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Quality systems — Medical devices — Guidance on the application of ISO 13485 and ISO 13488

Systèmes qualité — Dispositifs médicaux — Lignes directrices pour l'application de l'ISO 13485 et l'ISO 13488

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Contents

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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 3.

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.

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

Annexes A and B of this International Standard are for information only.

Introduction

This International Standard provides guidance to assist in the development, implementation, maintenance and improvement of medical device related quality systems that meet the requirements of ISO 13485 and ISO 13488. These standards specify, in conjunction with ISO 9001 and ISO 9002 respectively, the quality system requirements for medical devices (see Table A.1 in annex A). For this reason, this International Standard also contains guidance applicable to medical devices based on the generic requirements of ISO 9001 and ISO 9002. ISO 13488 differs from ISO 13485 in that the former does not contain requirements for design control. This International Standard also gives guidance on ways to meet globally harmonized regulatory quality system requirements for medical devices.

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

As used in this International Standard, the term “regulatory requirement” includes any part of a law, ordinance, decree or national and/or regional regulatory requirement which applies to quality systems of medical device manufacturers.

Quality systems — Medical devices — Guidance on the application of ISO 13485 and ISO 13488

1 Scope

This International Standard provides guidance for the application of the requirements for medical device quality systems contained in ISO 13485 and ISO 13488. It does not add to, or otherwise change, the requirements of ISO 13485 and ISO 13488. This guidance can be used to better understand alternative methods and approaches among many (not specifically included here) for applying the requirements of ISO 13485 and ISO 13488.

The guidance provided by this International Standard has value for:

— suppliers seeking to implement and maintain quality systems that comply with ISO 13485 and ISO 13488;

— organizations having the responsibility to assess the successful implementation and maintenance of such quality systems; and

— regulatory bodies seeking to enforce regulatory requirements based on the requirements of ISO 13485 and ISO 13488.

These organizations and regulatory bodies should understand the benefits of the guidance given in this International Standard and the special considerations associated with the use of this guidance.

a) For suppliers

The guidance given in this International Standard is applicable to the design, development (ISO 13485 only), production, installation, and servicing of medical devices of all kinds. It describes concepts and methods which can be considered by suppliers who are establishing and maintaining quality systems.

Special considerations: The supplier has the responsibility for determining which of the guidance contained in this International Standard is relevant to its operations and will be incorporated in its quality system. The supplier should understand that if it voluntarily incorporates guidance from this International Standard into its quality system, the guidance needs to be followed, consistent with the requirements of the supplier's quality system. Failure to comply with those incorporated guidance can be determined to be a deficiency by those charged with the responsibility of conducting internal or external quality system assessments, audits and inspections.

The supplier should also understand that its quality system cannot be found deficient for failure to incorporate guidance contained in this International Standard which the supplier determines are not relevant to its operations.

b) For quality system assessors, notified bodies, regulatory enforcement bodies

Guidance contained in this International Standard can be useful as background information for those representing quality system assessors, notified bodies and regulatory enforcement bodies.

Special considerations: The guidance contained in this International Standard should not be used for identifying specific deficiencies of quality systems, unless such guidance is voluntarily incorporated by the supplier into the documentation describing and supporting the supplier's quality system, or unless such guidance is specifically made part of the regulatory requirements relevant to the supplier's operation.

2 Normative references

The following normative documents contain provisions which, through reference in this text, constitute provisions of this International Standard. For dated references, subsequent amendments to, or revisions of, any of these publications do not apply. However, parties to agreements based on this International Standard are encouraged to investigate the possibility of applying the most recent editions of the normative documents indicated below. For undated references, the latest edition of the normative document referred to applies. Members of ISO and IEC maintain registers of currently valid International Standards.

ISO 8402:1994, *Quality management and quality assurance — Vocabulary.*

ISO 9000-2:1997, *Quality management and quality assurance standards — Part 2: Generic guidelines for the application of ISO 9001, ISO 9002 and ISO 9003.*

ISO 9001:1994, *Quality systems — Model for quality assurance in design, development, production, installation and servicing.*

ISO 9002:1994, *Quality systems — Model for quality assurance in production, installation and servicing.*

ISO 13485:1996, *Quality systems — Medical devices — Particular requirements for the application of ISO 9001.*

ISO 13488:1996, *Quality systems — Medical devices — Particular requirements for the application of ISO 9002.*

3 Terms and definitions

For the purposes of this International Standard, the tems and definitions given in ISO 8402, ISO 13485 and ISO 13488 apply, with the exception of “product”, where the definition in ISO 9001 and ISO 9002 applies.

NOTE The terms provided in annex B should be regarded as generic, as definitions provided in national regulatory requirements may differ.

4 Quality system requirements

4.1 Management responsibility

4.1.1 Quality policy

There is no specific medical device guidance beyond the generic guidance given in 4.1.1 of ISO 9000-2:1997.

4.1.2 Organization

4.1.2.1 Responsibility and authority

The generic guidance given in 4.1.2.1 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

When necessary, deputies for personnel having the responsibility and authority to make decisions that control the elements of the quality system and processes should be identified and be capable of assuming the responsibilities.

4.1.2.2 Resources

There is no specific medical device guidance beyond the generic guidance given in 4.1.2.2 of ISO 9000-2:1997.

4.1.2.3 Management representative

There is no specific medical device guidance beyond the generic guidance given in 4.1.2.3 of ISO 9000-2:1997.

4.1.3 Management review

There is no specific medical device guidance beyond the generic guidance given in 4.1.3 of ISO 9000-2:1997.

4.2 Quality system

4.2.1 General

There is no specific medical device guidance beyond the generic guidance given in 4.2.1 of ISO 9000-2:1997.

4.2.2 Quality system procedures

There is no specific medical device guidance beyond the generic guidance given in 4.2.2 of ISO 9000-2:1997.

4.2.3 Quality planning

The generic guidance given in 4.2.3 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

The file referred to in 4.2.3 of ISO 13485 is sometimes referred to by different terms (see annex B).

4.3 Contract review

4.3.1 General

There is no specific medical device guidance beyond the generic guidance given in 4.3.1 of ISO 9000-2:1997.

4.3.2 Review

There is no specific medical device guidance beyond the generic guidance given in 4.3.2 of ISO 9000-2:1997.

4.3.3 Amendment to contract

There is no specific medical device guidance beyond the generic guidance given in 4.3.3 of ISO 9000-2:1997.

4.3.4 Records

There is no specific medical device guidance beyond the generic guidance given in 4.3.4 of ISO 9000-2:1997.

4.4 Design control

4.4.1 General

The generic guidance given in 4.4.1 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

The extent of medical device evaluations, verifications and validations should be commensurate with the nature of the risks and the benefits associated with the use of the medical device.

Risk analysis using techniques such as fault tree analysis (FTA) and failure mode and effects analysis (FMEA) can be utilized at various stages of the design process. Such techniques can also help to determine the nature of possible design flaws and the risks associated with them. They may also identify changes required to increase reliability and safety. The application of risk analysis techniques are described in ISO 14971-1 (see Bibliography).

Design-related documents and records should form part of a file as described in row A of annex B.

4.4.2 Design and development planning

The generic guidance given in 4.4.2 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

Design and development planning can ensure that the design process is appropriately managed and that design objectives are met. The method chosen and the detail will vary depending on the complexity of the project and the level of risk associated with the medical device.

Generally, the design plan includes the specific quality practices, assessment methodology, documentation requirements, record keeping, resources and the sequence of activities relevant to a particular design or design category and the timing and content of design review. The plan should reference applicable codes, standards, regulatory requirements, specifications and acceptance criteria. Design activities should be specified to the level of detail necessary for carrying out the design process in a manner that permits the generation of objective evidence that the design activity has been completed. Design plans do not have to be elaborate. They may be as simple as a flow chart showing steps to be taken and who is responsible for taking them. If appropriate, applicable codes, standards, regulatory requirements, specifications and acceptance criteria can be considered for inclusion in the plan.

The decision process in deciding whether a clinical investigation and/or literature search as part of the clinical evaluation is necessary should be addressed (see note in 4.4.8 of ISO 13485:1996).

4.4.3 Organizational and technical interfaces

The generic guidance given in 4.4.3 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

For medical devices, the design process typically involves more than just design personnel. Other internal groups may also play a role. These include, but are not limited to, Marketing and Sales, Production, Testing, Purchasing, Quality Assurance, Clinical Affairs, and Regulatory Affairs. In addition, groups external to the device manufacturer may also be involved.

Operational procedures may be required to ensure that information from all levels of the organization, as required, is available to participants in the design activity. Failure to exercise the interfaces at all levels, when appropriate, can result in the organization's inability to use them when necessary.

4.4.4 Design input

The generic guidance given in 4.4.4 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

The design inputs should be specified to the level necessary to permit the design activity to be carried out effectively and to provide a consistent basis for design decisions, design verifications and design validation.

Examples of design inputs that should be defined, reviewed, approved and recorded by the supplier, include:

— intended clinical use;

— customer requirements, e.g. intended device performance (indications for use) and limits;

— performance requirements, e.g. during normal use, storage, handling and maintenance;

— specifications for various forms of labelling, e.g. instructions for use and servicing;

— environmental, safety and regulatory requirements;

— ergonomics and other human factors;

— other relevant standards;

— systems elements when a medical device is specified for use in combination with another device, e.g. other equipment or accessory. In this case the design input should completely define the interface requirement.

In defining the design inputs, the supplier should consider foreseeable use and misuse of the product and any related needs for specific labelling and customer/user training.

The design input document(s) should be regarded as a living document(s) and updated and reissued as necessary upon completion of design reviews. A record should be kept of all “agreed to” changes to the design input as it evolves during the design process.

The design transfer process should flow more smoothly if, during the design input stage, consideration is given to eventual production (producibility, parts/materials availability, production equipment needs, operator training etc.) and possible conformity assessment requirements (procedures, methods, equipment).

4.4.5 Design output

The generic guidance given in 4.4.5 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

Design outputs can also include specifications for:

— raw materials;

— component parts;

— sub-assemblies;

— finished devices;

— product and process software;

— quality assurance procedures, including acceptance criteria;

— manufacturing and inspection procedures;

— packaging and labelling;

— identification and traceability procedures;

— installation and servicing procedures and materials.

As part of, or in addition to, the design output documents, it is common practice to maintain a record/file to demonstrate that each design was developed and verified in accordance with the approved design plan.

The transfer of a design to production should occur after review and approval of specifications and procedures. The adequacy of specifications, methods and procedures can be demonstrated through process validation, including the testing of finished product under actual or simulated use conditions.

4.4.6 Design review

The generic guidance given in 4.4.6 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

In order to assure objectivity, it is advisable to involve one or more individuals, not having direct responsibility for the design activity in question, in the design review. This broader involvement also enables the reviewers to take into account all aspects of the supplier’s interest, e.g. manufacturing, marketing, design, after-sales servicing and support, and the likely medical effectiveness of the design. For medical devices, design reviews should also consider the following.

— Has a risk analysis been carried out to ensure that safety considerations are covered?

— Is the labelling adequate?

— Will the design reasonably accomplish the medical use intended ?

— Is the packaging adequate, particularly for sterile devices?

— Is the sterilization process adequate?

— Is the device compatible with the sterilization method?

At the completion of significant phases of the design process, design output documents should be reviewed and approved by designated functions prior to release for subsequent implementation; this is often accomplished through design review.

The records of design reviews should identify those involved and the decisions reached.

4.4.7 Design verification

The generic guidance given in 4.4.7 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

Once the design is translated into a tangible form, its safety, performance and reliability should be verified for conformance to the design inputs. Such verifications include:

— review of engineering specifications and drawings;

— physical and chemical laboratory testing (bench testing);

— *in vitro* testing;

— *in vivo* testing;

— packaging and labelling review (see 4.15.4).

4.4.8 Design validation

The generic guidance given in 4.4.8 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

Design validation goes beyond the technical issues of verifying that the design output meets the design input, and is intended to ensure that the medical device meets user needs and the intended use. This involves consideration of the knowledge and capabilities of the intended user, the operating instructions, compatibility with other systems, and any restriction on the use of the product.

The medical device units employed for validations should be produced under the conditions specified as “final” for the product, e.g. initial production units. The validation should be conducted under actual or simulated use conditions; this can involve clinical investigations.

4.4.9 Design changes

The generic guidance given in 4.4.9 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

Whether or not the device is currently on the market, the following considerations, among others, should be addressed before permitting a change to an approved design.

— Will the product still conform to the agreed-to product requirements?

— Will the product still conform to the agreed-to product specifications?

— Will the intended use be affected?

— Will different components of the product or system be affected by the change?

— Will there be a need for further interface design; i.e. physical contact with other components in a product or system?

— Will the change create problems in manufacture, installation or use?

— Will the design still be verifiable?

— Will the change affect the regulatory status of the product?

4.5 Document and data control

4.5.1 General

The generic guidance given in 4.5.1 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

Examples of documents and data which should be subject to formal control procedures are:

— quality manual;
— standard operating procedures, test methods and work instructions;
— technical data, e.g. purchase specifications, drawings, process specifications, packaging/labelling specifications;
— relevant promotional material, user manuals, service manuals, etc.;
— back-up of electronic versions of quality system documents and data.

To the extent applicable, copies of published external standards, regulatory requirements and codes of practice which relate to the quality system or product specification should be controlled in such a way as to identify clearly which version is being used.

4.5.2 Document and data approval and issue

The generic guidance given in 4.5.2 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

The established system for the control of documents and data should:

— include periodic review of documents, if required by the quality system;
— assign responsibilities for preparation, check release and issue of documents;
— require review of all quality related documents for accuracy completeness and correctness before approval and issue;
— identify recipients of controlled copies of documents;
— ensure prompt withdrawal of obsolete copies of controlled documents (see 4.5.2);
— define a method for recording the implementation date of a document change.

Document control procedures may be assisted by the adoption of a consistent structure for the documents within the quality system. These procedures should clearly indicate which document control information should be included in the individual controlled documents. 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, if periodic review is required by the quality system;
— revision history;
— the originator or author;
— the person(s) approving it;
— the person(s) issuing it;
— the distribution;
— pagination; and
— computer file reference, if applicable.

The document control system should allow controlled and non-controlled documents to be distinguished.

Retention of clearly marked obsolete and superseded controlled documents can assist in providing a full picture of the product's life cycle.

4.5.3 Document and data changes

The generic guidance given in 4.5.3 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

Changes to documents and data, including computer-based documents, should be made by authorized personnel (e.g. persons with an access code to the document and data file to be changed). The approval of authorized changes should be identified in the document (or data) or in its change history. Prevention of unauthorized changes to computer-based documents and data can be facilitated by making “read only” copies available to persons who have a need to use them but are not authorized to change them.

4.6 Purchasing

4.6.1 General

The generic guidance given in 4.6.1 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

A supplier can purchase, from a number of sources, products and services which can directly or indirectly affect the safety, effectiveness and general quality of the finished medical device. These products and services typically include:

— raw materials;
— components or sub-assemblies manufactured by others using equipment owned by, and/or materials provided by, the supplier;
— components or sub-assemblies available as standard items from other sources;
— components or sub-assemblies manufactured by others to the supplier’s specifications;
— completed product bearing the mark and/or name of the device manufacturer; this may be ready for sale or require some further processing such as packaging and/or sterilization;
— packaging material either as a standard item or manufactured to the supplier’s specification;
— labelling manufactured to the supplier’s specification;
— services, e.g. machining, heat treating, sterilization, calibration, testing, pest control, waste disposal, cleaning, environmental monitoring, laundry, transport, installation;
— specialist professional advice/consulting services.

4.6.2 Evaluation of subcontractors

The generic guidance given in 4.6.2 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

The term “subcontractor” is taken to include providers to the supplier of materials, components, sub-assemblies, finished medical devices or services.

The selection of potential subcontractors can typically include evaluation of the facilities, capabilities, skills, resources, etc. to demonstrate the subcontractor’s ability to meet the relevant requirements for medical devices.

Acceptable subcontractors should be added to a controlled master list, which may contain the following information:

— company name/address;
— contact persons;
— product or service which may be purchased.

If the supplier purchases sub-assemblies designed by a subcontractor, the supplier may have to obtain information from the subcontractor in order to enable servicing to be carried out by the eventual purchaser of the medical devices.

If the subcontractor delivers finished medical devices to the supplier to distribute under the supplier's name, the supplier should understand any deficiencies in the subcontractor's quality system that should be accommodated by the supplier.

If meeting the specification relies on the level of quality assurance attained by the subcontractors, the supplier and the potential subcontractors should:

— agree on the quality system standards;
— agree on methods of verification;
— make provisions for settlement of disputes about quality.

Where possible, the supplier should obtain agreement from the subcontractor to notify the supplier for approval of process changes that could affect the quality of the purchased product or service. When notified of such changes, the supplier should evaluate their effect on the finished device.

Monitoring of the subcontractor's quality system could involve one or more of the following activities.

a) For a provider of commercially available products:

— periodic inspection of products received;
— monitoring of inspection results;
— accepting certification of the subcontractor's quality system by third parties;
— accepting certificates of conformance and/or of analysis from the subcontractor.

b) For a provider of products to the specification of the supplier, auditing of the quality system by the product supplier may be required in addition to the items listed in a) above.

When designing its monitoring activities, the supplier should consider results of a contractor's third-party certification status, complaint trends and nonconformance history. The frequency of performance monitoring should be defined. Results of monitoring activities should be documented to demonstrate continued use as an acceptable subcontractor. This document should consider results of quality system audits.

Where information confirms the subcontractor does not continue to meet criteria, corrective action should be taken.

Examples of corrective and preventive actions include but are not limited to:

— working with the subcontractor to understand the root cause of the subcontractor failure and to facilitate their corrective and/or preventive action;
— instituting increased inspection and/or acceptance tests;
— increasing audit frequency;
— placing an employee within the subcontractor's operation; and
— selecting an alternative subcontractor.

4.6.3 Purchasing data

The generic guidance given in 4.6.3 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

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

4.6.4 Verification of purchased product

4.6.4.1 Supplier verification at subcontractor's premises

There is no specific medical device guidance beyond the generic guidance given in 4.6.4.1 of ISO 9000-2:1997.

4.6.4.2 Customer verification of subcontracted product

There is no specific medical device guidance beyond the generic guidance given in 4.6.4.2 of ISO 9000-2:1997.

4.7 Control of customer-supplied product

There is no specific medical device guidance beyond the generic guidance given in 4.7 of ISO 9000-2:1997.

4.8 Product identification and traceability

The generic guidance given in 4.8 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

a) Identification

Identification on products permits traceability in two directions: forward to customers; and backward to raw materials, components and processes used in manufacture. The former is important if it is necessary to trace products to the user, e.g. patients or hospitals, and the latter enables investigation of quality problems and feedback for the prevention of nonconforming product.

Identification can be achieved by batch/lot/serial numbers, or by electronic means.

Identification of raw materials, components and finished products is important for a number of reasons, such as:

— control of material throughout manufacture (see 4.9);
— demonstration of product source, status and compliance with safety requirements;
— permitting traceability;
— facilitating fault diagnosis in the event of quality problems.

The extent to which raw materials and components need to be identified and related to the finished product batch/lot or serial number may depend upon a number of factors such as:

— the material involved;
— the type of finished product;
— the effect of failure of finished product or materials used therein;
— specified requirements;
— traceability if necessary;
— design input;
— regulatory requirement.

b) Traceability

The supplier should determine the nature and extent of its traceability activities. Normally, such activities are conducted throughout the production and warehousing process, and up to the point when the product leaves the supplier's possession. The supplier may choose to limit the traceability activities to particular parts of its operation.

Additional guidance for active implantable medical devices and implantable medical devices

A traceability system for implantable and active implantable medical devices is useful because it might not be possible to inspect the device while it is in use. Traceability can, therefore, avoid unnecessary explant of implanted devices through precise identification of those implants which incorporated a subsequently identified faulty component, 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 supplier's possession and the quality system should take account of these as appropriate.

4.9 Process control

The generic guidance given in 4.9 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

Process control can be demonstrated through records that confirm compliance with established procedures, which may include:

— equipment and materials to be used;

— any process validations;

— precautions to be taken;

— step-by-step instructions;

— any in-process quality checks conducted by production personnel;

— process or material change;

— the procedure to be followed in the event of problems with quality;

— the disposition of accepted or rejected products.

The amount of documentation and level of detail should be commensurate with the degree of criticality of the process in achieving the requirements for quality and the degree of personnel training in any particular process control area. The procedure could be in the form of a simple flowchart or a processing sequence combined with a checklist of what is to be checked.

Procedures or instructions may be presented in graphic or audio-visual form. Frequently a simple set of pictures can convey the requirements more accurately than a lengthy detailed description. The supplier should make maximum use of existing documentation (e.g. engineering drawings, production schedules, internal work orders) to avoid an excess of forms, duplication of information and effort.

Whenever processes are computer-controlled, the adequate training of individuals, the availability of up-to-date databases and the adherence to systematic procedures are critical in order to meet requirements consistently.

Work in progress should be identified and/or segregated to avoid product mix-up (see 4.8). For small parts, for bulk manufacture and where the parts cannot be marked, the bulk containers and/or process equipment should be identified to indicate the product and/or batch and its status. This identification need not be the code used on the finished product but it should be easily related to the code. Any previously used labels should be removed or obliterated.

Ancillary materials should be adequately identified and labelled. Ancillary 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. Containers for temporary storage and handling should be suitably constructed and cleaned as necessary.

Equipment should be designed and selected so that product and process specifications are met. Equipment installation and operational performance qualification should be conducted. New equipment and significantly modified equipment should be evaluated to verify that it meets purchasing/design specifications and is capable of operating within its defined limits and the process operating limits.

Some processes require that operators have extra training and or be specially qualified, or the process itself should have specific approval, for example, as follows.

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

— The introduction of a new or significantly changed manufacturing process, including any new manufacturing and test methods, should be evaluated to determine whether process validation is necessary.

See additional guidance for special processes and additional guidance for sterile medical devices, below, for further elaboration on this feature.

a) Personnel

Persons, e.g. permanently employed personnel, temporary personnel (including subcontractors) and visitors, who can come in contact with product or its environment should be suitably clothed, clean and in good health if these factors could adversely affect the product, because individuals spread both micro-organisms and particles which constitute contamination risks.

Persons who have a medical condition which may 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 products to be supplied:

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

Temporary personnel, such as those involved in maintenance, cleaning, repair, etc., 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.

b) Environmental control in manufacture

The supplier should ensure that 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.

The following are examples of items that should be considered for control:

— lighting;
— temperature;
— an alarm system in case of accident or rapid and/or dangerous changes in environmental conditions.

Special consideration should be paid to microbial contamination levels. This is of particular importance in the manufacture of sterile products and therefore these should be produced in a specific controlled environment unless the microbial contamination can be reduced to a known, controlled level prior to sterilization and the particulate level has little or no significance for the clinical application.

The supplier should ensure that where environmental conditions at the manufacturing site could have an adverse effect on the fitness of material in use, these environmental conditions are controlled to limit contamination of the material and to provide proper conditions for all operations performed. Any environmental control system should be periodically inspected to verify that the system is functioning properly. Such systems and inspections should be documented.

The following should be considered specifically for environmentally controlled "clean room" areas.

— The provision of filtered air. The air pressure should be maintained above that of surrounding areas to prevent the ingress of unfiltered air or, if appropriate, below that of surrounding areas if a negative pressure is required (e.g. for handling of pathogens). Windows, if present, should be sealed. Doors should be tight fitting and self-closing. Air locks may be required to maintain the required pressure differentials. Openings (other than emergency exits) should not be sited near areas subject to extremes of temperature or give access to the exterior.

The required cleanliness level of the air should be established and will depend upon the nature of the work, the product and the degree of product handling and exposure. Work stations may be used to provide a higher standard of air cleanliness. Air cleanliness may be affected by products or production process and control should be such as

to prevent, as far as is reasonable practicable, any significant increase in the existing level of contamination. The control and monitoring of the "clean room" environment should be in accordance with documented procedures.

— They should not be used for general storage or as a thoroughfare either for personnel of for transport of unrelated material.

— The avoidance of dust and the facilitation of cleaning. Walls, floors, furniture and other surfaces should be of a smooth, non-shedding resistant finish able to withstand frequent cleaning. Coving is frequently used at the junctions between walls, floors and ceilings to eliminate dust traps. Care should be taken to ensure that contamination sources are not inadvertently created.

— Process materials such as adhesives, water or compressed air, should be controlled and verified periodically to ensure conformance to microbial and particulate contamination specifications in any process.

Documented cleaning procedures for all product-handling areas and equipment include:

— instructions for periodic cleaning, and

— instructions for effective decontamination following accidents and prior to equipment service.

When cleaning operations are carried out by a subcontractor, a written contract specifying the limits of responsibility of the device manufacturer and the subcontractor should be considered. This contract should include details of the documented cleaning procedure and specify the training to be given to cleaning staff (see also 4.6.2, 4.6.3 and 4.18).

Changing rooms and toilets should be provided as necessary and be segregated from production areas. They should be regularly cleaned and disinfected.

Changing areas and washing facilities should be adjacent at the lowest end of any air pressure gradient and maintained in a clean and tidy condition. Microbial contamination should be minimized by providing, for example: sinks without traps, plugs or overflows; taps or wash basins, or soap or hand detergent dispensers which are not hand operated; hand drying facilities (multiple-use towels should not be provided because they can become a significant source of microbiological contamination); nail brushes if used should be either clean and single-use or maintained in a hygienic condition, e.g. by sterilization; mirrors to assist in correct adjustment of head covering.

Other environmental features which can affect the quality of product include:

— general site cleanliness;

— special testing and laboratory facilities.

In cases where the fitness of a product for use could be affected by eating, drinking, smoking, the application of cosmetics or the wearing of jewelry by personnel, the supplier should not allow such practices in product-sensitive areas.

c) Cleanliness of product

The supplier should establish and maintain documented procedures for the protection of product against contamination by any substance which could reasonably be expected to have an adverse affect.

Cleaning processes may be required to remove ancillary materials and/or particulate contamination. Cleaning processes should be validated as to the effectiveness of the process for removing the contamination in accordance with a documented procedure. Records of validation should be retained (see 4.16). The cleaning process should be routinely monitored in accordance with documented procedures. Records of this monitoring should be maintained (see 4.16).

When a cleaning process is intended to remove microbiological contamination, the validation protocol, the results of the validation and the final operating procedure should be reviewed or approved by a person trained and qualified in microbiology. Where the effectiveness of cleaning is monitored microbiologically, the methods should be approved, and the results reviewed, in the same manner as the validation protocol and results.

d) Maintenance

Manufacturing equipment should be designed, constructed, correctly installed and located to facilitate maintenance, adjustment, cleaning and/or sterilization.

The supplier should ensure that, where applicable, any inherent limitations or allowable tolerances of manufacturing equipment should be documented on or near the equipment.

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

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

e) Installation

Installation of a medical device is the activity of putting the device into service in the location where it will be used. The activity might involve permanent connection to services, e.g. electrical supply, plumbing, waste disposal. Final testing of installed 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.

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

In certain cases (e.g. when required by a regulatory requirement or when performance parameters of a medical device have to be controlled) the supplier should provide instructions that allow the installer to confirm correct operation of the device. The results of installation or commissioning tests should be recorded.

f) Computer software used in process control

All software that is purchased, developed, maintained, or modified for process control purposes should be controlled. Software and changes to software may be controlled in the same manner as documents; i.e. the software program is formally approved by a documented system prior to issue, a master copy of the original program is retained, and any changes to software programs are validated, approved and documented (see 4.5).

Where automated production or process control systems are used, associated software should be validated for the intended application.

ISO 9000-3 (see Bibliography) may be used as a reference for software development.

Additional guidance for special processes

Special processes as indicated in ISO 9000-2 need special consideration. In the medical device industry, these considerations often lead to process validation.

Process validation is the documented procedure and process for obtaining, recording and interpreting the results required to establish that a process will consistently yield product complying with predetermined specifications and its intended use. Process validation covers three activities:

— verification of process installation and setup;

— qualification of process capability; and

— qualification of its long-term stability.

Most processes will only require verification of process installation and setup and qualification of short-term process capability in order to demonstrate the capability of the process to meet requirements. This should be considered adequate for most types of processes because the product can be fully verified.

However for special processes, since the product cannot be fully verified, process validation should demonstrate with a high degree of assurance that the process will meet requirements under the full range of process operating conditions.

When validation is performed for a special process, either by the supplier or subcontractor, the validation should include the following:

— 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;
— adequate control of any specific environmental parameters;
— the certification records maintained for personnel, processes and equipment, as appropriate;
— the appropriateness of the process result.

Records should provide objective evidence that validation procedures were followed.

Additional guidance for sterile medical devices

Sterilization is an example of a special process because the result of the process cannot be verified by inspection and testing of the product. 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 product is sterile. It may also be important that attention is given to the microbiological status of incoming raw materials and their subsequent storage, and to the control of the environment in which the product is manufactured, assembled and packaged. Also refer to ISO 11134, ISO 11135 and ISO 11137 (see Bibliography).

4.10 Inspection and testing

4.10.1 General

The generic guidance given in 4.10.1 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

Documented procedures for inspection and testing activities should include details of test methods, equipment to be used, and acceptance/rejection criteria.

The supplier‘s procedures should ensure the objectivity of the inspection and test results, including situations where inspection and testing is carried out by production personnel.

4.10.2 Receiving inspection and testing

The generic guidance given in 4.10.2 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

If the purchased items are claimed to conform to the subcontractor’s specification, the supplier should check that the items meet the agreed specification. This check may be accomplished by various approaches, such as certification of subcontractors, certificates of conformance, skip lot testing, 100 % or sampling inspection, as determined by the requirements of the supplier’s quality system.

4.10.3 In-process inspection and testing

The generic guidance given in 4.10.3 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

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 may be used both for process control and for the early identification of nonconforming product.

4.10.4 Final inspection and testing

The generic guidance given in 4.10.4 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

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 conformance for all designated release criteria that have not been confirmed through previous inspection and testing. Final testing may include, where practical, testing under simulated or actual conditions of use of products selected from a lot or batch.

In the case of equipment which is 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 are not necessarily carried out by the supplier, but the device manufacturer should ensure the availability of all necessary information about the inspection and test procedure and the results expected (see also 4.9).

Additional guidance for active implantable and implantable devices

For an implantable medical device, records should be made of the inspection of each completed sub-assembly, and these should be traceable from the manufacturing record.

4.10.5 Inspection and test records

The generic guidance given in 4.10.5 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

As applicable, records may:

— identify the inspection/test procedure(s) and revision level used (see also 4.5);

— 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 items examined and the number accepted;

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

4.11 Control of inspection, measuring and test equipment

4.11.1 General

The generic guidance given in 4.11.1 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

In addition to the calibration of test equipment, where it is necessary to have recording or controlling instruments on manufacturing equipment, these also should be calibrated initially and at defined intervals in accordance with a planned schedule.

The limits of accuracy of the calibration should exceed the limits of accuracy of the test for which the calibrated equipment is being used.

Some inspection, measurement and test equipment are not used for purposes that affect the quality of the product or service provided by the supplier. As a result the following examples are not necessarily part of the supplier's control programme:

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

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

— instruments that may be attached to process equipment, but are not used for process control.

Some inspection, measurement and test equipment which requires initial calibration or certification may not need to be included in the control programme. Examples of such equipment are:

— mercury-in-glass thermometers;

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

Inspection, measurement and test materials intended to provide a qualitative reference should be stored and maintained in a location that does not compromise the integrity of the material.

The following software applications related to the control and/or calibration of inspection, measuring and test equipment should be validated [see also 4.9 f)]:

— for controlling the instrument calibration process;

— for determining the control or calibration status of instruments based on the data generated during the process;

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

4.11.2 Control procedure

There is no specific medical device guidance beyond the generic guidance given in 4.11.2 of ISO 9000-2:1997.

4.12 Inspection and test status

The generic guidance given in 4.12 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

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

4.13 Control of nonconforming product

4.13.1 General

The generic guidance given in 4.13.1 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

In a quality system, process control (see 4.9) and inspection and testing (see 4.10) are the most likely internal sources to identify nonconforming product before distribution.

4.13.2 Review and disposition of nonconforming product

The generic guidance given in 4.13.2 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

Review procedures should ensure that the nonconforming product is assessed against the originally specified requirements to determine whether those specified requirements need to be revised.

Review procedures should ensure that the risk of the nonconforming product is assessed against the originally specified requirements to determine whether those specified requirements need to be revised. Where such changes are indicated, the supplier's quality system should specify the functions and/or personnel that should be notified.

If a nonconforming product is allowed to be released under concession, is reworked, or is destroyed, this should be recorded (see 4.16). Any concession should be adequately justified, and the justification should be recorded. It is important to ensure that any concession does not increase the safety risk above that allowed by regulatory requirements or internal quality standards.

Consideration should be given to the need for an investigation into the cause of the nonconformance. Records should be retained of:

— any investigation into the cause of the nonconformance;
— corrective action taken;
— disposition.

a) Rework (reprocessing)

The control of rework (reprocessing) is an important feature of the disposition of nonconforming product.

Reworking of products should be in accordance with an authorized and documented procedure which describes work instructions, equipment, method of inspection and tests to be used. Any rework should be documented and recorded.

The reworked products should meet the original, or formally revised, specification. Any previous inspection and test which could have been invalidated by the reworking should either be repeated, or the results from the original inspection and test should be confirmed as still being applicable.

Changes to approved reworking procedures should be subject to formal approval.

b) Returned products

Any product returned to the supplier should be treated as nonconforming product until it has satisfied a documented acceptance procedure. For any returned product for which there is a risk of biological contamination, consideration should be given to hazardous materials regulatory requirements and to ISO 12891-1 (see Bibliography).

c) Disposal of nonconforming product

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;
— it is disposed of safely.

4.14 Corrective and preventive action

4.14.1 General

The generic guidance given in 4.14.1 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

NOTE The term "recall" has different definitions in different national and regional regulatory systems. Consequently, its use in this subclause has been avoided in favour of terminology describing the field corrective activity.

Corrective and preventive action should be implemented without undue delay. The procedures for dealing with nonconformities discovered in product which has already been shipped can include, amongst others if necessary, taking such actions as:

— withdrawing products from sale;

— withdrawing products from distribution;

— giving advice to customers (this may 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);

— in extreme cases, a request for the physical return or destruction of products.

4.14.2 Corrective action

The generic guidance given in 4.14.2 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

The supplier's corrective action procedures should clearly establish responsibility for taking corrective action, how this action will be carried out and by when, and verification of the effectiveness of the corrective action. An important element in the programme is the dissemination of quality problem information to those directly responsible for ensuring quality.

Additional sources of data on which to base corrective actions are:

— experience from the post-production phase;

— reports from the marketing function;

— reports from authorized representatives;

— returned product [see 4.13.2 b)];

— solicited information on new or modified products;

— published literature;

— published reports of failures of similar products.

Key features of the documented procedure(s) necessary to implement corrective action effectively should include:

— clear and accurate identification of the product lot(s) concerned (as a result of comprehensive lot history documentation);

— the ability to identify in a timely manner and take appropriate action concerning related products/components;

— the ability to identify in a timely manner the initial recipient(s) [consignee(s)] of defective product;

— a summary of activities, findings and recommendations associated with the corrective action taken, prepared by a designated person able to assess the efficiency of any advisory notice;

— an adequate and effective system for controlling corrective action, reviewed and challenged at defined intervals;

— clearly describe course(s) of action with designated responsible persons identified.

a) Customer complaints

Any customer complaint received by the supplier on a product should be evaluated. Customer's complaints and warranty claims are the most common external indications of product deficiency that might be subject to corrective action.

In evaluating the complaint, it should be considered whether the product fails to conform to its specification or conforms with its specifications but nevertheless causes problems in use. For instance, a complaint with a product conforming to its specifications may be caused by a design fault. Complaints related to handling may indicate inadequate instructions for use.

Regulatory requirements may place requirements on suppliers to monitor the use of their products and inform regulatory authorities of certain defined experience in use.

The supplier should formally designate a person(s) (by role or position) to collect and coordinate all written and oral customer complaints about 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 documented complaints system should cover the following:

— establishing responsibility for operating the system;
— evaluation of the complaint;
— records and statistical summaries, enabling the major causes of complaints to be determined;
— any corrective action;
— segregation and disposition of customer returns and faulty stock (special attention may need to be given to decontamination);
— filing of customer correspondence and other relevant records (the retention time for these should be defined).

The records of complaint investigations should contain enough information to show that the complaint was properly reviewed, for example a determination of:

— whether there was an actual product failure to perform per specifications;
— whether the product was being used to treat or diagnose a patient;
— whether a death, injury or serious illness was involved, the relationship, if any, to the reported incident or adverse event.

An investigation record typically includes:

— the name of the product;
— the date the complaint was received;
— any control number used;
— the name and address of the complainant;
— the nature of the complaint;
— the results of the investigation, including:
— the corrective action taken;
— the justification for no action being taken;
— the dates of the investigation;
— the name of the investigator;
— the reply (if any) to the complainant.

b) Advisory notices

National or regional regulatory requirements may require that advisory notices be reported to the regulatory authorities.

The nature and seriousness of the hazard or nonconformity, the intended use of the product, 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 local or national authorities. These factors will also determine the speed and extent of the action.

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

— the management arrangements that 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, for example, rework, re-package, scrap;
— the communication system (which includes the necessity to report to local or national authorities), the points of contact and methods of communication between the supplier and national authorities.

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;
— advice of possible hazards and consequent action to be taken.

When a product is returned to the supplier, the progress of agreed corrective action should be monitored and, where appropriate, the quantities of product physically returned to the medical device manufacturer or scrapped locally or corrected locally should be reconciled.

4.14.3 Preventive action

The generic guidance given in 4.14.3 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

Sources of information for initiating preventive actions include:

— purchased items rejected on receipt, needing rework;
— difficulties with subcontractors (see 4.6.2);
— in-process problems, rework rates, wastage levels;
— final inspection failures;
— customer complaints and customer surveys;
— warranty claims;
— service reports;
— the need for concessions.

4.15 Handling, storage, packaging, preservation and delivery

4.15.1 General

There is no specific medical device guidance beyond the generic guidance given in 4.15.1 of ISO 9000-2:1997.

4.15.2 Handling

There is no specific medical device guidance beyond the generic guidance given in 4.15.2 of ISO 9000-2:1997.

4.15.3 Storage

There is no specific medical device guidance beyond the generic guidance given in 4.15.3 of ISO 9000-2:1997.

4.15.4 Packaging

The generic guidance given in 4.15.4 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

During storage and transportation up to the point of use, the packaging of medical devices is intended to provide appropriate protection against damage, deterioration or contamination of the product.

Before any packaging of the product is adopted, the appropriateness of the packaging for its intended use should be validated. Validation activities include defining the packaging materials, packaging process conditions, storage and handling conditions to be used during manufacture, warehousing and distribution. The following should be considered if applicable:

— bacterial barrier properties of packaging materials for sterile devices;

— integrity of the primary container/package to maintain sterility or maintain cleanliness as required and to prevent damage;

— compatibility with the device and packaging process;

— compatibility with the sterilization process, where applicable;

— journey hazard trials/shipping tests.

Labelling

The content of labels may be specified in regulatory requirements, general standards or product standards. Where product 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 internationally agreed symbols can reduce translation problems.

The risk of labelling and packaging errors may 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;

— the destruction of unused batch-coded materials on completion of packaging and labelling;

— use of roll-feed labels;

— use of 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;

— proper storage of labels in areas of restricted access.

4.15.5 Preservation

The generic guidance given in 4.15.5 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

The identification of items with a limited shelf life, or which require special protection during storage and transportation, is important to ensure that such items are not used if their shelf lives have expired.

The supplier therefore should have a procedure which identifies the shelf life applicable under specified storage conditions.

4.15.6 Delivery

There is no specific medical device guidance beyond the generic guidance given in 4.15.6 of ISO 9000-2:1997.

4.16 Control of quality records

The generic guidance given in 4.16 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

Quality records can be divided into three broad categories:

a) Preproduction records (those which relate to the design, and the purchasing, manufacturing, quality assurance processes, affecting all products of a particular type)

Examples of records in this category include:

— design documentation (see annex B);
— records of process validation and revalidation;
— sterilization validation and revalidation (where applicable).

b) Operations records (those which relate to the purchasing, manufacture, quality assurance, distribution, installation, and servicing of an individual product or batch of product)

Examples of operations records include:

— pertinent subcontractor quality records;
— product-related purchasing records;
— the quantity of the raw materials, components, and intermediate products, and their batch number (where appropriate);
— the date of start and completion of different stages of production, including sterilization records (where appropriate);
— the quantity of product manufactured;
— the results of all inspections and tests, including the quantity of product approved for distribution;
— designation of the production line used;
— any deviation from the manufacturing specifications or procedures, including the authorization for the deviation;
— the results of installation/commissioning tests where devices are assembled on site;
— service records;
— distribution records;
— retained samples.

Quality records of this category facilitate traceability and review of the manufacture of a product or batch, and should be collated or referenced in a single file (see annex B).

If it is not practicable to include all the relevant manufacturing records, then these records should list the titles of those documents and their locations to facilitate their retrieval.

It is to be understood that records are not limited to data and verbal information describing the procurement, processing or product, but can include any other means of recording the process or its result including, but not limited to, samples of components, raw materials, uncompleted in-process materials, finished product, or defective product brought to the attention of the manufacturer.

The data which constitute the operations records should be constructed and reproduced by an appropriate method to avoid clerical errors. Each operations record should be uniquely identified relating to an individual product or manufacturing batch; for example a set of affected product batches may be identified by including all batches processed during a designated time period.

Distribution records should contain enough information to enable the supplier, directly or indirectly, to identify affected customers in the event of the issue of an advisory notice. These records should facilitate product advisory notice reconciliation as described in this International Standard (see 4.14.2).

c) System records (those which demonstrate the effective operation of the overall quality system)

Examples of system records include:

— management review meeting minutes, action items, and follow-up records;
— contract review activities;
— general complaint-handling records;
— training records;
— internal audit logs and reports;
— cleaning and maintenance records;
— environmental monitoring records;
— manufacturing and inspecting equipment calibration logs and records.

It might be required to maintain additional records to meet regulatory requirements.

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

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. Where appropriate, the reason for the correction should be recorded.

Back-ups (hard copy or electronic) should be made of any quality system records stored on electronic media and should be capable of being retrieved.

A system should be in place that assures the integrity of electronic records and protects against unauthorized entries.

4.17 Internal quality audits

The generic guidance given in 4.17 of ISO 9000-2:1997 applies.

Additional guidance for all medical devices

The scope of the internal audit should include relevant regulatory requirements.

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

The audit records should indicate the time agreed for completion of corrective action(s) and identification of the function(s)/individual(s) responsible for carrying out any corrective actions needed.

Only records which demonstrate that an effective internal audit system is in operation may need to be made available for assessment made by external parties.

Such records may include:

— identification of the procedures used for the conduct of audits;
— audit schedules;
— records demonstrating that scheduled internal audits have been performed;
— records demonstrating the effectiveness of corrective actions.

In the case of suppliers with small numbers of direct employees, internal audits may be subcontracted.