the nature and level of its inspection controls; are they still essential or can some savings be made by modifying them or adopting other controls, since the cause of the problem has been addressed? If the rate of complaints is found to be increasing, a decision should be taken to explore the reasons and to set appropriate objectives.

5.6.2.5 Reviews and audits are not the same. This is clearly indicated by the requirement that the results of audits are part of the management review.

5.6.2.6 For the purposes of management review and even for the purposes of design input (see ISO 13485:2003, 7.3.2), the "regulatory requirements" referred to are any laws published or otherwise enacted by any government that establish legal prerequisite conditions in order

— to place a medical device on the market,
— to make a medical device available for use,
— to install a medical device, or
— to implement a related service.

Such regulatory requirements are only applicable to an organization if they have entered or plan to enter a particular market or region where such requirements exist. A portion of the management review should be devoted to an understanding of the organization's regulatory compliance status as well as action plans to ensure such compliance is established and maintained.

5.6.3 Review output

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

5.6.3 Review output

The output from the management review shall include any decisions and actions related to

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

b) improvement of product related to customer requirements, and

c) resource needs.

Review output should include a statement regarding the effectiveness of the quality management system and its processes established for the achievement of the quality policy and objectives and the extent to which those objectives have been achieved based on the established respective criteria. One possible output from a management review might be a decision to revise the planned interval for such reviews (see 5.6.1).

Top management should reach decisions as a result of the review and provide the necessary resources for implementation.

6 Resource management

6.1 Provision of resources

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

6 Resource management

6.1 Provision of resources

The organization shall determine and provide the resources needed

a) to implement the quality management system and to maintain its effectiveness, and

b) to meet regulatory and customer requirements.

The provision and maintenance of adequate resources is a prerequisite to the effective initiation, maintenance and management of a quality management system and its processes. The nature and quantity of such resources will be determined by the processes involved.

Consideration should be given by the organization's management to the identification and provision of adequate resources needed to implement its quality policy and to achieve its objectives, as well as to satisfy customer requirements, inclusive of applicable regulatory requirements.

Resources can be people, infrastructure, work environment, information, suppliers and partners, natural resources and financial resources. Responsibility for the provision of resources resides with the organization regardless of whether associated processes are performed by the organization itself or are outsourced.

6.2 Human resources

6.2.1 General

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

6.2 Human resources

6.2.1 General

Personnel performing work affecting product quality shall be competent on the basis of appropriate education, training, skills and experience.

There is no specific guidance for this subclause beyond that given in 6.2.2.

6.2.2 Competence, awareness and training

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

6.2.2 Competence, awareness and training

The organization shall

a) determine the necessary competence for personnel performing work affecting product quality,

b) provide training or take other actions to satisfy these needs,

c) evaluate the effectiveness of the actions taken,

d) ensure that its personnel are aware of the relevance and importance of their activities and how they contribute to the achievement of the quality objectives, and

e) maintain appropriate records of education, training, skills and experience (see 4.2.4).

NOTE National or regional regulations might require the organization to establish documented procedures for identifying training needs.

The organization should consider the experience, qualifications, capabilities and abilities of personnel, especially in those areas that can affect the safety and effectiveness of the medical devices being manufactured and provided to customers. The level of training required prior to performing a process is usually determined by the level of competence required for the personnel intended to perform that process.

Work allocation and assignment of personnel (6.2.1), management review (5.6), corrective action (8.5.2), preventive action (8.5.3) and internal quality audit (8.2.2) are all likely to identify areas which could indicate a need for improving the competence of personnel and the means for such improvement, be it replacement of personnel, further education or training.

Personnel working within the quality management system require a certain level of competence or training (internal or external) before they can perform tasks properly or safely. It might be necessary for people to be further qualified or formally certified for some tasks (e.g. chemical or microbiological analysis, radiation activities, laser operation, welding or soldering). Organizations typically provide general education and training for full-time, part-time and contract personnel, tailored to the person's assignment. Such training and education should cover

— the nature of the business,
— the health, safety and environmental regulations,
— the quality policy and other internal policies,
— the function of the employee, and
— the procedures and instructions of relevance to them.

Training may be carried out in stages, and usually includes follow-up or refresher training, as needed and planned. Persons and functions who are assigned responsibility via the documented procedures of the quality management system should receive training on those procedures.

Organizations should evaluate the effectiveness of training or other actions taken in order to ensure competency. Evaluation can consist of polling the trained employee to assess whether he or she feels they have learned the required information, evaluating the work performance of the trained individual, and reviewing the trainer assessment of training effectiveness.

Organizations should maintain records which show what competencies an employee possesses. Records should also be kept of the training an employee has received and any results of that training. The records which show that the training course has been successfully completed and that competence has been achieved may be as simple or complex as necessary. At their simplest, the records may consist of 'sign-off' to confirm that personnel are now able to use certain equipment, carry out specific processes or follow certain procedures. The records should include a clear statement that a person is now deemed to be competent to do

the task for which they were trained. The effectiveness of any further education and training should be re-evaluated, after a period, to confirm that the competence achieved is continuing.

Training should be carried out by personnel with appropriate skills, qualifications and experience. Records are typically kept to document the qualifications of the personnel used as trainers.

6.3 Infrastructure

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

6.3 Infrastructure

The organization shall determine, provide and maintain the infrastructure needed to achieve conformity to product requirements. Infrastructure includes, as applicable

a) buildings, workspace and associated utilities,

b) process equipment (both hardware and software), and

c) supporting services (such as transport or communication).

The organization shall establish documented requirements for maintenance activities, including their frequency, when such activities or lack thereof can affect product quality.

Records of such maintenance shall be maintained (see 4.2.4).

Manufacturing equipment should be designed, constructed, correctly installed and located to facilitate proper operation, maintenance, adjustment and cleaning.

The organization should ensure that, if applicable, any inherent limitations or allowable tolerances of production, measurement and test equipment are documented and are readily available to the operators.

Documented procedures should be available for the maintenance, cleaning and checking of all equipment used in production, and for the control of the work environment. The determination of the necessary adjustments and maintenance intervals should be established.

The maintenance schedule should normally be posted on or near the equipment, or should be readily available. Maintenance should be carried out on schedule.

The organization should ensure that the buildings utilized are of suitable design and contain adequate space to facilitate cleaning, maintenance and other necessary operations. The premises should be laid out in such a way, and with sufficient allocation of space, to facilitate orderly handling and to prevent mixing between incoming material, in-process batches, material scrapped, re-worked, modified or repaired, any other nonconforming material, finished devices, manufacturing equipment, inspection aids, documents and drawings.

6.4 Work environment

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

6.4 Work environment

The organization shall determine and manage the work environment needed to achieve conformity to product requirements.

The following requirements shall apply.

a) The organization shall establish documented requirements for health, cleanliness and clothing of personnel if contact between such personnel and the product or work environment could adversely affect the quality of the product (see 7.5.1.2.1).

b) If work environment conditions can have an adverse effect on product quality, the organization shall establish documented requirements for the work environment conditions and documented procedures or work instructions to monitor and control these work environment conditions (see 7.5.1.2.1).

c) The organization shall ensure that all personnel who are required to work temporarily under special environmental conditions within the work environment are appropriately trained or supervised by a trained person [see 6.2.2 b)].

d) If appropriate, special arrangements shall be established and documented for the control of contaminated or potentially contaminated product in order to prevent contamination of other product, the work environment or personnel (see 7.5.3.1).

6.4.1 General

Product quality can be influenced by the production work environment. The most significant factors within the work environment that can affect product quality are

— the process equipment,
— the work environment established, and
— the personnel within that work environment.

6.4.2 Environmental control in product realization

6.4.2.1 The need for control of the work environment and the extent to which that control is exercised depend upon the type of the product being produced. To control the work environment means to direct, regulate, coordinate and monitor activities and variables that affect the conditions such that the quality of the work environment is known. Qualified and quantified limits for the desired quality of the work environment should be established and may be used to describe the extent to which control capabilities are implemented. The extent of the control required will influence the type of facility construction, equipment, resources and documentation needed to establish, monitor and maintain the work environment. An environmental control system should be validated if the resulting output cannot be verified (see 7.5.2 and 7.5.2.1), and should be regularly inspected to verify that the system is functioning properly. Such systems and inspections should be documented.

NOTE Additional information regarding cleanrooms and associated environments is available in the various parts of ISO 14644.

6.4.2.2 Examples of situations in which the work environment can have an effect on product quality include medical devices which

— are to be supplied labelled sterile (this also includes medical devices labelled “pyrogen free”),
— are to be supplied non-sterile and are intended to be sterilized before use,
— have a limited shelf life,
— have special handling or storage requirements,
— are susceptible to electrostatic discharge (ESD) due to electronic microcircuits or imbedded software, and
— are affected in their use by microbiological and/or particulate cleanness or other environmental conditions.

6.4.2.3 During the manufacture of sterile product or product intended to be sterilized before use, or product for which viable or non-viable particulate contamination (including pyrogens) has significance in their manufacture or use, special consideration should be paid to microbial and particulate contamination levels. The organization should ensure that if the work environment could have an adverse effect on the fitness of product in use, this environment is controlled to limit contamination of product and to provide proper conditions for all operations performed. Such product should be produced and packaged in a qualified, controlled environment with established specifications. An exception to the need for a controlled environment during the entirety of manufacturing processes would be if contamination can be reduced to a known, consistent, controlled level by validated product cleaning, and maintained at this level by controlled packaging. However, even when a validated cleaning procedure is relied upon, a controlled environment might need to be established to contain the validated cleaning and packaging process.

6.4.2.4 There are various parameters, indicators and controls associated with the work environment. Some examples of these are

— temperature,
— humidity,
— airflow,
— air filtration,
— air ionization,
— pressure differentials,
— lighting (both spectral content and intensity),
— sound,
— vibration,
— cleanliness of work surfaces and process,
— water quality, and
— number of people in the work environment.

6.4.2.5 Each of the parameters, indicators and controls should be considered for evaluation to determine if lack of control could increase the risk posed by product when put into use; i.e. the need and extent of environmental control should be traceable through records of risk management activities for product. If the environmental conditions are of significance in its manufacturing processes, the organization should establish requirements for the work environment to which product is exposed. For some product it might also be necessary to ensure traceability to environmental exposure, such as records of continuous monitoring of environmental parameters even during times when product is not undergoing manufacturing processes (e.g. evenings or weekends).

6.4.3 Personnel

6.4.3.1 Any personnel, including those entering the area on a temporary or transient basis, who can come in contact with product or work environment, should be suitably clothed, clean and in good health if these factors could adversely affect the product. This is because individuals spread both microorganisms and particles, which constitute contamination risks.

Examples of persons who might enter the work environment are

— manufacturing personnel, their supervisors and managers,
— material handlers,
— manufacturing engineers,
— design and development engineers,
— quality control, quality assurance, quality engineering personnel,
— suppliers of any material or service (including cleaning services),
— persons responsible for process equipment maintenance,
— customers,
— auditors, and
— visitors.

It is also important to remember that contact with product or work environment includes those times when product is not actually being produced, such as evenings, weekends and holidays.

6.4.3.2 Persons who have a medical condition that can adversely affect the product should be excluded from those operations, or prevented from entry into such areas until they have recovered. Personnel should be instructed and encouraged to report such conditions to their supervisor. This is of particular importance in the manufacture of medical devices which are to be supplied

— sterile,
— for sterilization before use, or
— for purposes in which microbiological cleanliness is of significance.

6.4.3.3 Special training and/or supervision should be provided to persons required to perform work under special environmental conditions (e.g. in a room where the temperature or humidity is controlled to such high or low levels that prolonged exposure might be hazardous, or a room or area where exhaust fans keep hazardous fumes at an acceptable level) or within a controlled environment. Any personnel, including temporary personnel such as those involved in manufacturing, maintenance, cleaning or repair, who have not been trained for performing specific tasks in a controlled environment, should not be allowed to enter unless supervised by an appropriately trained person.

6.4.4 Contaminated or potentially contaminated product

Examples of aspects to consider for special arrangements designed to prevent cross-contamination of product, work environment or personnel, are

— identification of the product, and

— handling, cleaning, and decontamination procedures for product, work surfaces, or personnel which have been or might have been contaminated.

7 Product realization

7.1 Planning of product realization

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

7 Product realization

7.1 Planning of product realization

The organization shall plan and develop the processes needed for product realization. Planning of product realization shall be consistent with the requirements of the other processes of the quality management system (see 4.1).

In planning product realization, the organization shall determine the following, as appropriate:

a) quality objectives and requirements for the product;

b) the need to establish processes, documents, and provide resources specific to the product;

c) required verification, validation, monitoring, inspection and test activities specific to the product and the criteria for product acceptance;

d) records needed to provide evidence that the realization processes and resulting product meet requirements (see 4.2.4).

The output of this planning shall be in a form suitable for the organization's method of operations.

The organization shall establish documented requirements for risk management throughout product realization. Records arising from risk management shall be maintained (see 4.2.4).

NOTE 1 A document specifying the processes of the quality management system (including the product realization processes) and the resources to be applied to a specific product, project or contract, can be referred to as a quality plan.

NOTE 2 The organization may also apply the requirements given in 7.3 to the development of product realization processes.

NOTE 3 See ISO 14971 for guidance related to risk management.

7.1.1 General

7.1.1.1 "Product realization" is the term used in ISO 13485 to describe the processes starting with planning and proceeding through

- determination of customer requirements and customer communication (ISO 13485:2003, 7.2),
- design and development (ISO 13485:2003, 7.3),
- purchasing (ISO 13485:2003, 7.4),
- production and servicing (ISO 13485:2003, 7.5),
- control of monitoring and measuring devices (of ISO 13485:2003, 7.6),

and including the delivery of the medical device.

Product realization also includes certain post-delivery activities such as customer service, spare parts supply and technical support.

7.1.1.2 Organizations whose quality management systems exclude design and development control (ISO 13485:2003, 7.3) are still required to comply with the product verification and validation requirements as specified in ISO 13485:2003, 7.1, dealing with product realization. In such organizations, the controls included in 7.3 should be considered for all changes made to the product. Such changes will require objective evidence (e.g. product verifications and validations, inspection and test specifications, revised procedures) of the results of the activities described in ISO 134857:2003, 7.3.

Note 1 in ISO 13485:2003, 7.1, is consistent with the definition of "quality plan" in ISO 9000 as being related to the planning for product realization.

NOTE Additional information regarding quality plans is available in ISO 10005.

7.1.1.3 In planning for product realization, the organization should consider the scope of its quality management system (see 1.2). If the organization has used a regulatory approach which allows exclusion of design and development control from the scope of quality management system, the design information related to necessary verification and validation may be part of, or referenced within, the records of planning product realization. This information may be contained or referenced in a file (see Annex A, section A).

7.1.1.4 ISO 13485:2003, 7.1, lists several needs or requirements relating to product realization which are to be considered "as appropriate." However, ISO 13485:2003, 1.2, also states that when a requirement is qualified by this phrase, it is considered to be appropriate *unless* the organization can document justification otherwise. A requirement should always be considered "appropriate" if it is necessary for the product to meet specified requirements, or for the organization to carry out corrective action.

A requirement need not be stated in order to be appropriate to an organization; applicable regulatory requirements in the markets for which an organization's medical devices are destined are also considered requirements.

7.1.1.5 Some examples of such requirements which are typically associated with medical devices include

- quality objectives and product requirements,
- established processes, documents and required resources specific to the product,
- required verification, validation, monitoring, measurement, inspection and test activities specific to the product, and
- records needed to provide evidence that the realization processes and resulting product meet requirements (see 4.2.4).

7.1.1.6 The organization's procedures should ensure the objectivity of the inspection and test results, if inspection and testing is carried out by production personnel.

The resultant records referred to in ISO 13485:2003, 4.2.4, 7.1 d), 7.1 (Note 1) and 7.3.3 are sometimes referred to by different terms (see Annex A, section C).

7.1.2 Risk management

ISO 13485:2003, 7.1, requires the establishment of documented requirements for risk management activities throughout the product realization, and that records of the same be maintained. The key elements of such risk management include risk assessment (made up of risk analysis and risk evaluation) and risk control. Special attention should be paid to the word “throughout.” The intent of ISO 13485 in using this term is that all processes within ISO 13485:2003, Clause 7, should be considered as to how they provide input to, or benefit from the results of, risk management activities.

To make risk management activities complete, information from the post-production phase (e.g. feedback, see 8.2.1, or customer complaints, see 8.5.1) should be considered and included in a risk management file.

The results of risk management activities influence the organization’s product realization processes by, for example

- helping to determine the nature and extent of purchasing controls,
- influencing supplier approval activities,
- providing important design inputs,
- serving as criteria for evaluating design outputs,
- establishing the need for design change, and
- helping to determine production and process control requirements, and monitoring and measurement devices controls, as well as acceptance activities.

It is also important to note that the output of risk management activities can influence decisions and activities outside of the area of product realization, ISO 13485:2003, Clause 7. For example, management review decisions, personnel training, infrastructure, monitoring and measurement, handling of nonconforming product, and corrective and preventive actions can be significantly influenced by information derived from the output of risk management activities.

Additional information on how to establish a risk management process over the life cycle of the medical device can be found in ISO 14971.

7.1.3 Lifetime of the medical device

Decisions related to product lifetime can be made, in part, to control identified residual risks that can increase to unacceptable levels as the period of use of a medical device is extended.

Organizations are required by ISO 13485 to define the lifetime of the medical device for document and record control purposes (see 4.2.3 and 4.2.4). Medical device lifetime may be based on technical, legal, commercial or other considerations.

The basis of the defined lifetime of the medical device should be documented. To assist in determining the lifetime of the medical device, the rationale for the determination should be recorded and may involve consideration of the following:

a) shelf life of the medical device;

b) expiry date for medical devices or components which are subject to degradation over time;

c) number of cycles or periods of use of the medical device, based on life testing of the medical device;

d) anticipated material degradation;

e) stability of packaging material;

f) for implantable devices, the residual risk that results from the entire period of residence of the device inside the patient’s body;

g) for sterile medical devices, the ability to maintain sterility;

h) organization’s ability/willingness or contractual or regulatory obligation to support service;

i) spare parts cost and availability;

j) legal considerations including liability.

7.2 Customer-related processes

7.2.1 Determination of requirements related to the product

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7.2 Customer-related processes

7.2.1 Determination of requirements related to the product

The organization shall determine

a) requirements specified by the customer, including the requirements for delivery and post-delivery activities,

b) requirements not stated by the customer but necessary for specified or intended use, where known,

c) statutory and regulatory requirements related to the product, and

d) any additional requirements determined by the organization.

7.2.1.1 This subclause of ISO 13485 deals with customer-related processes associated with

- design input/output for new product development,
- customer expectations for the delivery of existing product, and
- customer feedback and communications relative to orders placed or product delivered.

7.2.1.2 This subclause focuses mainly on the products and services which the organization is going to provide to its customers. Product and service requirements can cover additional factors, such as

- regulatory or legal requirements of the countries or regions where the product is placed on the market,
- intended use,
- performance expectations,
- design related factors,
- delivery schedules, and
- unspecified customer expectations.

7.2.1.3 For medical devices, an understanding of both stated intended use and any reasonably foreseeable misuse, and indications for use, should be documented. This is of particular importance in the development of new products. The guidance in 7.3 will help the organization to determine if requirements for design and development apply.

The stated intended use and any reasonably foreseeable misuse should also be included in risk management activities (see 7.1 above regarding risk management activities).

7.2.1.4 All parts of a customer's order, contract and expectations need to be understood and reviewed to ensure that they can be met; these activities have previously been referred to as "contract review".

If there are any requirements that are not covered by the organization's usual work processes, particularly any requirements which are felt to be unrealistic or unachievable, the organization might need to discuss them with the customer.

7.2.1.5 The manner in which a customer provides the order might vary in form and could be, for example, a written order, a verbal agreement, a telephone order or an order made via an e-business web address.

One of the most common problems encountered is misunderstanding what was ordered or how it is to be used. Good communication between the organization and the customer is essential to resolve any

misunderstandings and, if possible, the organization should develop communication processes to identify and resolve any such misunderstandings.

Written or electronic orders, such as those received by mail, facsimile, email or the Internet, can provide a permanent record of the order details. If telephone and direct computer link orders are received, special provisions need to be made to record and confirm the order. The organization will need methods of handling such orders.

Two examples follow.

a) One approach to telephone orders is to provide a pad (or even pre-printed forms) for the order receiver to record the details of the order and to read it back to the customer, asking for confirmation.

b) Another approach is to enter the details directly into a computer system, again seeking confirmation, which could be verbal, by fax or by e-mail, with the information being saved directly to disk or printed out in hard copy form.

7.2.1.6 At the time the order is received, an appropriate person in the organization should review the order to ensure that the requirements listed in 7.2.2 can be met. In a small business, the appropriate person is frequently the manager.

The organization also needs to determine if there are any design requirements in the order and whether the requirements of 7.3 will apply. The guidance in 7.3 will help the organization to determine if a requirement for design and development apply.

The record of the review may be as simple as a notation on the order that it can be fulfilled, together with the signature of the reviewer and the date. If a more complex review is called for, the organization can determine how the review is recorded but the record should include at least the main details.

7.2.1.7 If the organization tenders for a contract or submits a proposal to a potential customer, the same approach should be taken. Any differences between the organization's offer and the requirements of the customer should be resolved. The organization should make sure that the agreed requirements are appropriately recorded.

If changes to an order or tender, or both, arise for whatever reason, the changes should be reviewed and agreed to in the same manner as the original order or tender. If the changes are accepted, it is essential that everyone in the organization who is affected by the changes is informed.

The relevant documents affected by these changes should be amended as well.

7.2.2 Review of requirements related to the product

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7.2.2 Review of requirements related to the product

The organization shall review the requirements related to the product. This review shall be conducted prior to the organization's commitment to supply a product to the customer (e.g. submission of tenders, acceptance of contracts or orders, acceptance of changes to contracts or orders) and shall ensure that

a) product requirements are defined and documented,

b) contract or order requirements differing from those previously expressed are resolved, and

c) the organization has the ability to meet the defined requirements.

Records of the results of the review and actions arising from the review shall be maintained (see 4.2.4).

Where the customer provides no documented statement of requirement, the customer requirements shall be confirmed by the organization before acceptance.

Where product requirements are changed, the organization shall ensure that relevant documents are amended and that relevant personnel are made aware of the changed requirements.

NOTE In some situations, such as internet sales, a formal review is impractical for each order. Instead the review can cover relevant product information such as catalogues or advertising material.

There is no specific medical device guidance beyond the general guidance given in 5.2 and 7.2.1.

7.2.3 Customer communication

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7.2.3 Customer communication

The organization shall determine and implement effective arrangements for communicating with customers in relation to

a) product information,

b) enquiries, contracts or order handling, including amendments,

c) customer feedback, including customer complaints *(see 8.2.1), and*

d) advisory notices (see 8.5.1).

In addition to stating the need to implement effective means for customer communication and feedback, ISO 13485:2003, 7.2.3, addresses customer complaints and advisory notices. See also applicable guidance provided in 7.2.1.

Advisory notices are addressed in ISO 13485:2003, 8.5.1, and additional guidance is provided for that subclause.

Advisory notices and customer complaints are defined in ISO 13485:2003, 3.3 and 3.4. Medical device regulatory schemes existing in today's world markets have subtle differences in terms, definitions and reporting requirements with regard to complaints, corrective actions and preventive actions. These schemes also have differing responsibilities for the organization, regulators, customers and third parties. It is very important that an organization make provisions to understand and comply with the regulatory schemes of each of the markets intended for its product. Customer communication can also have an effect on the ability of an organization to establish or verify traceability to an end user. This is particularly important for implantable medical devices for which there are specific traceability requirements (see 7.5.3.2.2) or other high-risk devices which might have tracking requirements put upon them by regulators.

7.3 Design and development

7.3.1 Design and development planning

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7.3 Design and development

7.3.1 Design and development planning

The organization shall establish documented procedures for design and development.

The organization shall plan and control the design and development of product.

During the design and development planning, the organization shall determine

a) the design and development stages,

b) the review, verification, validation and design transfer activities (see Note) that are appropriate at each design and development stage, and

c) the responsibilities and authorities for design and development.

The organization shall manage the interfaces between different groups involved in design and development to ensure effective communication and clear assignment of responsibility.

Planning output shall be documented, and updated as appropriate, as the design and development progresses (see 4.2.3).

NOTE Design transfer activities during the design and development process ensure that design and development outputs are verified as suitable for manufacturing before becoming final production specifications.

Guidance given in 5.4.2 and 7.1 of this Technical Report also applies.

Design and development planning is needed to ensure that the design process is appropriately controlled and that the quality objectives of the medical device are met. The plans should be consistent with the organization's quality management system provisions for quality planning and product realization requirements, including design and development controls.

The following elements would typically be addressed in the design and development plan or plans:

a) a description of the goals and objectives of the design and development programme; i.e., what is to be developed;

b) the markets intended (at least a broad preliminary assessment) for the product;

c) an identification of quality management system documents, procedures and resulting records applicable to controls for design and development;

d) an identification of organizational responsibilities with respect to assuring quality during the design and development phase, to include interface with any suppliers;

e) the identification of the major tasks to be undertaken (or stages/phases of the design and development control), expected outputs (deliverables and records) resulting from each task or stage/phase, and individual or organizational responsibilities (staff and resources) for completing each task or stage/phase;

f) the schedule of major tasks or stages/phases to meet overall programme time constraints;

g) the identification of appropriate existing and anticipated measurement and monitoring devices for the development of product specifications, verification, validation and production related activities (see also guidance given in 7.6 of this Technical Report);

h) the selection of reviewers, the composition of review teams, and procedures to be followed by reviewers appropriate to each task or stage/phase;

i) the risk management activities;

j) the selection of the suppliers.

Planning enables management to exercise control over the design and development process while providing for predictable timeframes and records. Planning accomplishes all this by clearly communicating policies, procedures and goals to members of the design and development team. It also provides a basis for measuring conformance to quality management system objectives.

Design and development activities should be specified at the level of detail necessary to carry out the design process. The extent of design and development planning is dependent on the size of the developing organization and the complexity of the product to be developed. Some organizations have documented policies and procedures which apply to all design and development activities. For each specific development programme, such organizations can also prepare a plan which spells out the project-dependent elements in

detail, and incorporates the general policies and procedures by reference. Other organizations develop a comprehensive design and development plan that is specifically tailored to each individual project.

The inter-relationship of design control and process development can, for some technologies, be very closely related. For others, the relationship is remote. The product should be designed robustly enough to withstand variations in the manufacturing process, and the manufacturing process should be capable and stable to assure continued safe products that perform adequately. Often this results in very interactive product development and process development activities.

The transfer of a design to production should occur after review and approval of specifications and procedures. Planning of product realization should take into account the production (producibility, parts/materials availability, production equipment needs, operator training, etc.) and possible conformity assessment requirements (procedures, methods, equipment). This planning should encompass all of the specifications to ensure that each specification is correctly incorporated into the specific processes or procedures associated with product realization. Failure to do so can lead to production delays and nonconforming product for reasons such as purchase of incorrect raw material grades or quantities, inappropriate manufacturing methods, unvalidated processes, unclear work instructions, incorrect labelling, etc. The adequacy of specifications, methods and procedures can be demonstrated through process validation (see 7.5.2).

7.3.2 Design and development inputs

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7.3.2 Design and development inputs

Inputs relating to product requirements shall be determined and records maintained (see 4.2.4). These inputs shall include

a) functional, performance and safety requirements, according to the intended use,

b) applicable statutory and regulatory requirements,

c) where applicable, information derived from previous similar designs,

d) other requirements essential for design and development, and

e) output(s) of risk management (see 7.1).

These inputs shall be reviewed for adequacy and approved.

Requirements shall be complete, unambiguous and not in conflict with each other.

7.3.2.1 General

The guidance given in 7.2.1 of this Technical Report also applies.

Design and development inputs are typically in the form of product requirement specifications and/or product description with specifications relating to intended use, configuration, composition, incorporated elements, and other design features. The design and development inputs should be specified to the level necessary to permit the design activities to be carried out effectively and to provide a consistent basis for design decisions, design verifications and design validation.

The design and development inputs should describe all requirements to the greatest possible extent. Details agreed upon between customer and organization as to the customer, statutory, and regulatory requirements to be met should be included. The record of the design inputs should also include the resolutions of any incomplete, ambiguous or conflicting requirements which have been identified through feedback during other design and development activities. The design and development inputs should identify design criteria, materials, and processes requiring development and analysis, including prototype testing to verify their

feasibility and adequacy. Design inputs should be prepared in a way that facilitates periodic updates. If design inputs have to be changed, a record should indicate what caused the input to be changed, who is responsible for the change, and who needs to be notified. Design and development inputs prepared in this way serve as the definitive up-to-date reference document as the design progresses to completion.

Examples of design and development inputs which are typically defined, reviewed, approved and recorded by the organization, include

— intended use of the device,
— indications for use of the device,
— performance claims,
— performance requirements (including normal use, storage, handling and maintenance),
— user and patient requirements,
— physical characteristics,
— human factors/usability requirements,
— safety and reliability requirements,
— toxicity and biocompatibility requirements,
— electromagnetic compatibility requirements,
— limits/tolerances,
— measurement and monitoring instruments to be used,
— risk management or risk reduction methods suggested by hazard/risk analysis,
— reportable adverse events (see 8.5.1)/complaints/failures for previous products,
— other historical data,
— documentation for previous designs,
— compatibility requirements with respect to accessories and auxiliary devices,
— compatibility requirements with respect to the environment of intended use,
— packaging and labelling (including considerations to deter foreseeable misuse),
— customer/user training requirements,
— regulatory and statutory requirements of intended markets,
— relevant voluntary standards (including industry standards, national, regional or international standards, “harmonized” and other consensus standards),
— manufacturing processes,
— sterility requirements,
— economic and cost aspects,
— lifetime of the medical device requirements, and
— need for servicing.

The design and development input documents should be updated and re-issued as necessary upon completion of design and development reviews. A record should be kept of all “agreed to” changes to the design and development input as it evolves during the design and development process.

The design transfer process (see 7.3.1) should flow more smoothly if, during the design and development input stage, consideration is given to subsequent production (producibility, parts/materials availability, production equipment needs, operator training etc.) and possible conformity assessment requirements (procedures, methods, equipment). Thus the need for process validation should be considered during design and development planning, and is a significant input to design and development.

7.3.2.2 Packaging

Design and development input activities should also address packaging requirements. The packaging material, the packaging process conditions and the anticipated storage and handling conditions during manufacturing, warehousing and distribution are typically considered.

The following should be considered, if applicable:

— compatibility with the device and packaging process;
— compatibility with the sterilization process;
— transportation hazard trials/shipping tests;
— microbial barrier properties of packaging materials for sterile devices;
— integrity of the primary container/package to prevent damage and to maintain sterility or cleanliness as required.

NOTE Additional information relating to packaging of terminally sterilized medical devices is available in ISO 11607.

7.3.2.3 Labelling

The content of labels may be specified in regulatory requirements, general standards and medical device standards. If the medical device is to be supplied to countries with different languages, and the language to be used on the labels has been specified, it is advisable that the label translations be checked by a person with adequate expertise in the specified language and who has technical knowledge of medical devices.

The use of international symbols (if applicable) can reduce translation problems, however such symbols should only be used if they have the appropriate regulatory acceptance in the countries where the medical device has been placed on the market. Product liability aspects might also need to be considered before deciding on the use of symbols.

NOTE Additional information relating to the use of symbols for medical devices is available in ISO 15223 and EN 980.

7.3.3 Design and development outputs

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7.3.3 Design and development outputs

The outputs of design and development shall be provided in a form that enables verification against the design and development input and shall be approved prior to release.

Design and development outputs shall

a) meet the input requirements for design and development,

b) provide appropriate information for purchasing, production and for service provision,

c) contain or reference product acceptance criteria, and

d) specify the characteristics of the product that are essential for its safe and proper use.

Records of the design and development outputs shall be maintained (see 4.2.4).

NOTE Records of design and development outputs can include specifications, manufacturing procedures, engineering drawings, and engineering or research logbooks.

Design and development outputs are the product requirements used for purchasing, production, inspection and testing, installation, servicing and service provision.

Throughout the design and development process, the requirements contained in the design description are translated by the organization into outputs. Design and development outputs should be recorded in terms which can be verified and validated against design and development input requirements and need to contain, or make reference to, acceptance criteria.

Design and development outputs can include

— specifications for raw materials, component parts and sub-assemblies,
— drawings and parts list,
— customer training materials,
— process and materials specifications,
— finished medical devices,
— product and process software,
— quality assurance procedures (including acceptance criteria),
— manufacturing and inspection procedures,
— work environment requirements needed for the device,
— packaging and labelling specifications,
— identification and traceability requirements (including procedures, if necessary),
— installation and servicing procedures and materials,
— documentation for submission to the regulatory authorities where the medical devices will be marketed, if appropriate, and
— a record/file to demonstrate that each design was developed and verified in accordance with the design and development planning.

7.3.4 Design and development review

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

7.3.4 Design and development review

At suitable stages, systematic reviews of design and development shall be performed in accordance with planned arrangements (see 7.3.1)

a) to evaluate the ability of the results of design and development to meet requirements, and

b) to identify any problems and propose necessary actions.

Participants in such reviews shall include representatives of functions concerned with the design and development stage(s) being reviewed, as well as other specialist personnel (see 5.5.1 and 6.2.1).

Records of the results of the reviews and any necessary actions shall be maintained (see 4.2.4).

7.3.4.1 General

The timing of design and development reviews will be influenced by the maturity and complexity of the product being designed and developed.

At the defined stages of design and development (see 7.3.1), reviews can consider topics such as the following, as appropriate.

a) Do designs satisfy specified requirements for the product?
b) Is the input adequate to perform the design and development tasks?
c) Are product design and processing capabilities compatible?
d) Have safety considerations been addressed?
e) What is the potential impact of the product on the environment?
f) Do designs meet functional and operational requirements, for example, performance and dependability objectives?

g) Have appropriate materials been selected?

h) Have appropriate facilities been selected?

i) Is there adequate compatibility of materials, components and/or service elements?

j) Is the design satisfactory for all anticipated environmental and load conditions?

k) Are components or service elements standardized and do they provide for reliability, availability and maintainability?

l) Is there a provision in tolerances, and/or configuration, for interchangeability and replacement?

m) Are plans for implementing the design technically feasible (e.g. purchasing, production, installation, inspection and testing)?

n) 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?

o) Have the inputs to such software, and the outputs, been appropriately verified and documented?

p) Are the assumptions made during the design and development processes valid?

q) Are the results of model or prototype testing considered?

r) Have risk management activities been carried out and, if so, are they adequate?

s) Is the labelling adequate?

t) Will the design reasonably accomplish the medical use intended?

u) Is the packaging adequate, particularly for sterile devices?

v) Is the sterilization process adequate?

w) Is the device compatible with the sterilization method?

x) How are changes and their effects controlled during the design and development process?

y) Are problems being identified and corrected?

z) Is the product meeting verification and validation goals?

aa) What is the progress of the planned design and development process?

bb) Are there opportunities for design and development process improvement?

7.3.4.2 Other specialist personnel

The requirement in ISO 13485 for “other specialist personnel”, in addition to those representing organizational functions who have direct concerns regarding the design and development being reviewed, obliges the organization to include person(s) who are capable of understanding the design and development information being reviewed.

Some national and regional regulatory bodies might require an individual(s) who does not have direct responsibility for the design and development stage being reviewed, as well as “other specialist personnel.”

7.3.5 Design and development verification

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7.3.5 Design and development verification

Verification shall be performed in accordance with planned arrangements (see 7.3.1) to ensure that the design and development outputs have met the design and development input requirements. Records of the results of the verification and any necessary actions shall be maintained (see 4.2.4).

Design and development verification is necessary to ensure that the design and development outputs conform to specified requirements (design and development inputs).

Verification activities can include, if appropriate,

— tests (e.g. bench tests, laboratory analyses),
— alternative calculations,
— comparison with proven design,
— inspections, and
— document reviews (e.g. specifications, drawings, plans, reports).

If tests and demonstrations are employed at any stage of the design and development verification, the safety and performance of the product should be verified under conditions which are representative of the full range of circumstances of actual use.

When alternative calculations or comparison with a proven design are employed as forms of design and development verification, the appropriateness of the alternative calculation method, and/or proven design, should be reviewed. This review should confirm that the alternative calculations or comparison with a proven design are actually scientifically valid methods of design verification for the design under consideration.

7.3.6 Design and development validation

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

7.3.6 Design and development validation

Design and development validation shall be performed in accordance with planned arrangements (see 7.3.1) to ensure that the resulting product is capable of meeting the requirements for the specified application or intended use. Validation shall be completed prior to the delivery or implementation of the product (see Note 1).

Records of the results of validation and any necessary actions shall be maintained (see 4.2.4).

As part of design and development validation, the organization shall perform clinical evaluations and/or evaluation of performance of the medical device, as required by national or regional regulations (see Note 2).

NOTE 1 If a medical device can only be validated following assembly and installation at point of use, delivery is not considered to be complete until the product has been formally transferred to the customer.

NOTE 2 Provision of the medical device for purposes of clinical evaluations and/or evaluation of performance is not considered to be delivery.

After successful design and development verification, a design and development validation should be performed under actual or simulated conditions for the use of the final medical device. However, validation might need to be performed at earlier stages during product development if there are features which are not possible or practical to validate at the final stage.

Design and development validation goes beyond the technical issues of verifying that the design and development outputs meet the design and development inputs, and is intended to ensure that the medical device meets user requirements and the intended use in the hands of the intended user. This involves consideration of the knowledge and capabilities of the intended user, the operating instructions, compatibility with other systems, the environment in which it will be used, and any restriction on the use of the product.

Some national or regional regulations require clinical evaluations as part of design and development validation. Clinical evaluation can include one or more of the following to ensure that the medical device performs as intended:

— a critical analysis of relevant scientific literature in relation to the medical device being designed and developed;
— historical evidence that similar designs and/or materials are clinically safe;
— a clinical investigation (or trial).

For additional guidance regarding clinical evaluations, see ISO 14155-1.

The medical devices employed for validations should be produced under the conditions specified as “final” for the product (e.g. initial production units recognizing that production equipment or processes might change between production for validation and production for commercial distribution). The validation should be conducted under actual or simulated use conditions; this can involve clinical investigations in accordance with national or regional regulations. These points are important as many validations can be irrelevant or misleading if not done using products representative of the final product and process conditions, or not done under conditions of actual or simulated use.

For medical devices used for *in vitro* diagnosis, evaluation of performance consists of *in vitro* studies undertaken to ensure that the medical device performs as intended in laboratories for medical analyses or other suitable environments outside of the organization’s premises.

7.3.7 Control of design and development changes

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7.3.7 Control of design and development changes

Design and development changes shall be identified and records maintained. The changes shall be reviewed, verified and validated, as appropriate, and approved before implementation. The review of design and development changes shall include evaluation of the effect of the changes on constituent parts and product already delivered.

Records of the results of the review of changes and any necessary actions shall be maintained (see 4.2.4).

7.3.7.1 Product design can be changed or modified for a number of reasons, and the change can happen during or after the design and development phase, for example,

— changes required following design and development review (see 7.3.4), design and development verification (see 7.3.5) or design and development validation (see 7.3.6),
— omissions or errors (e.g. in calculation, material selection) during the design phase which have been identified afterwards,
— difficulties in manufacturing, installation and/or servicing found after the design and development phases,
— change requests from engineering,
— change required in response to risk management activities,
— changes requested by the customer or supplier,
— changes required for corrective or preventive action (see 8.5),
— changes needed to safety, regulatory, or other requirements, and
— improvements to the function or performance of product.

7.3.7.2 Improving one characteristic might have an unforeseen adverse influence on another. For example, the following should be considered in order to help in avoiding this situation.

a) Will the product still conform to the product requirements?
b) Will the product still conform to the product specifications?
c) Will the intended use be affected?
d) Will the existing risk assessment be adversely affected?
e) Will different components of the product or system be affected?
f) Will there be a need for further interface design (e.g., physical contact with other components in a product or system)?
g) Will the change create problems in manufacture, installation or use?
h) Will the design still be verifiable?
i) Will the change affect the regulatory status of the product?

7.4 Purchasing

7.4.1 Purchasing process

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

7.4 Purchasing

7.4.1 Purchasing process

The organization shall establish documented procedures to ensure that purchased product conforms to specified purchase requirements.

The type and extent of control applied to the supplier and the purchased product shall be dependent upon the effect of the purchased product on subsequent product realization or the final product.

The organization shall evaluate and select suppliers based on their ability to supply product in accordance with the organization's requirements. Criteria for selection, evaluation and re-evaluation shall be established. Records of the results of evaluations and any necessary actions arising from the evaluation shall be maintained (see 4.2.4).

7.4.1.1 The control of suppliers is a process consisting of establishing criteria, evaluating, selecting and ongoing monitoring. The application of the process depend on the nature and risk associated with the product or service, including outsourced processes (see 4.1), being purchased or otherwise received.

For instance, the process of evaluation and selection, and control might differ when applied to

- an original equipment manufacturer (OEM),
- a logistics service,
- an information technology service,
- a contract sterilizer,
- a supplier of material to the organization's specifications,
- a design and development service,
- a clinical evaluator,
- a consultant,
- a testing and calibration service, or
- a supplier of off-the-shelf components.

7.4.1.2 The evaluation of a supplier can include

- testing of samples of product or service to be provided,
- review of third-party evaluation reports,
- review of historical data, such as records of past performance,
- certification by a third party of the supplier's quality management system, or
- auditing of the supplier's quality management system by the organization.

7.4.1.3 Regardless of the method of evaluation, the organization is required to demonstrate that it has control over the purchased product or outsourced process by possessing objective evidence that the selection of a supplier was based on appraisals appropriate to the product or service being purchased and the supplier's ability to enable the organization to meet the customer and regulatory requirements associated with the medical device.

When monitoring the performance of suppliers, the organization should consider a supplier's third-party certification status, compliance trends and conformance history. The organization should define the frequency

of supplier performance monitoring. The organization should also include in the supplier monitoring activities the need for their registration body to visit the supplier for the purpose of obtaining objective evidence that outsourced processes are under control, and that the products or services conform to the organization's specified requirements which might include customer and regulatory requirements.

7.4.2 Purchasing information

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

7.4.2 Purchasing information

Purchasing information shall describe the product to be purchased, including where appropriate

a) requirements for approval of product, procedures, processes and equipment,

b) requirements for qualification of personnel, and

c) quality management system requirements.

The organization shall ensure the adequacy of specified purchase requirements prior to their communication to the supplier.

To the extent required for traceability given in 7.5.3.2, the organization shall maintain relevant purchasing information, i.e. documents (see 4.2.3) and records (see 4.2.4).

The organization's purchasing information (including the requirement for supplier records) should define appropriate requirements and communicate them to the supplier to ensure the quality of the purchased product or service, including outsourced processes.

Typically, these requirements are formalized in an agreement between the organization and the supplier.

Examples of purchasing information include

- technical information and specifications,
- test and acceptance requirements,
- quality requirements for products, services and outsourced processes,
- environmental requirements,
- regulatory requirements,
- certification requirements,
- requirements for specific equipment,
- special instructions (e.g. traceability records), and
- conditions for the review and updating of the agreement.

The degree or specificity of the purchasing information should be dependent upon the effect of the purchased product or service on the medical device (see 7.4.1), for example, as determined during risk management activities.

For example, when cleaning operations in environmentally controlled areas are carried out by a supplier, a written contract specifying the limits of responsibility of the organization and the supplier should be considered in order that product is not contaminated by cleaning agents or personnel, or that areas are left uncleaned due to oversight. This contract should include details of the documented cleaning procedure and specify the training to be given to cleaning staff.

Specifications should define any special conditions required for storage or transport of the purchased product that could significantly affect the safety, effectiveness, or intended use of the medical device.

The organization may make reference to applicable technical information such as national or international standards and test methods. Another approach is for information to be clearly and precisely stated to the supplier on the purchase order. Responsibility for reviewing and approving the purchasing data should be clearly assigned to appropriate personnel to prevent the purchase of incorrect materials. The revision status of documents referenced in the purchasing data should be identified to ensure that the correct versions of materials are purchased.

Depending on an organization's traceability requirements (see 7.5.3.2 of this Technical Report), purchasing documents and records might need to be identified and retained; i.e. when evaluating the traceability requirements, consideration should be given to what purchasing information and records may also need to be retained to facilitate traceability. For example, if it is important to know to what specification revision a purchased part was ordered, then this information should be kept as part of the purchasing documents or records.

7.4.3 Verification of purchased product

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

7.4.3 Verification of purchased product

The organization shall establish and implement the inspection or other activities necessary for ensuring that purchased product meets specified purchase requirements.

Where the organization or its customer intends to perform verification at the supplier's premises, the organization shall state the intended verification arrangements and method of product release in the purchasing information.

Records of the verification shall be maintained (see 4.2.4).

Inspection on receipt is one method for the organization to verify that purchased product delivered to the organization's facilities fulfils specified requirements. If the purchased product is claimed to conform to the supplier's specification, the organization should check that the product meets the agreed specification. This check can be accomplished by various approaches, such as certification of suppliers, certificates of conformance, skip lot testing, 100 % or sampling inspection, as determined by the requirements of the organization's quality management system.

The organization's documented procedures (see ISO 13485:2003, 7.4.1) should specify the method of verifying that shipments received are in accordance with specifications, are complete, have proper identity, and are undamaged. The procedures should also include provisions for verifying that incoming product is accompanied by the required supporting documentation (e.g. certificates of conformity, acceptance test reports). Appropriate action in the event of nonconformities should be specified (see 8.3) so that the nonconformity can be dealt with in a consistent manner (including identification, segregation and documentation) and without undue delay. Analysis of previous receiving inspection data, in-plant rejection history or customer complaints will influence the organization's decisions regarding the amount of inspection required, and the need to reassess a supplier.

This subclause does not imply that incoming product has to be inspected and tested by the organization. Incoming inspection might not be required if the necessary confidence in the product can be obtained by other defined processes or procedures, particularly if the information given by a supplier is considered sufficient.

The organization's documented procedures should define who is authorized to allow incoming product to be used before conformity to specified requirements for quality is demonstrated. Such a procedure ensures that decisions are made at a level in the organization that is aware of the possible impact on product realization if the incoming products do not subsequently meet the requirements. The organization's procedures should also define how such product will be positively identified and controlled in the event that subsequent inspection finds nonconformities, in order to facilitate corrective action.

These requirements apply to all products received from outside the organization's quality management system, whether payment occurs or not.

7.5 Production and service provision

7.5.1 Control of production and service provision

7.5.1.1 General requirements

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

7.5 Production and service provision

7.5.1 Control of production and service provision

7.5.1.1 General requirements

The organization shall plan and carry out production and service provision under controlled conditions. Controlled conditions shall include, as applicable

a) the availability of information that describes the characteristics of the product,

b) the availability of documented procedures, documented requirements, work instructions, and reference materials and reference measurement procedures as necessary,

c) the use of suitable equipment,

d) the availability and use of monitoring and measuring devices,

e) the implementation of monitoring and measurement,

f) the implementation of release, delivery and post-delivery activities, and

g) the implementation of defined operations for labelling and packaging.

The organization shall establish and maintain a record (see 4.2.4) for each batch of medical devices that provides traceability to the extent specified in 7.5.3 and identifies the amount manufactured and amount approved for distribution. The batch record shall be verified and approved.

NOTE A batch can be a single medical device.

7.5.1.1.1 The generic guidance with respect to infrastructure given in 6.3 applies.

In considering which controlled conditions are applicable for a given process, an organization should consider the impact on quality or regulatory compliance. If, in the absence of the control, there is an adverse or potentially adverse affect on quality or regulatory compliance, then control is necessary. The amount of control and level of detail may be commensurate with the degree of criticality (e.g. based on the output of risk management activities) of the process in achieving the requirements for quality and the degree of training of product realization personnel.

Reference materials may be physical or visual, such as product examples indicating permissable colour variation, or visual such as photos of known non-conformities. Reference materials should be available at the point of use. An individual procedure could be in the form of a simple flowchart, or a processing sequence, combined with a checklist [see 4.2.1 d)].

Suitable equipment should be designed and selected so that process and product specifications are met. It should be verified that new and/or significantly modified equipment meets purchasing/design specifications and is capable of operating within its defined limits and the process operating limits.

7.5.1.1.2 The risk of labelling and packaging errors can be minimized by the introduction of appropriate controls such as

- segregation of packaging and labelling operations from other manufacturing (or other packaging and labelling) operations,
- avoidance of packaging and labelling product of similar appearance in close proximity,
- line identification,
- application of line clearance procedures,
- destruction of unused batch-coded materials on completion of packaging and labelling,
- use of roll-feed labels,
- use of a known number of labels and reconciliation of usage,
- on-line printing, including batch coding,
- use of electronic code encoders/readers and label counters,
- use of labels designed to provide clear product differentiation,
- inspection of label content before use, and
- proper storage of labels in areas of restricted access.

7.5.1.1.3 Records that facilitate traceability and review of the manufacture of a batch of product, derived during the manufacture of that batch, should be contained in a batch record, and are frequently collated in a single file. Such files can be referred to as a "Device History Record", "Batch Manufacturing Record", "Lot History Record" or "Lot Record" (see Annex A, section C).

If it is not practical to include all the relevant documents in the batch record, then the record should list the titles of those documents and their location(s).

Batch records should be prepared from the currently approved versions of the specifications.

The forms that constitute the batch records should be designed and reproduced by an appropriate method to avoid clerical errors. A batch record should have a unique batch identification and relate to an individual manufacturing batch.

During manufacture, relevant information should be entered onto the batch record. Such information can include:

- the quantity of raw materials, components and intermediate products, and their batch number, if appropriate,
- the date of start and completion of different stages of production, including sterilization records if appropriate,
- the quantity of product manufactured,
- the signed results of all inspections and tests,
- the designation of the product line used, and
- any deviation from the manufacturing specifications.

7.5.1.2 Control of production and service provision – Specific requirements

7.5.1.2.1 Cleanliness of product and contamination control

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7.5.1.2 Control of production and service provision — Specific requirements

7.5.1.2.1 Cleanliness of product and contamination control

The organization shall establish documented requirements for cleanliness of product if

a) product is cleaned by the organization prior to sterilization and/or its use, or

b) product is supplied non-sterile to be subjected to a cleaning process prior to sterilization and/or its use, or

c) product is supplied to be used non-sterile and its cleanliness is of significance in use, or

d) process agents are to be removed from product during manufacture.

If product is cleaned in accordance with a) or b) above, the requirements contained in 6.4 a) and 6.4 b) do not apply prior to the cleaning process.

The organization is required to define the product cleanliness requirements. In order to achieve these requirements (including the removal of process agents, if these agents could reasonably be expected to have an adverse affect on product quality), the organization can establish documented procedures, work instructions, and reference materials and reference measurement procedures as necessary.

Process agents, also known as ancillary materials, manufacturing materials or auxiliary materials, are any materials or substances used in, or used to facilitate, a manufacturing process, such as cleaning agents, mould-release agents, lubricating oils, or other substances which are not intended to be included in the finished devices. Process agents should be adequately identified and labelled to avoid confusion and processing errors. Consideration of the entire supply chain (components and manufacturing) are areas that are typically addressed (see also 7.5.5).

Some medical devices might need to be cleaned and/or decontaminated prior to servicing to ensure that employees and other product are not exposed to some form of contamination. In such cases, they should be decontaminated by appropriate, approved procedures.

NOTE Additional information relating to cleaning procedures is available in ISO 12891-1.

7.5.1.2.2 Installation activities

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7.5.1.2.2 Installation activities

If appropriate, the organization shall establish documented requirements which contain acceptance criteria for installing and verifying the installation of the medical device.

If the agreed customer requirements allow installation to be performed other than by the organization or its authorized agent, the organization shall provide documented requirements for installation and verification.

Records of installation and verification performed by the organization or its authorized agent shall be maintained (see 4.2.4).

Installation of a medical device is the activity of putting the device into service in the location where it will be used. This activity might involve permanent connection to services (e.g. electrical supply, plumbing, waste disposal). Final testing of installed medical devices is carried out after it is in its location for use and connected to all relevant services. For medical devices, installation does not mean implantation in, or fitting to, a patient. The responsibility for installation should be clearly defined to ensure proper functioning of the medical device.

If a medical device must be assembled or installed at the user's site, instructions should be provided by the organization to guide correct assembly, installation, testing and/or calibrations. Special attention should be paid to ensure correct installation of safety control mechanisms and safety control circuits.

In certain cases (e.g. if required by a regulation, or if performance parameters of a medical device have to be controlled), the organization should provide instructions which allow the installer to confirm correct operation of the device. The results of installation or commissioning tests should be recorded (see 4.2.4).

7.5.1.2.3 Servicing activities

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7.5.1.2.3 Servicing activities

If servicing is a specified requirement, the organization shall establish documented procedures, work instructions and reference materials and reference measurement procedures, as necessary, for performing servicing activities and verifying that they meet the specified requirements.

Records of servicing activities carried out by the organization shall be maintained (see 4.2.4).

NOTE Servicing can include, for example, repair and maintenance.

If the functionality of products depends on servicing or maintenance for proper use of the products, and if the organization provides for some or all of the product servicing by either warranty or contract, then the organization's quality management system should include provisions for the type and extent of servicing provided. The following activities are considered as appropriate:

a) clarification of servicing responsibilities among the organization, distributors and users;

b) planning of service activities, whether carried out by the organization or by a separate agent;

c) validation of design and function of special-purpose tools or equipment for handling and servicing products after installation;

d) control of measuring and test equipment used in field servicing and tests;

e) provision and suitability of documentation, including instructions for use in dealing with the spares or parts lists, and in servicing of the product;

f) provision for adequate back-up, to include technical advice and support, customer training, and spares or parts supply;

g) training of servicing personnel;

h) provision of competent servicing personnel;

i) feedback of information which would be useful for improving product or servicing design;

j) other customer support activities.

Even when not specified in a contract, the guidance given here can be helpful to the organization.

The organization should establish a system for receiving service requests to determine if there are customer complaints or requirements that are not being met.

7.5.1.3 Particular requirements for sterile medical devices

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7.5.1.3 Particular requirements for sterile medical devices

The organization shall maintain records of the process parameters for the sterilization process which was used for each sterilization batch (see 4.2.4). Sterilization records shall be traceable to each production batch of medical devices (see 7.5.1.1).

The process parameters for sterilization processes usually applied to medical devices are identified in the relevant International Standards.

NOTE Additional information regarding sterilization is available in ISO 11134, ISO 11135, ISO 11137, ISO 13683, ISO 14160 and ISO 14937.

7.5.2 Validation of processes for production and service provision

7.5.2.1 General requirements

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7.5.2 Validation of processes for production and service provision

7.5.2.1 General requirements

The organization shall validate any processes for production and service provision 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.

Validation shall demonstrate the ability of these processes to achieve planned results.

The organization shall establish arrangements for these processes including, as applicable

a) defined criteria for review and approval of the processes,

b) approval of equipment and qualification of personnel,

c) use of specific methods and procedures,

d) requirements for records (see 4.2.4), and

e) revalidation.

The organization shall establish documented procedures for the validation of the application of computer software (and changes to such software and/or its application) for production and service provision that affect the ability of the product to conform to specified requirements. Such software applications shall be validated prior to initial use.

Records of validation shall be maintained (see 4.2.4)

7.5.2.1.1 General

7.5.2.1.1.1 Process validation is the mechanism or activity used by the organization to ensure that a process whose output is not fully verifiable is capable of consistently providing product that meets specifications. Process validation includes the development of a plan, the staged conduct of a number of evaluations of a particular process, and the collection and interpretation of recorded data. These activities can be considered to fall into a model consisting of four phases:

a) review and approval of equipment specifications;

b) initial qualification of the equipment used and provision of necessary services — also known as installation qualification (IQ);

c) demonstration that the process will produce acceptable results and establishment of limits (worst case) of the process parameters — also known as operational qualification (OQ);

d) establishment of long-term process stability — also known as performance qualification (PQ).

7.5.2.1.1.2 The following is a list of examples of processes that normally

— should be validated, or

— can be satisfactorily covered by verification, or

— need individual consideration of the circumstances of use and the controls in place to determine whether some or all of the elements of validation are required.

7.5.2.1.1.3 Processes that should be validated include

— sterilization,
— maintenance of specified conditions in environmentally controlled areas,
— aseptic processing,
— sealing of sterile packaging,
— lyophilization, and
— heat-treatment.

7.5.2.1.1.4 Processes that can be satisfactorily covered by verification include

— manual cutting,
— testing for colour, turbidity, total pH for solutions,
— visual inspection of printed circuit boards, and
— manufacturing and testing of wiring harnesses.

7.5.2.1.1.5 Processes that need individual consideration of the circumstances of use and the controls in place to determine whether some or all of the elements of validation are required include

— cleaning,
— manual assembly,
— numerical control cutting, and
— filling.

7.5.2.1.1.6 Cleaning processes might be required to remove process agents and/or particulate contamination. Such cleaning processes should be validated as to the effectiveness of the process for removing the contamination in accordance with a documented procedure (see 7.5.2). Records of validation are maintained (see ISO 13485:2003, 4.2.4). The process parameters used for the cleaning processes should be routinely monitored in accordance with documented procedures. Records of this monitoring should be maintained (see ISO 13485:2003 4.2.4).

When a cleaning process is intended to remove contamination (e.g. microbiological, viral, chemical, radioactive), the validation protocol, the results of the validation and the final operating procedure should be reviewed or approved by a qualified person.

NOTE Additional information regarding microbial monitoring is available in ISO 11737-1.

7.5.2.1.1.7 Process validation planning should include, but not be limited to, the following considerations:

— the accuracy and variability of the process parameters, including the settings of the equipment used;
— the skill, capability and knowledge of operators to conform to quality requirements;
— the adequacy of control of all process, including environmental parameters;
— the qualification of processes and equipment, as appropriate;
— the acceptance criteria and the process for handling process performance that does not meet these criteria;
— the circumstances that require process revalidation.

7.5.2.1.1.8 Some processes require that operators have extra training and/or be specially qualified, or that the process itself should have specific approval, as in the following example.

When qualifying an operator in sterile package sealing, if visual or other non-destructive examination for soundness of the seal would give no information on weld strength, the operator is required to be trained and qualified to carry out the sealing process according to a validated process procedure in order to provide assurance of seal strength.

When introducing a new or significantly changed process, including any new manufacturing and test methods, the process should be evaluated to determine whether validation is necessary.

NOTE Additional guidance on process validation is available in GHTF.SG3.N99-10.

7.5.2.1.2 Statistical methods and tools for process validation

There are many statistical methods and tools which may be used in process validation. Control charts, capability studies, designed experiments, tolerance analysis, robust design methods, failure modes and effects analysis (FMEA), sampling plans and mistake-proofing are some examples.

7.5.2.1.3 Computer software used in process control

The requirements of ISO 13485 regarding the validation of the application of computer software used in process control apply, whether or not such software is purchased, developed, maintained, or modified for automated production or process control purposes.

NOTE Additional information relating to the validation of the application of computer software is available in, for example, Good Automated Manufacturing Practice (GAMP) guidelines.

7.5.2.2 Particular requirements for sterile medical devices

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7.5.2.2 Particular requirements for sterile medical devices

The organization shall establish documented procedures for the validation of sterilization processes. Sterilization processes shall be validated prior to initial use.

Records of validation of each sterilization process shall be maintained (see 4.2.4).

Sterilization is an example of a process that cannot be verified by inspection and testing of the medical device. Therefore, sterilization processes must be validated before use and the process must be closely controlled and monitored (see 7.5.2.1). International Standards are available covering the development, validation and routine control of sterilization process and the aseptic manufacture of sterile medical devices. Sterilization processes validated and controlled in accordance with the requirements of existing International Standards should not be assumed to be effective in inactivating the causative agents of spongiform encephalopathies, such as scrapie, bovine spongiform encephalopathy (BSE), and Creutzfeld-Jakob disease. Specific recommendations have been produced in certain countries or regions for the processing of materials which are potentially contaminated with these agents.

NOTE Additional information regarding sterilization is available in ISO 11134, ISO 11135, ISO 11137, ISO 13683, ISO 14160, ISO 14937. Additional information regarding aseptic processing of medical devices is available in ISO 13408-1.

It is important to be aware that exposure to a properly validated and accurately controlled sterilization process is not the only factor associated with ensuring that the medical device is sterile. It can also be important that attention be given to the microbiological status of incoming raw materials and their subsequent storage, and to the control of the environment in which the medical device is manufactured, assembled and packaged (see 6.4).

7.5.3 Identification and traceability

7.5.3.1 Identification

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

7.5.3 Identification and traceability

7.5.3.1 Identification

The organization shall identify the product by suitable means throughout product realization, and shall establish documented procedures for such product identification.

The organization shall establish documented procedures to ensure that medical devices returned to the organization are identified and distinguished from conforming product [see 6.4 d)].

7.5.3.1.1 Identification of raw materials, components and finished medical devices is important for a number of reasons, including

- controlling material throughout manufacture,
- demonstrating product source, status and safety requirements,
- permitting traceability, and
- facilitating fault diagnosis in the event of quality problems.

Identification of product may be achieved by marking, tagging, or specifying a physical location for the product or its container. For example, on visually identical parts, if the functional characteristics are different, then different colours could be used. For bulk product or product from continuous processes, the identification could be by marking of batches or well-defined lots and accompanying documents.

7.5.3.1.2 It is usual for finished medical devices to be identified by a batch/lot/serial number or by electronic means. The extent to which raw materials and components need to be identified and related to the finished medical device batch/lot or serial number can depend upon a number of factors such as

- raw materials involved,
- type of medical device,
- effect of failure of the medical device or components, or raw materials used therein,
- specified requirements,
- traceability, if necessary,
- design and development input, and
- regulatory requirements.

Any marking materials used for product identification, if applied to medical devices or components, should not have a deleterious effect on the safety or performance of the medical device.

7.5.3.2 Traceability

7.5.3.2.1 General

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7.5.3.2 Traceability

7.5.3.2.1 General

The organization shall establish documented procedures for traceability. Such procedures shall define the extent of product traceability and the records required (see 4.2.4, 8.3 and 8.5).

Where traceability is a requirement, the organization shall control and record the unique identification of the product (see 4.2.4).

NOTE Configuration management is a means by which identification and traceability can be maintained.

Identification of product by batch/lot/serial number or electronic means permits traceability in two directions: forward to customers (also known as “device tracking”); and backward to raw materials, components and processes used in manufacturing. The former is important if it is necessary to track medical devices to the user (e.g. patients or hospitals), and the latter enables investigation of quality problems and feedback for the prevention of nonconforming product.

Product traceability involves the ability to trace the history, application or location of a product or activity by means of recorded identification. Traceability is typically required when there is a need to trace a nonconformity back to its source and to determine the location of the remainder of the affected batch.

The organization typically ensures traceability throughout the production and warehousing process, and up to the point when the medical device leaves the organization's possession. The organization may choose to limit the traceability activities to particular parts of its operation.

NOTE Additional information regarding the use of configuration management as a means to maintain identification and traceability is available in ISO 10007.

7.5.3.2.2 Particular requirements for active implantable medical devices and implantable medical devices

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7.5.3.2.2 Particular requirements for active implantable medical devices and implantable medical devices

In defining the records required for traceability, the organization shall include records of all components, materials and work environment conditions, if these could cause the medical device not to satisfy its specified requirements.

The organization shall require that its agents or distributors maintain records of the distribution of medical devices to allow traceability and that such records are available for inspection.

Records of the name and address of the shipping package consignee shall be maintained (see 4.2.4).

A traceability system for implantable and active implantable medical devices is essential because it might not be possible to inspect the device while it is in use. Traceability can, therefore, avoid unnecessary explanation of implanted devices by precisely identifying those implants which incorporated a component subsequently identified to be faulty, or for which some process control has subsequently been shown to be inadequate. Regulatory requirements for certain higher risk implants may require additional traceability beyond the organization's possession, and the quality management system should take account of these as appropriate.

The organization can achieve traceability by each individual product having an identifier (e.g. serial number, date code, batch code, lot number) unique to the source of operation. Separate identifiers could be required for changes in operative personnel, changes in raw materials, changes in tooling, new or different machine set-ups, changes in process methods, etc. Traceability identifiers should appear on applicable inspection and stock records (see 4.2.4).

There can be situations where traceability requires identification of the specific personnel involved in each phase of medical device processing or delivery. A sequence of individuals may perform successive service functions, each of which is to be traceable. The recording of identification evidence through signatures on serially numbered documents is an example. Each individual's identification evidence should be traceable.

7.5.3.3 Status Identification

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7.5.3.3 Status identification

The organization shall identify the product status with respect to monitoring and measurement requirements.

The identification of product status shall be maintained throughout production, storage, installation and servicing of the product to ensure that only product that has passed the required inspections and tests (or released under an authorized concession) is dispatched, used or installed.

Status can be indicated by marking, location, tagging or signing, either physically or by electronic means.

The status should indicate whether or not product has been inspected and tested, and

— accepted as fully meeting requirements,
— accepted with identified nonconformities under concession,
— on hold awaiting further analysis/decision, or
— rejected as unsatisfactory.

Separate physical location of these categories of product is often the most certain method of assuring both the status and accurate disposition. However, in an automated process, accurate disposition can equally as well be achieved by other means, such as by using a computer database.

Any marking materials, used for indication of inspection and test status, applied to medical devices or components should not have a deleterious effect on medical device safety or performance.

7.5.4 Customer property

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7.5.4 Customer property

The organization shall exercise care with customer property while it is under the organization's control or being used by the organization. The organization shall identify, verify, protect and safeguard customer property provided for use or incorporation into the product. If any customer property is lost, damaged or otherwise found to be unsuitable for use, this shall be reported to the customer and records maintained (see 4.2.4).

NOTE Customer property can include intellectual property or confidential health information.

The organization should identify responsibilities in relation to property and other assets owned by customers and under the control of the organization, in order to protect the value of the property.

Examples of such property are

— raw materials or components supplied for inclusion in product (including packaging materials),
— product supplied for repair, maintenance or upgrading,
— product supplied for further processing (e.g. packaging, sterilization or testing),
— services provided on behalf of the customer (such as transport of customer property to a third party), and
— customer intellectual property (including specifications, drawings and proprietary information).

The organization retains the responsibility for the protection of customer property awaiting further processing when it provides these to external organizations for services such as storage and contract sterilization.

7.5.5 Preservation of product

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7.5.5 Preservation of product

The organization shall establish documented procedures or documented work instructions for preserving the conformity of product during internal processing and delivery to the intended destination.

This preservation shall include identification, handling, packaging, storage and protection. Preservation shall also apply to the constituent parts of a product.

The organization shall establish documented procedures or documented work instructions for the control of product with a limited shelf-life or requiring special storage conditions. Such special storage conditions shall be controlled and recorded (see 4.2.4).

Consideration should be given to the various types of delivery and variations in environmental conditions which can be encountered.

The organization's method for handling product might need to consider providing equipment (such as anti-static wrist straps, gloves and protective clothing) and transportation units (such as pallets, containers, conveyors, vessels, tanks, rigging, pipelines and vehicles). This is necessary so that damage, deterioration or contamination due to vibration, shock, abrasion, corrosion, temperature variation, electrostatic discharge, radiation or any other conditions occurring during handling and storage, can be prevented. Maintenance of handling equipment is another factor to be considered.

Packaging materials and the packaging process should provide adequate protection against damage to the product. During storage and transportation up to the point of use, the packaging materials and labelling (see also 7.3.3) of medical devices are intended to provide appropriate protection against damage, deterioration or contamination.

The organization must provide suitable storage facilities, considering not only physical security but also environmental conditions (e.g. temperature and humidity). It might be appropriate to check product periodically in storage to detect possible deterioration. Consideration might need to be given to administrative procedures for product expiration dates, stock rotation and lot segregation.

Examples of preservation measures include the maintaining of

— sterile conditions for medical equipment,
— dust- and static-free conditions for semiconductors,
— temperature/humidity and hygienic conditions, and
— protection for fragile products.

The identification of product with a limited shelf life or expiration date, or product which requires special protection during storage and transportation, is important to ensure that such product is not used if the shelf life or expiration date has expired. The organization therefore should define the medical device shelf life applicable under specified storage conditions. Such special storage conditions must be controlled and recorded (see ISO 13485:2003, 4.2.4).

7.6 Control of monitoring and measuring devices

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

7.6 Control of monitoring and measuring devices

The organization shall determine the monitoring and measurement to be undertaken and the monitoring and measuring devices needed to provide evidence of conformity of product to determined requirements (see 7.2.1).

The organization shall establish documented procedures to ensure that monitoring and measurement can be carried out and are carried out in a manner that is consistent with the monitoring and measurement requirements.

Where necessary to ensure valid results, measuring equipment shall

a) be calibrated or verified at specified intervals, or prior to use, against measurement standards traceable to international or national measurement standards; where no such standards exist, the basis used for calibration or verification shall be recorded;

b) be adjusted or re-adjusted as necessary;

c) be identified to enable the calibration status to be determined;

d) be safeguarded from adjustments that would invalidate the measurement result;

e) be protected from damage and deterioration during handling, maintenance and storage.

In addition, the organization shall assess and record the validity of the previous measuring results when the equipment is found not to conform to requirements. The organization shall take appropriate action on the equipment and any product affected. Records of the results of calibration and verification shall be maintained (see 4.2.4).

When used in the monitoring and measurement of specified requirements, the ability of computer software to satisfy the intended application shall be confirmed. This shall be undertaken prior to initial use and reconfirmed as necessary.

NOTE See ISO 10012 for guidance related to measurement management systems.

7.6.1 The requirements refer explicitly to monitoring and measuring devices, including test software. It is helpful to approach the subject of control of monitoring and measuring devices from the perspective that measuring is itself a process involving materials, equipment and procedures. The intent of the requirements is to give the organization confidence in the monitoring and measuring devices that it uses to ensure that product meets customer and regulatory requirements.

Statistical methods are important in showing which monitoring and measuring devices are used in a manner which ensures that the measurement uncertainty is known and is consistent with the required measurement capability.

The requirements of this subclause are also applied by the organization when demonstrating the conformity of product to the specified requirements. This can involve measurements subsequent to production and inspection of product (e.g. during handling, storage, packaging, preservation, delivery or servicing).

Documented procedures should include details of equipment type, unique identification, location, frequency of checks, check method and acceptance criteria.

7.6.2 Some monitoring and measuring devices are not used for purposes which affect the quality of the product or service provided by the organization. As a result, the following examples are not necessarily part of the organization's control programme:

— instruments which are used to provide an indication only (e.g. a pressure gauge used only to determine the existence of line pressure), but are not used to control the actual manufacturing process, or a pressure gauge on a fire extinguisher or on a sprinkler system;

— instruments which are associated with business administration (e.g. clocks to control working times, thermostats to control operator comfort);

— instruments which can be attached to process equipment, but are not used for process control.

7.6.3 Some monitoring and measuring devices which require initial calibration or certification need not be included in the control programme. Examples of such equipment are

— mercury-in-glass thermometers,

— steel rulers, and

— laboratory volumetric measurement glassware that is not exposed to processes or environments which might affect its calibration.

Monitoring and measuring materials intended to provide a qualitative reference should be stored and maintained in a location which does not compromise the integrity of the material.

7.6.4 Software applications related to the control and/or calibration of monitoring and measuring devices should be validated. Examples include software used for

— controlling the instrument calibration process,

— determining the control or calibration status of instruments based on the data generated during the process, and

— scheduling the calibration of equipment, if the scheduling is not backed up by a manual (e.g. calibration label or other system).

NOTE Additional information regarding the management of monitoring and measuring equipment is available in ISO 10012.

8 Measurement, analysis and improvement

8.1 General

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

8 Measurement, analysis and improvement

8.1 General

The organization shall plan and implement the monitoring, measurement, analysis and improvement processes needed

a) to demonstrate conformity of the product,

b) to ensure conformity of the quality management system, and

c) to maintain the effectiveness of the quality management system.

This shall include determination of applicable methods, including statistical techniques, and the extent of their use.

NOTE National or regional regulations might require documented procedures for implementation and control of the application of statistical techniques.

8.1.1 If documented procedures for inspection and testing activities are required, they usually include details of test methods, acceptance and rejection criteria, and equipment to be used.

The organization‘s procedures should ensure that the integrity of the inspection and test results are not compromised, particularly if testing is done by persons with potential conflicts of interest, such as suppliers or production personnel.

Measurement, and analysis include the following considerations:

— measurement data should be converted to information and knowledge to be of benefit to the organization;
— measurement, and analysis of products and processes, should be used to establish appropriate priorities for the organization;
— measurement methods employed by the organization should be reviewed as necessary.

8.1.2 The use of statistical methods can be beneficial to the organization in a wide range of circumstances, including data collection, analysis and application. These techniques are useful for demonstrating process capability, as well as product conformity to specified requirements. They assist in deciding what data to obtain, and in making the best use of the data to gain a better understanding of customer requirements and expectations. Statistical methods can also find uses in

— designing product and processes,
— controlling processes,
— avoiding nonconformity,
— analysing problems,
— determining risk,
— investigating root causes,
— establishing product and process limits,
— forecasting,
— verifying and validating products or processes, and
— measuring or assessing quality characteristics.

8.1.3 Among the statistical methods which can be beneficial for these purposes are the following:

- graphical methods (histograms, sequence charts, scatter plots, Pareto diagrams, cause and effect diagrams, etc.) which help diagnose problems and suggest appropriate computational approaches for further statistical diagnosis;
- statistical control charts for monitoring and controlling production and measurement processes for all types of product (hardware, software, processed materials and services);
- design of experiments for determining which candidate variables have significant influence on process and product performance, and for quantifying the effect;
- regression analysis, which provides a quantitative model for the behaviour of a process or a product when the conditions of process operation or product design are changed;
- analysis of variance (separating the total observed variability), leading to variance component estimates useful for designing sample structures for control charts, for product characterization and release, and for prioritizing quality improvement efforts based on the magnitudes for the variance components;
- methods of sampling and acceptance;
- sampling at all stages of production;
- statistical methods for inspections and testing.

8.1.4 Once the appropriate statistical techniques are chosen, it is important to implement those techniques in such a manner that appropriate data are collected and evaluated, and the results are reported to the relevant departmental functions, so that necessary actions can be taken. The data resulting from the application of statistical techniques can be an effective means of demonstrating conformity to requirements for quality and can be used as quality records. The documentation of such techniques and the records resulting from them might be subject to regulatory requirements.

NOTE Additional information regarding statistical techniques is available in ISO/TR 10017.

8.2 Monitoring and measurement

8.2.1 Feedback

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

8.2 Monitoring and measurement

8.2.1 Feedback

As one of the measurements of the performance of the quality management system, the organization shall monitor information relating to whether the organization has met customer requirements.

The methods for obtaining and using this information shall be determined.

The organization shall establish a documented procedure for a feedback system [see 7.2.3 c)] to provide early warning of quality problems and for input into the corrective and preventive action processes (see 8.5.2 and 8.5.3).

If national or regional regulations require the organization to gain experience from the post-production phase, the review of this experience shall form part of the feedback system (see 8.5.1).

Management should recognise that many sources exist for obtaining customer-related information. This information is useful for providing feedback related to the quality of medical devices and related services. The organization should identify relevant sources of such information and establish an effective process to collect, analyse and use the information for monitoring quality problems. The process established has to be documented, so that regulatory requirements are met.

Examples of customer-related information that demonstrates whether or not the requirements of customers have been met, include

— customer and user surveys,
— feedback on aspects of the medical device,
— customer complaints (see 8.5.1),
— customer requirements and contract information,
— regulatory authority compliance-related communications,
— peer-reviewed journals, and
— service delivery data.

As part of a regulated organization's requirement to provide early warning of quality problems, vigilance or post-market surveillance systems are typically implemented.

NOTE Additional information regarding vigilance and post-market surveillance systems is available on the websites of many regulatory authorities.

8.2.2 Internal audit

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

8.2.2 Internal audit

The organization shall conduct internal audits at planned intervals to determine whether the quality management system

a) conforms to the planned arrangements (see 7.1), to the requirements of this International Standard and to the quality management system requirements established by the organization, and

b) is effectively implemented and maintained.

An audit programme shall be planned, taking into consideration the status and importance of the processes and areas to be audited, as well as the results of previous audits. The audit criteria, scope, frequency and methods shall be defined. Selection of auditors and conduct of audits shall ensure objectivity and impartiality of the audit process. Auditors shall not audit their own work.

The responsibilities and requirements for planning and conducting audits, and for reporting results and maintaining records (see 4.2.4) shall be defined in a documented procedure.

The management responsible for the area being audited shall ensure that actions are taken without undue delay to eliminate detected nonconformities and their causes. Follow-up activities shall include the verification of the actions taken and the reporting of verification results (see 8.5.2).

NOTE See ISO 19011 for guidance related to quality auditing.

Planning for internal audits should be flexible in order to permit changes in emphasis based on findings and objective evidence obtained during the audit. Relevant input from the area to be audited, as well as from other interested parties such as customers, corporate audit plans, or third-party assessment organizations, should be considered in the development of internal audit plans.

The results of audits are usually stated in a written report (see 4.2.4) which indicates the deficiencies found. Avoiding undue delay is usually accomplished by including appropriate target dates for responding to audit findings. The audit results can be communicated and used as an input to management review (see ISO 13485:2003, 5.6.2).

A series of limited, well-defined audits can be as effective as one single comprehensive audit. Such an audit system can be operated flexibly to give special, or repeat, attention to any areas of weakness or of other concern.

In addition to the periodic internal audits, a special internal audit can be initiated for the following purposes:

— when verifying that the quality management system continues to meet specified requirements and is being implemented, if required, within the framework of a contractual relationship;

— when undergoing significant changes in functional areas (e.g. reorganizations or procedural revisions);

— when investigating safety, performance or dependability of the products which are, or which are suspected to be, in jeopardy due to nonconformities;

— when verifying which required corrective actions have been taken and have been effective.

Internal audits may be partially or fully subcontracted.

8.2.3 Monitoring and measurement of processes

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

8.2.3 Monitoring and measurement of processes

The organization shall apply suitable methods for monitoring and, where applicable, measurement of the quality management system processes. These methods shall demonstrate the ability of the processes to achieve planned results. When planned results are not achieved, correction and corrective action shall be taken, as appropriate, to ensure conformity of the product.

No additional guidance is provided for this subclause.

8.2.4 Monitoring and measurement of product

8.2.4.1 General requirements

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

8.2.4 Monitoring and measurement of product

8.2.4.1 General requirements

The organization shall monitor and measure the characteristics of the product to verify that product requirements have been met. This shall be carried out at appropriate stages of the product realization process in accordance with the planned arrangements (see 7.1) and documented procedures (see 7.5.1.1).

Evidence of conformity with the acceptance criteria shall be maintained. Records shall indicate the person(s) authorizing release of product (see 4.2.4).

Product release and service delivery shall not proceed until the planned arrangements (see 7.1) have been satisfactorily completed.

8.2.4.1.1 In-process inspection and testing includes all such activities between the acceptance of incoming materials and submission of the medical device for final inspection. The results of in-process inspection and testing can be used both for process control and for the early identification of nonconforming product.

Final inspection involves activities (examination, inspection, measurement or test) upon which the final release of product is based. Records of previously performed inspection and testing results can also be reviewed.

The specified requirements forming the basis of final inspection and test should include all designated release criteria. These should be directly related to the type of medical device involved and its intended use. Final inspection and testing should provide objective evidence of conformity with all designated release criteria that have not been confirmed through previous inspection and testing. Final testing can include, if practical, testing under simulated or actual conditions of use, and using medical products selected from a lot or batch.

In the case of medical devices that are assembled and/or installed at the user's premises, any additional inspection and testing should be carried out after completion of assembly/installation. In such cases, these inspection and testing activities might not be carried out by the organization, but the organization should ensure the availability of all necessary information about the inspection and test procedure and the results expected (see also 6.3, 6.4, 7.5.1, 7.5.1.2 and 7.5.2).

8.2.4.1.2 When selecting measurement methods for ensuring that product conforms to requirements and when considering customer requirements, the organization should consider the following:

— the types of product characteristics, which then determine the types of measurement, suitable measurement means, the accuracy required and skills needed;

— the equipment, software and tools required;

— the location of suitable measurement points in the realization process sequence;

— the characteristics to be measured at each point, and the documentation and acceptance criteria to be used;

— the customer-established points for observation or verification of selected characteristics of the product;

— the inspections or testing required to be observed or performed by regulatory authorities;

— the timing and manner in which the organization intends, or is required by the customer or regulatory authorities, to engage qualified third parties to perform activities within the quality management system;

— the qualification of people, materials, products, processes and the quality management system;

— the final inspection to confirm that verification activities have been completed and accepted;

— recording the results of product measurements.

The organization's inspection and test records (see 4.2.4) should facilitate assessment of in-process and finished products having fulfilled the requirements for quality. Purchased product is verified under the provisions of ISO 13485:2003, 7.4.3.

8.2.4.1.3 As applicable, records of monitoring and measurements can

— identify the inspection/test procedure(s) and revision level used (see also 4.2.3),

— identify the test equipment used,

— include test data,

— be signed and dated by the person responsible for the inspection or test,

— clearly identify the number of products examined and the number of products accepted, and

— record the disposition of any products failing inspection or test, and the reasons for failure.

8.2.4.2 Particular requirements for active implantable and implantable devices

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

8.2.4.2 Particular requirement for active implantable medical devices and implantable medical devices

The organization shall record (see 4.2.4) the identity of personnel performing any inspection or testing.

In addition to inspection and test records (see 4.2.4), the organization should record the identity of personnel performing any inspection or testing of active implantable or implantable devices to facilitate failure investigation, and corrective and preventive actions.

8.3 Control of nonconforming product

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

8.3 Control of nonconforming product

The organization shall ensure that product which does not conform to product requirements is identified and controlled to prevent its unintended use or delivery. The controls and related responsibilities and authorities for dealing with nonconforming product shall be defined in a documented procedure.

The organization shall deal with nonconforming product by one or more of the following ways:

a) by taking action to eliminate the detected nonconformity;

b) by authorizing its use, release or acceptance under concession;

c) by taking action to preclude its original intended use or application.

The organization shall ensure that nonconforming product is accepted by concession only if regulatory requirements are met. Records of the identity of the person(s) authorizing the concession shall be maintained (see 4.2.4).

Records of the nature of nonconformities and any subsequent actions taken, including concessions obtained, shall be maintained (see 4.2.4).

When nonconforming product is corrected it shall be subject to re-verification to demonstrate conformity to the requirements.

When nonconforming product is detected after delivery or use has started, the organization shall take action appropriate to the effects, or potential effects, of the nonconformity.

If product needs to be reworked (one or more times), the organization shall document the rework process in a work instruction that has undergone the same authorization and approval procedure as the original work instruction. Prior to authorization and approval of the work instruction, a determination of any adverse effect of the rework upon product shall be made and documented (see 4.2.3 and 7.5.1).

8.3.1 People in the organization should be empowered with the authority and responsibility to report nonconformities at any stage of a process in order to ensure timely detection and disposition of nonconformities.

Top management of the organization should ensure the establishment of an effective process to provide for review and disposition of identified nonconformities.

Nonconforming product includes nonconforming product occurring in the organization's own facilities as well as to nonconforming product received or delivered by the organization.

8.3.2 Procedures established and maintained by the organization should have the following purposes:

— to determine which product is involved in the nonconformity (e.g. what production time interval, production machines or products) and the number of products involved;
— to identify the nonconforming product to make sure that it can be distinguished from the conforming product (see 7.5.3);
— to document the existence and source of the nonconformity;
— to evaluate the nature of the nonconformity;
— to consider the alternatives for the disposition of the nonconforming product;
— to decide upon and record what disposition should be made;

— to control (e.g. by physical segregation) the subsequent processing of the nonconforming product consistent with the disposition decision;
— to notify others who might be affected by the nonconformity including, if appropriate, the customer.

8.3.3 When a nonconformity is determined, the organization should take steps to investigate and eliminate the reason for the occurrence of the nonconformity as well as determine what do to with (disposition of) the nonconforming product.

"Correction" refers to repair, rework, or adjustment and relates to the disposition of an existing nonconformity, whereas the "Corrective Action" relates to the elimination of the causes of nonconformity (see 8.5.2).

If the nonconforming product is to be used, accepted or released, the organization should decide to do so either by correcting the nonconforming product and then reevaluating it, or by using the product as is.

If the organization chooses to use, accept or release nonconforming product when a nonconformity exists, the organization has made a "concession." Concessions are a tool used to minimize the financial impact to the organization as it relates to the disposition of nonconforming products. In such instances of concessions being made, the organization may not relinquish regulatory responsibilities for medical devices and related services. Each concession should be reviewed to ensure that the nonconformity does not conflict with any regulatory requirement. The identity of the person(s) within the organization who authorizes each concession is maintained in a record, and this record should include information documenting that regulatory requirements have been fully met.

Actions taken when nonconforming product is detected after delivery or use has started is sometimes referred to as "product recall." Because the term "recall" has different definitions in different national or regional jurisdictions, its use in ISO 13485 has been avoided when describing such activities.

8.3.4 The procedures for dealing with nonconformities discovered in product which has already been shipped can include taking such actions as

— withdrawing products from sale,
— withdrawing products from distribution,
— giving advice to customers (this can take the form of checks to be carried out before use, providing additional guidance on the use of the product or the replacement of certain products), or
— in extreme cases, requesting the physical return or destruction of products.

Information concerning nonconforming product should be provided to all appropriate personnel, so that action is taken, if necessary, to identify and correct the cause of the nonconformity and prevent recurrence (see 8.5). Information concerning nonconforming products might require the review and updating of risk management activities.

Any product returned to the organization should be treated as nonconforming product.

For any returned product for which there is a risk of contamination (e.g. microbiological, viral, chemical, radioactive), consideration should be given to regulatory requirements for hazardous materials.

NOTE Additional information regarding decontamination is available in ISO 12891-1.

8.3.5 Control should be established over the disposal of nonconforming material designated as scrap to ensure that

— its status is clearly identified,
— it cannot be confused with conforming product,
— it cannot re-enter the production system, and
— it is disposed of safely.

8.4 Analysis of data

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

8.4 Analysis of data

The organization shall establish documented procedures to determine, collect and analyse appropriate data to demonstrate the suitability and effectiveness of the quality management system and to evaluate if improvement of the effectiveness of the quality management system can be made.

This shall include data generated as a result of monitoring and measurement and from other relevant sources.

The analysis of data shall provide information relating to

a) feedback (see 8.2.1),

b) conformity to product requirements (see 7.2.1),

c) characteristics and trends of processes and products including opportunities for preventive action, and

d) suppliers.

Records of the results of the analysis of data shall be maintained (see 4.2.4).

Data should be collected and analysed in order to verify the ongoing suitability and effectiveness of the quality management system, and to determine if there are any trends or patterns that require attention. Negative trends should be considered for improvement. The results of the analysis of data should be considered for input to management reviews and risk management activities.

Analysis of data can help to determine the root cause of existing or potential problems, and thereby to guide decisions about the corrective and preventive actions needed for improvement.

For an evaluation of the effectiveness of the quality management system, data and information from relevant parts of the organization should be integrated and analysed. The results of this analysis can be used by the organization to determine

- trends in product conformance,
- the extent to which customer requirements are being met,
- process effectiveness,
- supplier performance, and
- success of performance improvement objectives.

8.5 Improvement

8.5.1 General

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

8.5 Improvement

8.5.1 General

The organization shall identify and implement any changes necessary to ensure and maintain the continued suitability and effectiveness of the quality management system through the use of the quality policy, quality objectives, audit results, analysis of data, corrective and preventive actions and management review.

The organization shall establish documented procedures for the issue and implementation of advisory notices. These procedures shall be capable of being implemented at any time.

Records of all customer complaint investigations shall be maintained (see 4.2.4). If investigation determines that the activities outside the organization contributed to the customer complaint, relevant information shall be exchanged between the organizations involved (see 4.1).

If any customer complaint is not followed by corrective and/or preventive action, the reason shall be authorized (see 5.5.1) and recorded (see 4.2.4).

If national or regional regulations require notification of adverse events that meet specified reporting criteria, the organization shall establish documented procedures to such notification to regulatory authorities.

8.5.1.1 Improvement activities

For the purposes of ISO 13485, “improvement” activities are those which identify and implement any changes necessary to ensure and maintain the continued suitability and effectiveness of the quality management system to meet the requirements of the customer. If the need for corrective or preventive action is identified, this is an indication that the quality management system has not been suitable or fully effective in a particular area. Correcting the problem or potential problem by implementing corrective or preventive action to bring the quality management system back to a fully suitable and effective state is considered to be improvement.

8.5.1.2 Customer complaints

8.5.1.2.1 Any customer complaint received by the organization on a product should be evaluated. Customer complaints and warranty claims are the most common external indications of product deficiency that might be subject to correction, corrective action to prevent recurrence of the problem, or preventive action to prevent the occurrence of the problem.

Some organizations might consider other sections within the same organizations to be customers. In this case internal complaints can be treated as customer complaints and processed accordingly. If nonconforming product is involved, this should also be handled according to the requirements of ISO 13485:2003, 8.3.

In evaluating the complaint, the organization should consider whether the medical device

— fails to conform to its specification, or

— conforms with its specifications but nevertheless causes problems in use.

For instance, a complaint with a medical device conforming to its specifications might be caused by a design fault. Complaints related to handling might indicate inadequate instructions for use.

Regulatory requirements can place requirements on organizations to monitor the use of their medical devices and to inform regulatory authorities of certain defined experience in use.

The organization should formally designate a person(s) (by role or position) to collect and coordinate all written and oral customer complaints about medical devices. This person(s) should have the authority to ensure immediate review of any complaint, particularly those relating to injury, death or any hazard.

The investigation of a complaint can determine that activities outside the organization might be involved. The other organization site can be unrelated (e.g. a supplier or representative/agent), but can also be within the same organization (e.g. another division or the Head Office). Whoever the other party is, arrangements have to be such that there is two-way communication of whatever information is needed to properly investigate and resolve the complaint. This will normally be provided for in the contract with the other party.

8.5.1.2.2 The documented complaints system should cover the following:

— establishing responsibility for operating the system;

— evaluating the complaint;

— creating records and statistical summaries to enable the major causes of complaints to be determined;

— taking any corrective action;

— segregating and disposing of customer returns and faulty stock (special attention might need to be given to decontamination);
— filing of customer correspondence and other relevant records (the retention time for these should be defined).

8.5.1.2.3 The records of complaint investigations should contain enough information to show that the complaint was properly reviewed, for example a determination of whether or not

— there was an actual medical device failure to perform per specifications,
— the medical device was being used to treat or diagnose a patient,
— a death, injury or illness was involved, or
— there was any relationship between the medical device and the reported incident or adverse event.

“Illness” and “injury” are frequently defined by national and regional regulations.

8.5.1.2.4 An investigation record typically includes

— the name of the medical device,
— the date the complaint was received,
— the control number used,
— the name and address of the complainant,
— the nature of the complaint,
— the results of the investigation,
— the correction(s) made
— the corrective action taken,
— the justification if no action is taken,
— the dates of the investigation,
— the name of the investigator, and
— the reply (if any) to the complainant.

Customer complaints should be considered for review and update of risk management activities.

8.5.1.3 Advisory notices

8.5.1.3.1 National or regional regulatory requirements might require that advisory notices be reported to designated regulatory authorities.

In some countries “advisory notices” are considered to include notices of medical devices that need to be corrected in order to be safe and perform as intended, as well as nonconforming devices that cannot be corrected and have to be removed from the market. In other countries, an advisory notice is a notice of correction needed to a medical device in order to maintain its safety and effectiveness and a notice of nonconforming devices that have to be removed from the market is defined as a “recall”. Many countries have specific regulatory procedures for processing advisory notices and recall. These must be included in the quality management system.

The nature and seriousness of the hazard or nonconformity, the intended use of the medical device, and the potential for patient injury or failure to meet regulatory requirements, will determine whether it will be necessary to issue an advisory notice and to report to national or regional regulatory authorities. These factors will also determine the urgency and extent of the action.

8.5.1.3.2 The procedures for generating, authorizing and issuing an advisory notice should specify

— the management arrangements which enable the procedure to be activated, even in the absence of key personnel,
— the level of management authorized to initiate corrective action, and the method of determining the affected products,

— the system for determining the disposition of returned product (e.g. rework, repackage, scrap), and

— the communication system (which includes the necessity to report to local or national authorities), the points of contact and the methods of communication between the organization and national or regional regulatory authorities.

8.5.1.3.3 An advisory notice should provide

— 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, and

— any consequent actions to be taken.

If a medical device is returned to the organization, the progress of agreed corrective actions should be monitored and, if appropriate, the quantities of product physically returned to the organization or scrapped locally or corrected locally should be reconciled.

8.5.2 Corrective action

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

8.5.2 Corrective action

The organization shall take action to eliminate the cause of nonconformities in order to prevent recurrence. Corrective actions shall be appropriate to the effects of the nonconformities encountered.

A documented procedure shall be established to define requirements for

a) reviewing nonconformities (including customer complaints),

b) determining the causes of nonconformities,

c) evaluating the need for action to ensure that nonconformities do not recur,

d) determining and implementing action needed, including, if appropriate, updating documentation (see 4.2),

e) recording of the results of any investigation and of action taken (see 4.2.4), and

f) reviewing the corrective action taken and its effectiveness.

8.5.2.1 Corrective action is the action taken to prevent recurrence of a nonconformity which has already occurred. If nonconforming product is involved, this is handled according to ISO 13485:2003, 8.3, and the action taken to prevent recurrence of the nonconforming product is handled under ISO 13485:2003, 8.5.2.

The organization's corrective action procedures should clearly establish

— who is responsible for taking the corrective action,

— when and how this corrective action will be carried out, and

— how the effectiveness of the corrective action will be verified.

An important element in the programme is the dissemination of information on corrective actions to those directly responsible for ensuring quality.

8.5.2.2 Causes of detected nonconformities should promptly be identified so that corrective action can be taken and recurrence prevented. These causes can include the following:

— failures, malfunctions or nonconformities in incoming materials, processes, tools, equipment or facilities in which products are processed, stored or handled, including the equipment and systems therein;
— inadequate or non-existent procedures and documentation;
— non-compliance with procedures;
— inadequate process control;
— poor scheduling;
— lack of training;
— inadequate working conditions;
— inadequate resources (human or material);
— inherent process variability.

8.5.2.3 Input to corrective action can come from many sources, including the following:

— inspection and test records;
— validation study results;
— nonconformity records;
— observations during process monitoring;,
— audit observations;
— field, service or customer complaints;
— regulatory authority or customer observations;
— observations and reports by personnel;
— supplier problems;
— management review results;
— solicited information on new or modified products;
— published literature;
— published reports of failures of similar products.

8.5.2.4 Effective implementation of corrective action typically includes

— clear and accurate identification of the nonconformity and the affected medical device(s),
— identification of the recipient(s) of the affected medical devices (see 7.5.3.2),
— consideration of what other medical device(s), process(es) or procedure(s) might have been affected,
— identification of the root cause of the nonconformity,
— identification of the action required to prevent recurrence of the problem,
— any necessary approvals required before any action is taken,
— a record that the identified corrective action was taken, and
— a check that the corrective action taken was effective (i.e. verification that the nonconformity is unlikely to recur and that no new risks have been introduced by the corrective action).

8.5.2.5 The degree of corrective action taken should be dependent upon and related to the risk, size and nature of the problem and its effect(s) on product quality. For example, the level of investigation to determine the cause of the nonconformity, the work done to determine and verify the appropriateness of corrective action, and the level of documentation kept, would be far more extensive for a nonconformity relating to the failure of a medical device compared to a less serious nonconformity such as the failure to conduct an internal audit when scheduled.

Corrective action should be implemented without undue delay.

8.5.3 Preventive action

ISO 13485:2003, Medical devices — Quality management systems — Requirements for regulatory purposes

8.5.3 Preventive action

The organization shall determine action to eliminate the causes of potential nonconformities in order to prevent their occurrence. Preventive actions shall be appropriate to the effects of the potential problems.

A documented procedure shall be established to define requirements for

a) determining potential nonconformities and their causes,

b) evaluating the need for action to prevent occurrence of nonconformities,

c) determining and implementing action needed,

d) recording of the results of any investigations and of action taken (see 4.2.4), and

e) reviewing preventive action taken and its effectiveness.

Preventive action is taken when a potential nonconformity is identified as the result of an analysis of records and other relevant sources of information.

The degree of preventive action taken should be dependent upon and related to the risk, size and nature of the problem and its effect(s) on product quality.

Sources for information for initiating preventive actions include

- purchased product rejected on receipt,
- evidence that previous decisions affecting product conformity were false,
- products requiring rework,
- in-process problems, wastage levels,
- final inspection failures,
- customer feedback,
- warranty claims,
- process measurements,
- statistical process control documents,
- identification of results that are out-of-trend but not out-of-specification,
- difficulties with suppliers (see 7.4.1),
- service reports, and
- the need for concessions.

Annex A
(informative)

Terms used in certain regulatory administrations to describe documents referenced in this Technical Report

	Document	USA	EU	Japan
A	A compilation of records which describes and records the history of the design activity (see ISO 13485:2003, 4.2.4 and 7.3). Examples include (but are not limited to): calculations, design inputs, requirements and specifications, design testing reports, risk analyses, design reviews, design verification and validation reports (including clinical investigation results), product labelling, and design changes and related records.	DHF Design History File	Part of the Technical Documentation and Design Dossier	Part of Seihin Hyojunsho
B	A compilation of documents based on the device design activity which specify how the device is to be produced, including the criteria for testing and acceptance (see ISO 13485:2003, 4.2.1 and 7.1). Examples include (but are not limited to): specifications for raw materials, packaging, and labelling, process/product specifications, engineering drawings, parts lists, work instructions (including equipment operation), sterilization procedures (if applicable), quality plan, and manufacturing/-testing/inspection procedures and acceptance criteria, installation procedures, servicing requirements.	DMR Device Master Record	Part of the Technical Documentation and Design Dossier	Seihin Hyojunsho
C	A compilation of records containing the production/ manufacturing history to demonstrate conformity with (approved) pre-production documents (see ISO 13485:2003, 4.2.4). Examples include (but are not limited to): manufacturing test reports, lot or batch records, travellers, functional test reports, actual labelling.	DHR Device History Record	Manufacturing Records	Quality Records

Annex B
(informative)

Analysis of significant changes from ISO 13485:1996 to ISO 13485:2003

Clauses in ISO 9001:1994	Corresponding clauses in ISO 13485:2003	Significant differences
1 Scope	1	ISO 13485:2003 is targeted specifically at harmonizing internationally the QMS regulatory requirements for medical device organizations. Because ISO 13485:2003 does not contain the requirements of ISO 9001:2000 that are inconsistent with regulatory objectives, compliance with ISO 13485:2003 does not ensure compliance with ISO 9001:2000. Because ISO 13485:2003 contains requirements that are regulatory in nature that are not contained in ISO 9001:2000, compliance with ISO 9001:2000 does not ensure compliance with ISO 13485:2003. Exclusions of design and development from the QMS is allowed if allowed by regulation. “Non-inclusion” of product realization requirements is allowed if those functions are not required by the nature of the medical device being provided by the organization. QMS requirements related to outsourced functions must be accounted for in the organization’s QMS.
2 Normative references	2	The only normative reference is ISO 9000:2000 because ISO 13485:2003 does not contain all the requirements of ISO 9001:2000; ISO 8402 has been withdrawn (ISO 9000:2000 contains all the relevant definitions); and other standards have been included only as informative references in the Bibliography.
3 Definitions	3	ISO 13485:2003 contains an explanation of the relationship between the organization, its suppliers, and its customers. ISO 13485:2003 contains more description in the definition of “medical device”. ISO 13485:2003 includes “services” or “related services” when it refers to either “product” or “medical device”. ISO 13485:2003 broadens the definition of “sterile medical device”.

Clauses in ISO 9001:1994	Corresponding clauses in ISO 13485:2003	Significant differences
4 Quality system requirements [title only] **4.1 Management responsibility** [title only] **4.1.1 Quality policy**	5.1 + 5.3 + 5.4.1	This clause in ISO 13485:2003 begins the focus of on "maintaining the effectiveness" of the QMS rather than the "continual improvement" of the QMS as in ISO 9001:2000. ISO 13485:2003 provides more description by separating out the quality policy and the quality objectives.
4.1.2 Organization [title only] **4.1.2.1 Responsibility and authority**	5.5.1	ISO 13485:2003 treats more generally the requirement for independence of persons whose work can effect quality. ISO 13485:2003 notes potential regulatory requirements related to experience reporting.
4.1.2.2 Resources	6.1 + 6.2.1	ISO 13485:2003 explicitly allows that competency can come from education, inherent skill and experience, as well as training.
4.1.2.3 Management representative	5.5.2	ISO 13485:2003 gives the management representative responsibility for promoting the awareness of regulatory and customer requirements throughout the organization.
4.1.3 Management review	5.6.1 + 8.5.1	ISO 13485:2003 includes the focus of assessing opportunities for QMS improvement as one of the objectives of management review. ISO 13485:2003 expands on the requirements associated with management review input and output.
4.2 Quality system [title only] **4.2.1 General**	4.1 + 4.2.2 + 7.2.1 c + 7.2.2 a	ISO 13485:2003 contains text that reinforces the process focus of the Standard. The QMS must take into account the methods to be used to control the outsourced processes. ISO 13485:2003 requires inclusion in the quality manual of justification for any processes that are excluded from the QMS.
4.2.2 Quality system procedures	4.2.1	ISO 13485:2003 does not have a separate clause devoted specifically to quality system procedures. ISO 13485:2003 provides more detailed description of the various types of documentation that can be found in the QMS. ISO 13485:2003, without calling it a special name, requires a file for each device model containing or referring to product requirements and related QMS requirements and procedures.

Clauses in ISO 9001:1994	Corresponding clauses in ISO 13485:2003	Significant differences
4.2.3 Quality planning	4.2.1 + 5.4.2 + 7.1	ISO 13485:2003 sets out the requirements related to general QMS planning in a different clause (5.4.2) from the requirements associated with product realization (7.1). As it relates to product realization planning, ISO 13485:2003 requires documentation of risk management requirements.
4.3 Contract review [title only] **4.3.1 General**		ISO 13485:2003 does not require documented procedures for determining customer requirements related to product or the transactions between the organization and the customer.
4.3.2 Review	5.2 + 7.2.1 + 7.2.2 + 7.2.3	ISO 13485:2003 addresses the identification and confirmation of requirements that are not explicited stated by the customer. ISO 13485:2003 contains guidance related to catalogue and Internet sales situations. ISO 13485:2003 contains requirements related to customer communications.
4.3.3 Amendment to a contract	7.2.2	
4.3.4 Records	7.2.2	
4.4 Design control [title only] **4.4.1 General**	7.1	
4.4.2 Design and development planning	7.3.1	ISO 13485:2003 explicitly requires documentation of the design and development planning process. ISO 13485:2003 provides guidance related to verification of the suitability of the design output for manufacturing purposes during design transfer.
4.4.3 Organizational and technical interfaces	7.3.1	
4.4.4 Design input	7.2.1 + 7.3.2	ISO 13485:2003 provides a listing of examples of design inputs, including statutory and regulatory requirements, information from previous designs, and outputs from risk management activities.
4.4.5 Design output	7.3.3	ISO 13485:2003 includes the requirement that design outputs be suitable to facilitate the purchasing process. ISO 13485:2003 provides guidance by listing

Clauses in ISO 9001:1994	Corresponding clauses in ISO 13485:2003	Significant differences
		examples of design outputs.
4.4.6 Design review	7.3.4	ISO 13485:2003 explains in more detail the objectives of the design review.
4.4.7 Design verification	7.3.5	ISO 13485:1996 provided guidance by giving a number of examples of design verification activities.
4.4.8 Design validation	7.3.6	ISO 13485:2003 requires design validation to be completed prior to delivery or implementation of the medical device or related service. ISO 13485:2003 also provides guidance for those situations where validation cannot be completed until after installation of the device in the user's location.
4.4.9 Design changes	7.3.7	ISO 13485:2003 requires the consideration of the effects of design changes on parts and product already delivered. ISO 13485:2003 explicitly requires records be kept of design changes and related activities.
4.5 Document and data control [title only] **4.5.1 General**	4.2.3	ISO 13485:2003 outlines in some detail elements of document control that are important. ISO 13485:1996 broke down the various aspects of document control into subclauses; ISO 13485:2003 handles them in one subclause.
4.5.2 Document and data approval and issue	4.2.3	ISO 13485:2003 specifies a minimum period for which documents that form the basis for the medical device manufacture must be kept (not less than the retention period of any resulting record (see 4.2.4), or as specified by relevant regulatory requirements).
4.5.3 Document and data changes	4.2.3	
4.6 Purchasing [title only] **4.6.1 General**		
4.6.2 Evaluation of subcontractors	7.4.1	
4.6.3 Purchasing data	7.4.2	
4.6.4 Verification of purchased product	7.4.3	ISO 13485:1996 indicated that customer verification of product at the subcontractor's location does not relieve the subcontractor nor the organization of its responsibility to control quality and provide

Clauses in ISO 9001:1994	Corresponding clauses in ISO 13485:2003	Significant differences
		acceptable product.
4.7 Control of customer-supplied product	7.5.4	ISO 13485:1996 required documented procedures to control customer supplied product; ISO 13485:2003 does not. ISO 13485:1996 indicated that organization verification of customer-supplied product does not absolve the customer of the responsibility to provide acceptable product. ISO 13485:2003 indicates that intellectual property is covered by this subclause.
4.8 Product identification and traceability	7.5.3	ISO 13485:2003 indicates that configuration management is one way to establish identification and traceability. ISO 13485:2003 requires that records of consignees be kept for implantable and active implantable medical devices. ISO 13485:2003 requires the product identification and acceptance status be maintained throughout production and preparation for distribution to ensure that product released for distribution has passed all inspections and required testing.
4.9 Process control	6.3 + 6.4 + 7.5.1 + 7.5.2	ISO 13485:2003 includes a requirement for the establishment of a batch record that provides traceability to the extent specified in 7.5.3 and identifies the amount manufactured and amount approved for distribution. The batch record shall be verified and approved. ISO 13485:2003 requires validation of all process for which the output cannot be verified. These differs from the requirements for special processes contained in the 1996 version of the standard which required those processes to be closely monitored and supervised. For sterile medical devices, ISO 13485:2003 requires the establishment of sterilization batch records. ISO 13485:2003 requires validation of process software before it is put into use.
4.10 Inspection and testing [title only] **4.10.1 General**	7.1 + 8.1	

Clauses in ISO 9001:1994	Corresponding clauses in ISO 13485:2003	Significant differences
4.10.2 Receiving inspection and testing	7.4.3 + 8.2.4	ISO 13485:2003 treats the acceptance activities generally, while ISO 13485:1996 broke acceptance activities into receiving, in-process, and final categories. ISO 13485:2003 treats verification of purchased product as a separate item. ISO 13485:1996 allowed for the use of incoming materials prior to verification as long as the product was properly identified to facilitate recall or replacement. ISO 13485:2003 allows for release according to planned arrangement, which may allow for such release prior to verification.
4.10.3 In-process inspection and testing	8.2.4	
4.10.4 Final inspection and testing	8.2.4	
4.10.5 Inspection and test records	7.5.3 + 8.2.4	
4.11 Control of inspection, measuring and test equipment [title only] **4.11.1 General**	7.6	ISO 13485:2003 explicitly requires the confirmation that software used to control or as part of inspection, measurement, or testing is appropriate for the task it is asked to do.
4.11.2 Control procedure	7.6	ISO 13485:2003 requires the organization to check the validity of previous test results when the measurement or test equipment is found to be out of specification. The organization must record these activities and take appropriate action with respect to the equipment and affected product.
4.12 Inspection and test status	7.5.3	
4.13 Control of nonconforming product [title only] **4.13.1 General**	8.3	
4.13.2 Review and disposition of nonconforming product	8.3	

Clauses in ISO 9001:1994	Corresponding clauses in ISO 13485:2003	Significant differences
4.14 Corrective and preventive action [title only] **4.14.1 General**	8.2.1 + 8.5.1 + 8.5.2 + 8.5.3	
4.14.2 Corrective action	8.5.2	
4.14.3 Preventive action	8.5.3	
4.15 Handling, storage, packaging, preservation and delivery [title only] **4.15.1 General**	6.4 + 7.5.3.1 + 7.5.5	
4.15.2 Handling	7.5.5	
4.15.3 Storage	7.5.5	
4.15.4 Packaging	7.5.1.1 + 7.5.5	ISO 13485:2003 no longer contains the requirement contained in the 1996 version which required the recording of the name of the persons who performed the final labelling operation on active and nonactive implantable medical devices.
4.15.5 Preservation	7.5.5	
4.15.6 Delivery	7.5.1 + 7.5.3.2.2	
4.16 Control of quality records	4.2.4 + 7.5.1.1	
4.17 Internal quality audits	8.2.2 + 8.2.3	
4.18 Training	6.2.2	ISO 13485:2003 alerts organizations that national or regional regulations might require the establishment of documented procedures for the identification of training needs. ISO 13485:1996 required such documented procedures. ISO 13485:2003 requires the organization to evaluate the effectiveness of its training activities. ISO 13485:2003 requires that personnel understand the relevance of their activities on the achievement of quality objectives.

Clauses in ISO 9001:1994	Corresponding clauses in ISO 13485:2003	Significant differences
4.19 Servicing	7.5.1	
4.20 Statistical techniques [title only] **4.20.1 Identification of need**	8.1 + 8.2.3 + 8.2.4 + 8.4	
4.20.2 Procedures	8.1 + 8.2.3 + 8.2.4 + 8.4	

Bibliography

NOTE ISO TC 210/WG1 does not endorse the content of any of the following standards or guidance documents. They are offered by way of providing additional information relating to requirements of ISO 13485. ISO 16142 may also be consulted as a source of additional standards in support of recognized essential principles of safety and performance of medical devices that might be of assistance.

[1] ISO 9001:2000, *Quality management systems — Requirements*

[2] ISO 9004:2000, *Quality management systems — Guidelines for performance improvements*

[3] ISO 10005:1995, *Quality management — Guidelines for quality plans*

[4] ISO 10007:2003, *Quality management systems — Guidelines for configuration management*

[5] ISO 10012:2003, *Measurement management systems — Requirements for measurement processes and measuring equipment*

[6] ISO/TR 10013:2001, *Guidelines for quality management system documentation*

[7] ISO/TR 10017:2003, *Guidance on statistical techniques for ISO 9001:2000*

[8] ISO 11134:1994, *Sterilization of health care products — Requirements for validation and routine control — Industrial moist heat sterilization*

[9] ISO 11135:1994, *Medical devices — Validation and routine control of ethylene oxide sterilization*

[10] ISO 11137:1995, *Sterilization of health care products — Requirements for validation and routine control — Radiation sterilization*

[11] ISO 11607:2003, *Packaging for terminally sterilized medical devices*

[12] ISO 11737-1:1995, *Sterilization of medical devices — Microbiological methods — Part 1: Estimation of population of microorganisms on products*

[13] ISO 12891-1:1998, *Retrieval and analysis of surgical implants — Part 1: Retrieval and handling*

[14] ISO 13408-1:1998, *Aseptic processing of healthcare products — Part 1: General requirements*

[15] ISO/TS 13409:2002, *Sterilization of health care products — Radiation sterilization — Substantiation of 25 kGy as a sterilization dose for small or infrequent production batches*

[16] ISO 13683:1997, *Sterilization of health care products — Requirements for validation and routine control of moist heat sterilization in health care facilities*

[17] ISO 14155-1:2003, *Clinical investigation of medical devices for human subjects — Part 1: General requirements*

[18] ISO 14160:1998, *Sterilization of single-use medical devices incorporating materials of animal origin — Validation and routine control of sterilization by liquid chemical sterilants*

[19] ISO 14644-1:1999, *Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness*

[20] ISO 14644-2:2000, *Cleanrooms and associated controlled environments — Part 2: Specifications for testing and monitoring to prove continued compliance with ISO 14644-1*

[21] ISO14644-3:—[1] *Cleanrooms and associated controlled environments — Part 3: Test methods*

[22] ISO 14644-4:2001, *Cleanrooms and associated controlled environments — Part 4: Design, construction and start-up*

[23] ISO 14644-5:2004, *Cleanrooms and associated controlled environments — Part 5: Operations*

[24] ISO 14644-6:—[1], *Cleanrooms and associated controlled environments — Part 6: Vocabulary*

[25] ISO 14644-7:2004, *Cleanrooms and associated controlled environments — Part 7: Separative devices (clean air hoods, gloveboxes, isolators and mini-environments)*

[26] ISO 14644-8:—[1], *Cleanrooms and associated controlled environments — Part 8: Classification of airborne molecular contamination*

[27] ISO 14937:2000, *Sterilization of health care products — General requirements for characterization of a sterilizing agent and the development, validation and routine control of a sterilization process for medical devices*

[28] ISO 14971:2000, *Medical devices — Application of risk management to medical devices*

[29] ISO 15223:2000, *Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied*

[30] ISO/TR 16142:1999 *Medical devices — Guidance on the selection of standards in support of recognized essential principles of safety and performance of medical devices.*

[31] ISO 19011:2002, *Guidelines for quality and/or environmental management systems auditing*

[32] ISO Handbook, 2nd Edition*, ISO 9001 for Small Businesses — What to do*

[33] *ISO 9000 Introduction and Package module*

[34] EN 724:1994, *Guidance on the application of EN 29001 and EN 46001 and of EN 29002 and EN 46002 for non-active medical devices*

[35] EN 928:1995, *In vitro diagnostic systems — Guidance on the application of EN 29001 and EN 46001 and of EN 29002 and EN 46002 for in vitro diagnostic medical devices*

[36] EN 980:2003*, Graphical symbols for use in the labelling of medical devices*

[37] EN 50103:1995, *Guidance on the application of EN 29001 and EN 46001 and of EN 29002 and EN 46002 for the active (including active implantable) medical device industry*

[38] Global Harmonization Task Force (GHTF) — Study Group 3 (SG3), Document No. N99-8, dated June 29, 1999, *Guidance On Quality Systems For The Design And Manufacture Of Medical Devices*

[39] Global Harmonization Task Force (GHTF) — Study Group 3 (SG3), Document No. N99-9, dated , June 29, 1999, *Design Control Guidance For Medical Device Manufacturers*

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