FINAL DOCUMENT

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The document herein was produced by the Global Harmonization Task Force, which is comprised of representatives from medical device regulatory agencies and the regulated industry. The document is intended to provide *non-binding* guidance for use in the regulation of medical devices, and has been subject to consultation throughout its development.

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Preface

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1.0 Introduction

This document gives guidance to regulators and auditing organizations conducting audits of quality management systems of medical device manufacturers based on the process approach to quality management system requirements (e.g., ISO 13485:2003 and 21 CFR Part 820).

The incorporation of quality management system requirements, based on ISO 13485, into regulations applicable to manufacturers of medical devices, provides the opportunity for developing mechanisms that would lead to global harmonization. Regulators can use these guidelines when introducing regulatory systems for medical devices.

Note: For the purpose of these guidelines, "audit" means a regulatory audit.

Potential benefits for the patients/users, regulators, auditing organizations or auditees include:

- a high degree of assurance (along with technical evaluation, where required in addition) that safe and effective devices will be available
- independent, reliable, objective evaluation of compliance with regulatory requirements of the manufacturer's quality management system
- if satisfactory, results are evidence (or part thereof) of compliance with regulatory requirements necessary to market devices

In this document the terms "compliance" and "conformity" are used interchangeably whereas in some jurisdictions they may have distinct and different meanings.

The auditing of a medical device manufacturer's quality management system may represent only one part of the conformity assessment procedure required by the applicable regulations.

2.0 Scope

This document provides guidance for auditing organizations responsible for establishing, planning, carrying out, and documenting audits of medical device manufacturers' quality management systems. The document also covers related requirements on the follow-up of corrections, corrective, preventive, or improvement actions, as applicable. In addition, it describes the competence criteria that the audit team should meet.

3.0 Purpose

The purposes of this document are:

- To harmonize and to provide guidance on auditing quality management systems of medical device manufacturers
- To help the auditing organization develop their auditing procedures
- To assist auditors and auditees in preparing for, facilitating and responding to audits

4.0 Rationale

This guideline promotes consistency in auditing of medical device manufacturers' quality management systems which is important in harmonization and mutual acceptance of audit results.

5.0 References

GHTF/SG4/N30R20:2006 Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers – Part 2: Regulatory Auditing Strategy

GHTF/SG4/N33R14:2007 Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers – Part 3: Regulatory Audit Reports

GHTF/SG4 (00) 3 Training Requirements for Auditors

ISO 13485:2003 Medical devices - Quality management systems – Requirements for regulatory purposes

ISO 17000:2004 Conformity assessment - Vocabulary and general principles

ISO/IEC 17021:2006 Conformity assessment – Requirements for bodies providing audit and certification of management systems

ISO 19011:2002 Guidelines for quality and/or environmental management systems auditing

ISO 9000:2005 Quality management systems – Fundamentals and vocabulary

6.0 Definitions

6.1 Audit

Systematic, independent, documented process for obtaining records, statements of fact or other relevant information and assessing them objectively to determine the extent to which specified requirements are fulfilled.

ISO 17000:2004 4.4

For the purpose of these guidelines, "audit" means audit of the auditee's quality management system to determine compliance with the relevant regulatory requirements.

6.2 Audit Criteria

Set of policies, procedures, or requirements.

Note: Audit criteria are used as a reference against which audit evidence (3.9.4) is compared.

ISO 9000:2005 3.9.3

6.3 Audit Evidence

Records, statements of fact or other information, which are relevant to the audit criteria and verifiable.

Note: Audit evidence may be qualitative and/or quantitative and is used to substantiate audit observations.

ISO 9000:2005 3.9.4

6.4 Audit findings

Results of the evaluation of the collected audit evidence against audit criteria.

Note: Audit findings can indicate either conformity or nonconformity with audit criteria or opportunities for improvement.

ISO 9000:2005 3.9.5

6.5 Audit language

The language(s) routinely used for the communication or exchange of information between auditee's personnel and auditors.

6.6 Audit program

Set of one or more audits planned for a specific time frame and directed towards a specific purpose.

Note: An audit program includes all activities necessary for planning, organizing and conducting the audits.

ISO 9000:2005 3.9.2

6.7 Auditee

Any organization whose quality management system is to be audited for compliance with relevant medical device regulatory requirements. The organization may be the manufacturer and/or their supplier(s).

Note: ISO 9000:2005 3.9.8 defines auditee as "organization being audited".

6.8 Auditing organization

A body designated, on the basis of specific regulations, to carry out audits according to assigned tasks.

Note: ISO 17000:2004 2.5 defines the term conformity assessment body as "body that performs conformity assessment services".

6.9 Auditor

A person with relevant qualifications and competence to perform audits or specified parts of such audits and who belongs to, or is authorized by, the auditing organization.

Note: ISO 9000:2005 3.9.9 defines auditor as "person with the demonstrated personal attributes and competence to conduct an audit".

6.10 Compliance

Overall conformity to regulatory requirements.

6.11 Conformity

Fulfillment of a requirement.

ISO 9000:2005 3.6.1

6.12 Establish

Establish means define, document (in writing or electronically), and implement.

Note: This definition differs from the usage of the word "establish" in ISO 13485:2003 in that the ISO 13485:2003 term is not defined and is less prescriptive.

6.13 Lead auditor

An auditor appointed to manage an audit

See ISO 9000:2005 3.9.10 Note 1

6.14 Manufacturer

Any natural or legal person who designs and/or manufactures a medical device with the intention of making the finished medical device available for use, under his name; whether or not such a medical device is designed and/or manufactured by that person himself or on his behalf by a third party(ies).

SG1(PD)/N055R6

Note: In some internationally recognized Standards and Guidelines on auditing, specific responsibilities are assigned to the client (i.e. a person or the organization requesting or commissioning the audit). These responsibilities are assigned on the basis that the client, as the financial supporter and primary customer of the audit, has the ultimate authority regarding the audit. The ultimate authority for the audit of medical device manufacturers is the auditing organization and the term "client" is not used therefore in these guidelines.

6.15 Nonconformity

Non-fulfillment of a requirement.

ISO 9000:2005 3.6.2

Other terms may be used to mean the same as nonconformity (e.g. 'non compliance', 'deficiency').

6.16 Objective evidence

Verifiable information or records pertaining to the quality of an item or service or to the existence and implementation of a quality management system requirement, which is based on visual observation, measurement, testing, or other means.

Note: ISO 9000:2005 3.8.1 defines objective evidence as "data supporting the existence or verity of something".

6.17 Quality management system

The organizational structure, responsibilities, procedures, processes and resources for implementing quality management. For the purpose of these guidelines 'implementing quality management' is taken to include both the establishment and maintenance of the system.

Note: ISO 9000:2005 3.2.3 defines quality management system as "management system to direct and control an organization with regard to quality".

6.18 Regulatory Audit

The audit of a quality management system to demonstrate conformity with quality management system requirements for regulatory purposes.

Note: For the purpose of these guidelines, "audit" means a regulatory audit.

6.19 Supplier

Organization or person that provides a product.

ISO 9000:2005 3.3.6

7.0 General requirements for auditing organizations

General principles applicable for auditing organizations include impartiality, competence, responsibility, openness, confidentiality, and responsiveness to complaints. (See ISO/IEC 17021:2006 section 4)

7.1 Legal responsibility

The auditing organization shall be a legal entity, or a defined part of a legal entity, such that it can be held legally responsible for all its activities. A governmental auditing organization is deemed to be a legal entity on the basis of its governmental status. The auditing organization shall be responsible for its decisions.

7.2 Independence and impartiality

The auditing organization and their auditors and experts shall be impartial and free from engagements and influences which could affect their objectivity, and in particular shall not be:

a) involved in the design, manufacturing, marketing, installation, servicing or supply of the device categories within the scope of the audit

b) involved in the design, manufacturing, implementation or maintenance of quality management systems within the scope of the audit

c) involved in consulting concerning design, manufacturing, implementation or maintenance of the quality management system of the auditee

d) an authorized representative of the manufacturer

Examples where independence could be compromised would include the following:

i. the auditor having a financial interest in the company being audited or a competitor to this company (e.g. holding stock in the company)

ii. the auditor being employed currently by a manufacturer producing medical devices

iii. the auditor being, or having recently been, a member of staff from a research or medical institute or a consultant having a commercial contract or equivalent interest with the manufacturer or manufacturers of similar devices

All persons and organizations involved with an audit should respect and support the independence and integrity of the auditors.

The impartiality of the auditing organization, auditors, and experts shall be established and documented.

7.2.1 Management of impartiality

In order to ensure the objectivity of its auditing activities, the auditing organization shall identify, analyze and document the possibilities for conflict of interests. Having relationships does not necessarily present the auditing organization with a conflict of interest. However, if any relationship creates a threat to impartiality, the auditing organization shall document and be able to demonstrate how it eliminates or minimizes such threats. The demonstration shall cover all potential sources of conflict of interests that are identified, whether they arise from within the auditing organization or from the activities of other persons, bodies or organizations. (See ISO/IEC 17021:2006 section 5.2)

7.3 Confidentiality, due professional care and code of ethics

The confidentiality of all documents and information obtained in association with an audit should be safeguarded. There should be no disclosure of such documents and information to any other party without the explicit approval of the auditee, unless it is a regulatory requirement.

Due professional care, diligence and good judgment should be practiced at all times in the conduct of an audit and in the management of supporting activities in accordance with an established and documented code of ethics.

7.3.1 Management of confidentiality

The auditing organization shall have a policy and arrangements to safeguard the confidentiality of the information obtained or created during the performance of auditing activities at all levels of its structure, including committees and external bodies or individuals acting on its behalf.

7.4 Liability and financing

The non-governmental auditing organization shall have adequate arrangements (e.g. insurance or reserves) to cover liabilities arising from its operations. The non-governmental auditing organization shall be able to demonstrate that commercial, financial or other pressures do not compromise its impartiality. (See ISO/IEC 17021:2006 section 5.3)

8.0 Management

8.1 Structural requirements

The auditing organization shall document its organizational structure, showing duties, responsibilities, and authorities of management and other personnel and any committees. (See ISO/IEC 17021:2006 section 6)

8.2 Quality management system

The auditing organization shall implement and maintain a quality management system to ensure that the audits conducted are of the highest quality to satisfy the requirements of the regulatory authority.

The quality management system shall cover at least:

a) control of documents

b) control of records

c) management review

d) internal audits

e) corrective and preventive actions

(See ISO/IEC 17021:2006 section 10.3)

8.3 Consistency

The management system must ensure that audits are performed in accordance with defined and documented methodologies and techniques designed to provide consistency of approach and depth among audits of the same type and scope. The management of audit activities should be in accordance with documented, systematic procedures designed to provide the necessary technical and administrative support for the audits.

9.0 Resources

9.1 Resources

Adequate resources in terms of competent staff, financial support, time to conduct effective audits and, where necessary, access to technical information and expertise from external sources should be committed to the conduct and implementation of audits and all supporting audit activities in order to ensure that audit results and conclusions are of the highest possible reliability within the limitations of the sampling aspects of auditing. (See ISO/IEC 17021:2006 section 7)

9.2 Audit team competence

Audits of medical device manufacturers should only be performed by audit teams possessing as a whole the education, skills and experience with respect to the relevant regulatory requirements and to the device technologies and related processes, as well as those required for auditing. (See GHTF/SG4 (00) 3 and ISO 19011:2002 section 7)

9.2.1 Audit team competence criteria

The competence requirements for all auditors in the team should be based on the qualification criteria for quality management system auditors as well as personal attributes (e.g. tact, diplomacy, effective communication skills).

The competence of the team as a whole should be appropriate to cover the scope of the audit. In particular:

a) The team should have competence (i.e. training and knowledge/ experience) in the following:

   i) assessment of the quality management system for medical device manufacturers and determination of the effectiveness of its implementation

   ii) understanding the regulations and applicable standards specific to quality management system requirements for medical device manufacturers

   iii) intended use of and risks associated with the devices being produced

   iv) the assessment of the design, manufacturing processes and the technologies involved

b) The competence must be present within the audit team as a whole but not necessarily by each member. In assessing the quality management systems of manufacturers the audit team may include additional experts in processes and technology relevant to the scope of the audit and ideally these experts should meet the requirements of clause 9.2.1 (a). The experts authorized by the auditing organization and who are not qualified as auditors should only assess the processes related to their specialized knowledge and under the supervision of an auditor.

   Alternatively, the members of the audit team may be given additional training and/or specialized knowledge related to those processes and technology (e.g. the achievement of a controlled environment and validation of the sterilization process).

c) The lead auditor shall be competent to plan and direct the team members so that in carrying out their separate tasks, the appropriate competence is applied effectively and fairly.

9.2.2 Audit team competence records

The auditing organization shall maintain records to demonstrate the competence of its auditors. (See ISO/IEC 17021:2006 section 7.4)

9.2.3 Auditor qualifications, training and experience

In addition to basic auditing skills (clause 9.2.1), the competencies specifically required for auditing medical device manufacturers may be achieved through a variety of means including a combination of qualification and one or more of the training or experience elements listed below.

a) Qualification: Auditor qualification is most likely to be in one or more of the following:

   i) biology or microbiology

   ii) chemistry or biochemistry

   iii) computer and software technology

   iv) electrical, mechanical or bioengineering

   v) human physiology

   vi) medicine

   vii) pharmacy

   viii) physics or biophysics

b) Training: Special programs may be established for training technically qualified staff in the following:

   i) understanding the regulatory requirements and related laws/ordinances/statutes/standards, etc.

   ii) auditing of medical device manufacturers' quality management systems

   iii) understanding the design and manufacturing processes and the technologies involved

   iv) safety aspects relating to the intended use of medical devices

c) Experience: Auditor experience is most likely to be in the following:

i) working in closely related industries and the workplace such as research and development, manufacturing

ii) working in the application of the device technology and its use in health care services and with patients

iii) testing the devices concerned for compliance with the relevant national or international standards

iv) conducting performance testing, evaluation studies or clinical trials of the devices

These competencies are to be regarded as the tools to address the relevant safety and performance aspects of the quality management system being audited arising from the way in which the devices are made, how they work, and how they are used.

9.3 Outsourcing

The auditing organization shall have a process in which it describes the conditions under which outsourcing (which is subcontracting to another auditing organization to provide part of the auditing activities on behalf of the auditing organization) may take place. (See ISO/IEC 17021:2006 section 7.5.)

The auditing organization may not outsource decisions with respect to certification.

In cases where outsourced auditors or experts are used, the auditing organization shall ensure that those auditors meet the same requirements that apply to the auditors within the auditing organization.

10.0 Audit Process

10.1 Audit objectives and scope

Audit objectives and scope should be clearly defined and documented by the auditing organization and the audit team and, as permitted by the regulatory requirements, agreed to by the manufacturer and/or auditee in the initial planning stages of the audit. However, based on the audit findings, the audit scope and objectives may be modified. (See ISO 19011:2002 section 6.2.2)

10.1.1 Audit objectives

Audits are designed to:

a) determine compliance of a manufacturer's quality management system with regulatory requirements

b) determine the effectiveness of the implemented quality management system for the purposes of meeting specified quality objectives which include all of the appropriate medical device regulatory requirements

c) audit the quality management system as the manufacturer has defined it (see note below)

d) in the case of audits subsequent to the initial audit, ensure that corrective actions agreed upon as a result of the previous audit have been completed effectively

Note: A manufacturer may have a quality management system that is more extensive than that defined in the regulations.

10.1.2 Audit scope

The audit scope describes the extent and the boundaries of the audit in terms of:

a) the subject medical devices controlled by the quality management system to be audited

b) the quality management system requirements against which the quality management system is to be audited

c) the type of audit required (see section 10.2)

d) physical location of activities and documentation to be audited

Audits for regulatory purposes should not impose an increase in the scope of quality management system requirements over and above those necessary to meet regulatory requirements.

10.2 Types of audits

10.2.1 Full audit

A full audit is an audit of all applicable subsystems of the quality management system to assess conformity with regulatory requirements. (See SG4/N30R20:2006 section 6.2)

Full audits are generally used to conduct initial audits.

10.2.2 Partial audit

A partial audit is an audit of some subsystems or aspects of subsystems of the quality management system to assess conformity with regulatory requirements.

Partial audits are generally used to conduct surveillance audits. Partial audits may also be used to conduct special audits.

10.2.3 Surveillance audit

Surveillance audits are audits conducted after the initial audit to confirm the ongoing conformity of the quality management system with regulatory requirements.

Surveillance audits shall be carried out at predetermined intervals in accordance with the audit program (e.g., ISO/IEC 17021:2006 clause 9.1.1) and/or regulatory requirements.

Surveillance audits should be conducted annually. The time interval between surveillance audits should not be greater than 3 years, and in the case of high risk devices not greater than 2 years.

The auditing organization may specify certain aspects or subsystems of the quality management system which are always included in a surveillance audit (e.g., corrective action or follow-up of audit findings from the last audit).

If partial audits are used for surveillance, all applicable subsystems of the quality management system should be audited within a recommended maximum period of 5 years.

The time interval between surveillance audits will depend upon:

a) the risk associated with the intended use of the medical devices

b) the number of quality management system subsystems to be examined

c) the nature of the quality management system subsystems to be examined

d) the scope and results of the previous audits

e) the post market surveillance data available on the subject devices indicating a possible deficiency in the quality management system

10.2.4 Special audit

Full or partial audits may be used to conduct special audits. These audits may be required when:

a) external factors apply such as:

    i) available post-market surveillance data on the subject devices indicate a possible significant deficiency in the quality management system

ii) significant safety related information becoming known to the auditing organization

b) significant changes occur which have been submitted as required by the regulations or become known to the auditing organization, and which could affect the decision on the manufacturer's state of compliance with the regulatory requirements

The following are examples of such changes which could be significant and relevant to the auditing organization when considering that a special audit is required, although none of these changes should automatically trigger a special audit:

i. Quality Management System – impact and changes:
- New ownership
- Extension to manufacturing and/or design control
  - Addition of a quality management system subsystem (extension, upgrade audits)
- New facility, site change
  - Modification of the site operation involved in the manufacturing activity (e.g. relocation of the manufacturing operation to a new site or centralizing the design and/or development functions for several manufacturing sites)
- New processes, process changes
  - Significant modifications to special processes (e.g. change in production from sterilization through a supplier to an on site facility or a change in the method of sterilization)
- Quality management personnel
  - Modifications to defined authorities, e.g. the management representative, that impact:
    - quality management system effectiveness or regulatory compliance
    - the capability and authority to assure that only safe and effective medical devices are released

ii. Product related changes:
- New products, categories
- Addition of a new device category to the manufacturing scope within the quality management system (e.g. addition of sterile single use dialysis sets to an existing scope limited to hemodialysis equipment, or the addition of magnetic resonance imaging to an existing scope limited to ultrasound equipment)

iii. Quality Management System & Product related changes:
- Changes in standards, regulatory requirements
- Post-market surveillance, vigilance

10.2.5 Combined audit

Combined audits occur when a quality management system is assessed against multiple regulatory requirements.

10.2.6 Joint audit

Joint audits occur when two or more auditing organizations audit an auditee against the same regulatory requirements simultaneously.

10.3 Flow Chart

Figure 1 provides an overview of typical audit activities. The extent to which these provisions are applicable depends on the scope and complexity of the specific audit and the intended use of the audit conclusions. (See ISO 19011:2002 section 6.1)

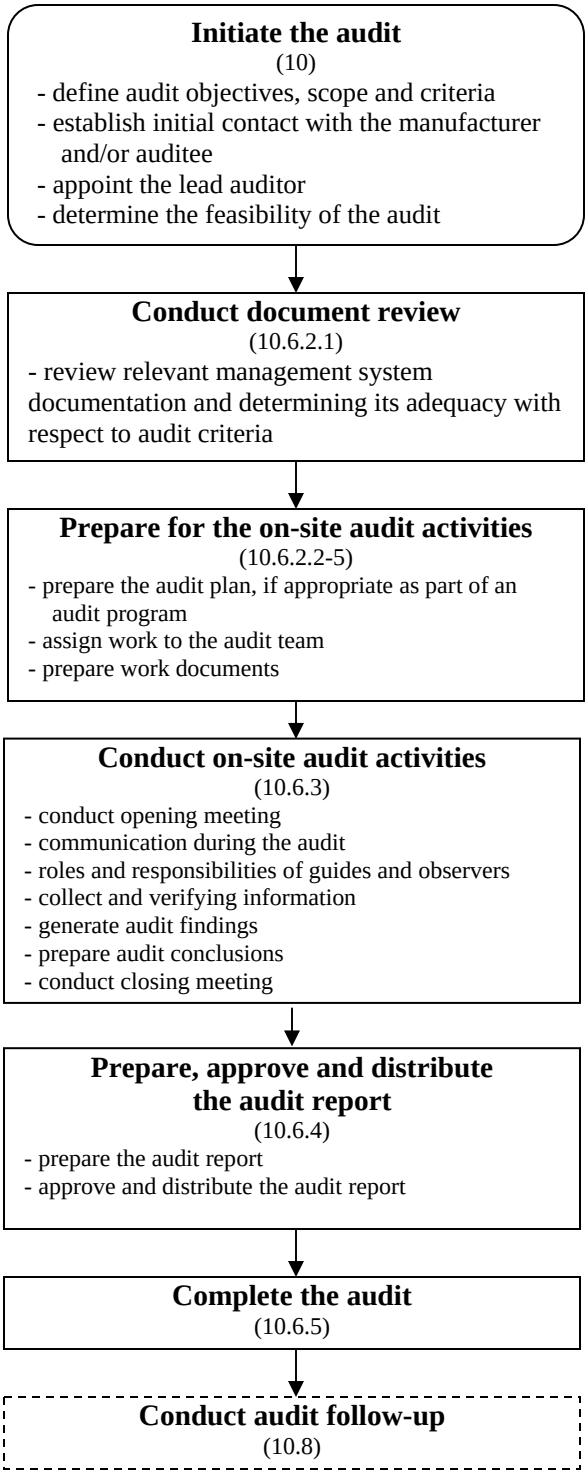


Figure 1 - Flow Chart – Overview of Typical Audit Process

10.4 Roles, responsibilities and authorities

All the organizations involved in the audit process should be identified and their respective roles, responsibilities and authorities should be clearly defined and documented to:

a) ensure a clear understanding of mutual expectations throughout the audit process

b) provide a means of accountability with respect to relevant regulatory requirements

10.4.1 Auditing organization

The auditing organization has the regulatory authority or is designated by the regulatory authority to perform audits, the results of which are evidence of the auditee's compliance or non-compliance with the regulatory requirements for quality management systems. Associated with this authority are the responsibilities for management and performance of all audit activities.

The responsibilities of the auditing organization for audit management include:

a) complying with relevant regulatory requirements for audit management

b) following the principles of these guidelines

c) following applicable standards

d) training, authorizing, selecting and supervising auditors

e) establishing methods to ensure consistency in the interpretation of the regulatory requirements

f) maintaining the means of providing prompt guidance which may be required by the audit team during the audit

g) safeguarding the confidentiality of all documents and information obtained in association with the audit

h) establishing and complying with a code of ethics

i) informing the appropriate authority on decisions taken when required by the regulatory requirements

Audits do not result in a transfer of the responsibility to achieve quality objectives from the manufacturer to the auditing organization.

In conjunction with the lead auditor, the responsibilities of the auditing organization for audit performance include:

a) complying with relevant regulatory requirements for auditing

b) agreeing on the scope of the audit, including the standards or other documents to be used, with the manufacturer as necessary to comply with and as permitted by the regulatory requirements

c) planning, organizing, evaluating and reporting on the audit

d) selecting the auditors

e) agreeing to the language of the audit

f) decision making with regard to applicable regulatory requirements resulting from nonconformities discovered during the audit and subsequent verification of corrections and/or corrective actions

10.4.2 Auditors

The responsibilities of auditors include:

a) complying with the applicable regulatory requirements for auditing

b) helping the auditee understand the regulatory requirements

c) planning and carrying out assigned responsibilities objectively, effectively and efficiently within the audit scope and in accordance with a code of ethics for auditors established and documented by the auditing organization

d) co-operating with and supporting the lead auditor

e) collecting, analyzing and, where appropriate, documenting objective evidence that is relevant and sufficient to permit the establishment of conclusions regarding compliance of the quality management system with regulatory requirements and the effectiveness of its implementation in meeting quality objectives

f) establishing the extent to which the procedures, documents and other information describing or supporting the required elements of the quality management system are known, available, understood and used by the auditee's personnel

g) remaining alert to any indications or evidence that can influence the audit results and possibly require more extensive auditing

h) informing the lead auditor of audit findings in a timely manner

i) assisting the lead auditor in preparing the report of the audit

j) informing the lead auditor immediately of any major obstacles encountered in performing the audit

k) safeguarding the confidentiality of all documents and information obtained in association with the audit:

   i) when submitting such documents to the auditing organization through the lead auditor

   ii) treating privileged information with discretion

l) verifying that corrective actions have been taken and have been effective:

   i) as a result of a previous audit

   ii) during the audit, as feasible

   iii) based on experience gained with devices on the market (e.g. post market surveillance)

   iv) based on incidents of a serious nature

m) minimizing disruption to the auditee's personnel and processes during the audit while attaining the audit's objectives

n) complying with any health and safety or other applicable requirements of the auditee

10.4.3 Lead auditor

The lead auditor is ultimately responsible to the auditing organization for all phases of the audit. During the audit, the lead auditor shall have authority to make final decisions regarding the conduct of the audit and any audit findings.

The responsibilities of the lead auditor include, in addition to those of the auditors:

a) identifying the requirements of each audit assigned to the lead auditor by the auditing organization

b) assisting the auditing organization with the selection of the other audit team members

c) previewing the quality management system description (where appropriate) for adequacy in meeting applicable regulatory requirements, prior to the on-site audit

d) preparing the audit plan (if appropriate, as part of an audit program) and working

documents and briefing the audit team

e) representing the audit team with the auditee's management

f) communicating any nonconformities to the auditee as soon as possible after they are identified and indicating whether such nonconformities may affect compliance with the regulatory requirements

g) reporting to the auditee and to the auditing organization any major obstacles encountered in performing the audit as planned

h) preparing and presenting the audit results clearly and conclusively to the auditee at the closing meeting

i) preparing and submitting the audit report to the auditing organization in a timely manner

10.4.4 Auditees

The responsibilities of the auditee include:

a) defining the scope and objectives of the audit in conjunction with the auditing organization

b) informing relevant employees about the objectives and scope of the audit

c) appointing responsible members of staff to accompany members of the audit team and ensuring that audit team members are aware of health, safety and other applicable requirements

d) providing resources needed for the audit team in order to ensure an effective and efficient audit process

e) providing access to the facilities and evidential material pursuant to the regulatory requirements as requested by the auditors

f) co-operating with the auditors to permit the audit objectives to be achieved

g) receiving the audit findings

h) determining what follow-up corrective actions are to be taken to address nonconformities and other audit findings, and implementing such actions in a timely and effective manner and informing the auditing organization as required

i) informing the auditing organization of any significant change to the quality management system as required

j) informing any other auditees that may be affected by the audit, of its objectives, scope and any other relevant arrangements

Where auditees, other than the manufacturer, are involved in the audit (i.e., suppliers), sections (a), (b) and (h) through (k) remain with the responsibility of the manufacturer.

The manufacturer should establish and maintain documented procedures to ensure that purchased product or services from their suppliers meet the relevant regulatory requirements. In cases when the manufacturer is not able to give satisfactory evidence to the audit team that purchased product or services meet the specified requirements, the auditing organization may need to audit the control of processes on the premises of the manufacturer's suppliers (e.g. sterilization suppliers).

10.4.5 Observers

a) With the auditee's consent (unless it is a regulatory requirement) observers may be present at an audit for:

- the purpose of an observer's training for auditing

or

- observing the effectiveness of the audit process according to the requirements for the designation of the auditing organization or in the course for assessing the auditing organization for the purpose of their recognition as specified in agreements.

b) Confidentiality

Observers are required to meet to the same level of confidentiality as other audit team members. This shall be established prior to any audit activity. (See also section 7.4)

c) Function

During the audit, the observer(s) take no active part in the audit process but "observe" the activities, interviews and documents reviewed by the auditors. Observers may provide feedback to the audit team at previously agreed intervals.

10.4.6 Language requirements

The auditees are expected to prepare their quality management system documentation in the company's operational language(s). The audit team must therefore have available:

a) as a minimum one member able to read and understand the quality management system documentation and to interview the auditee's personnel;

or

b) an audit interpreter, arranged and agreed in advance.

10.5 Audit team composition

The audit team shall include a lead auditor who shall be in overall charge of the audit team. Where the audit team is comprised of one individual then this person shall be the lead auditor. The lead auditor should have the capability and experience to manage an audit.

The audit team shall include one or more persons with experience of assessing the relevant medical device technology incorporated in the manufactured products and the associated manufacturing processes within the specified regulatory environment. Decisions with regard to the extent of inclusion of such expertise in the audit team should be made case by case (see also clause 9.2.1). When determining the size and composition of an audit team for a given audit, due consideration should be given to the audit objectives, scope and criteria, the language of the audit, and the auditee's particular social and cultural characteristics.

When the auditing organization chooses the audit team, it may take into account the auditee's opinion on the suitability of the auditor(s), trainees, observers, and interpreters, in particular when a conflict of interest may exist (see 7.2). (See ISO 19011:2002 section 6.2.4)

10.6 Audit activities

The audit process as illustrated in 10.3 applies to all types of audits – e.g., initial audits, surveillance audits, and special audits (see also 10.2).

The auditing organization should have documented procedures for planning and performing on-site audits in accordance with the relevant guidance provided in this document, (See GHTF/SG4/N30R20:2006, ISO 19011:2002 section 6, and ISO/IEC 17021:2006 section 9).

10.6.1 Notification

Where permitted by the regulatory requirements, the auditee should be notified in advance that an audit is to be conducted.

The purpose of this notification is:

- to establish communication channels with the auditee's representative
- to confirm the authority to conduct the audit, if appropriate
- to request relevant information on the auditee's quality management system documentation

An unannounced audit may be necessary if the auditing organization has justifiable concerns about implementation of corrective actions or compliance with regulatory requirements.

10.6.2 Preparation

The auditing organization should define the audit objectives, scope and criteria (for details see 10.1) and should appoint the audit team including the lead auditor for the specific audit.

The auditing organization should determine the feasibility of the audit. (See ISO 19011:2002 6.2.3)

In case of joint audits, the auditing organizations involved should reach agreement on the specific responsibilities of each organization, particularly with regard to the authority of the appointed lead auditor.

10.6.2.1 Preliminary review of quality management system description

As a basis for planning the audit, the lead auditor may carry out a preliminary review of the auditee's documented quality management system, such as the quality manual and relevant procedures, for meeting the regulatory requirements.

This preliminary review should be considered to be part of the execution of the audit and should help determine the feasibility of the audit.

If this review reveals that the quality management system is not adequate to meet the regulatory requirements, further resources should not be expended on the audit until such concerns are resolved to the satisfaction of the auditing organization.

10.6.2.2 Audit plan

If required, an audit plan should be drawn up in accordance with international guidance (See ISO 19011:2002 section 6.4.1). The plan should facilitate scheduling and coordination of the audit activities. The audit plan should be communicated to and agreed to by the auditee, preferably in advance of the site visit.

The audit plan should be designed to be flexible in order to permit changes in emphasis based on information gathered during the audit, and to permit effective use of resources.

The audit plan shall be based on the audit scope and objectives, and should take into account:

a) the type of audit to be conducted

b) information from the preliminary review of the quality management system documentation, if available

and in addition, in the case of surveillance or special audits:

c) information from previous quality management system audits

d) available post market surveillance information

GHTF SG4/N30R20:2006 Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers – Part 2: Regulatory Auditing Strategy provides additional input for drawing up the audit plan.

The audit plan should include:

a) the audit scope and objectives

b) the audit criteria and any reference documents

c) identification of the auditee

d) identification of audit team members

e) the language of the audit

f) the date and location(s) where the site visit is to be conducted

   i. Where the auditee has multiple sites, or the audit also covers a supplier, the audit plan should adequately address this issue.

   ii. Any offsite activities related to the scope of the audit should be identified.

g) identification of the auditee's organizational/functional units

h) identification of the auditee's management responsible for the audit

i) the expected time and duration for each major audit activity

j) the schedule of meetings, including any necessary daily briefings, to be held with the auditee's management

k) the audit report distribution

10.6.2.3 Audit plan changes

During the audit the lead auditor may make changes to the auditor's work assignments and to the audit plan in order to ensure the optimal achievement of the audit objectives. However, the auditee should be aware that, based on the audit findings, the plan may be modified to allow flexibility in the depth of each area investigated. The auditee should be advised of the changes.

If the audit objectives appear to become unattainable, the lead auditor should report

the fact and the reasons to the auditee and the auditing organization.

10.6.2.4 Audit team assignments

Each audit team member should be assigned specific tasks, such as auditing specific quality management subsystems or processes. These assignments should be made by the lead auditor in consultation with the audit team members and should be appropriate to each auditor's particular technical expertise.

10.6.2.5 Working documents

Working documents should be prepared by the lead auditor with the assistance of the other audit team members according to the auditing organization's procedures. These documents should be designed in relation to the audit plan and are for the purpose of facilitating the collection of objective evidence and the reporting of audit results.

Working documents may include:

a) check-lists used for evaluating quality management system compliance with applicable regulatory requirements

b) forms for reporting audit findings

c) forms for documenting supporting evidence for conclusions reached by the auditors

Sample working documents should be made available to the auditee on request.

Working documents should be designed so that they do not restrict additional audit activities or investigations which may become necessary as a result of information gathered during the audit.

10.6.3 Audit execution

10.6.3.1 Opening meeting

The purpose of an opening meeting is to:

a) introduce the audit team to the auditee's management or others as appropriate

b) review scope, objectives, and criteria of the audit

c) provide a summary of the audit process including methods and procedures to be used to conduct the audit

d) confirm the audit plan, clarify unclear details of the audit plan, and revise the

audit plan when necessary

e) confirm the official communication links between the audit team and the auditee, and confirm the audit language, confidentiality, audit progress, etc.

f) confirm that the resources and facilities needed by the audit team are available

g) confirm the time and date for the closing meeting and any interim meetings of the audit team and the auditee's management

h) explain the rationale for note taking, sampling, audit termination, audit evidence and reporting nonconformities

i) confirm safety, emergency and security procedures for the audit team

j) confirm and agree on roles of observers, trainees, interpreters, and guides

(See ISO 19011:2002, 6.5.1)

10.6.3.2 Examination

An on-site examination shall be performed by the audit team to:

a) determine compliance of the auditee's documented quality management system with the regulatory requirements

b) confirm implementation of the auditee's procedures

c) verify effectiveness of the auditee's quality management system

d) report significant risks (safety, environment, regulatory or quality) without delay to the auditee, and if required, to the appropriate regulatory authority

Note: Issues outside the audit scope should be brought to the attention of the lead auditor for possible forwarding information to the auditee. Audit process obstacles may require changes to the audit plan.

10.6.3.2.1 Depth of audit

The audit team should:

a) review the quality management system as contained in the audit scope with respect to the regulatory requirements

b) use an approach as described in GHTF/SG4/N30R20:2006 Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers – Part 2: Regulatory Auditing Strategy, section 6.3

c) sample documents and randomly select records for review from all levels in the quality management system

d) choose samples reflecting the risks associated with the intended use for the device, the complexity of the manufacturing technologies, the range of devices covered by the scope of the audit and any available post market surveillance data

e) investigate all audit findings to establish their extent, particularly if there are concerns about product safety

10.6.3.2.2 Objective evidence

Objective evidence should be collected through interviews, examination of documents and visual observation of activities and conditions in the areas audited and should be verified. Additional sources of objective evidence may include data summaries, samples, customer feedback, and web sites.

Suggested interview techniques include:

- Conducting interview with person(s) from appropriate levels and functions being audited during normal business hours
- Placing the interviewee at ease
- Explaining the purpose of note taking
- Asking interviewee to describe duties and tasks
- Avoiding the use of leading questions
- Using open-ended questions
- Summarizing and reviewing the audit results with the interviewee
- Thanking the interviewee when interview finished

Information gathered through interviews may be tested by acquiring additional information from other independent sources, such as visual observation, measurements and records. Based on this objective evidence, audit findings should be noted where there are indications of nonconformities.

Objective evidence may be further documented by collecting copies of documents or, on occasion, taking photographs. Collection of evidence in this manner should be accurately recorded and acknowledged by the auditor and the auditee.

The audit includes collecting evidence of procedures and their implementation to determine compliance with regulatory requirements for post production surveillance (such as complaint handling) and, where appropriate, the design process including risk analysis and clinical evaluation.

Documents or copies collected by the auditors during the audit should be noted and acknowledged.

10.6.3.3 Audit findings

All audit findings should be recorded. The audit team should meet as needed to discuss the audit findings at appropriate stages during the audit. Audit findings which may be nonconformities should be reviewed with the auditee as soon as possible after they are observed.

In preparation for the closing meeting, the audit team reviews audit findings and audit evidence and compare to audit criteria and objectives.

Any resulting nonconformities should:

a) be written in a clear, concise manner

b) be supported by objective evidence

c) identify the specific requirements which have not been met

d) be identified as a major or minor nonconformity

Examples of audit findings that may be classified as major nonconformities are as follows:

a) failure to address applicable regulatory requirements for quality management systems (e.g. failure to have a complaint handling or training system)

b) failure to implement applicable regulatory requirements for quality management systems

c) an excessive number of minor nonconformities against a particular regulatory requirement for quality management systems

d) failure to implement appropriate corrections and/or corrective actions when an investigation of post market data indicates a pattern of product defects

e) failure to implement appropriate preventive actions when an investigation of post market data indicates the potential for product defects

f) products which are put onto the market which cause undue risk to patient and/or users when the device is used according to the product labeling

g) the existence of products which clearly do not comply with the manufacturer's specifications and/or the regulatory requirements

h) repeated nonconformities from previous audits

10.6.3.4 Audit conclusions

In preparation for the closing meeting, the audit team should hold a conference to:

a) assess the conformity of the quality management system against the audit criteria

One or more major nonconformities will indicate that the manufacturer's quality management system is not in compliance with the regulatory requirements.

b) determine effective implementation of the quality management system

c) agree on the nonconformities, if any, and audit conclusions

d) generate recommendations to the auditee for improvement of the quality management system, if applicable

e) confirm audit is complete with respect to the audit scope and objectives

f) determine the need for audit follow-up activities

10.6.3.5 Closing meeting

At the end of the audit the audit team should hold a formal meeting, chaired by the lead auditor, with the auditee's management and management's designated attendees. A list of attendees should be recorded. The main purpose of this meeting is to present audit findings to the management in such a manner as to ensure that the results of the audit are understood, and acknowledged. If there are nonconformities, these should be provided in writing.

The lead auditor should present the audit team's conclusions with respect to the quality management system's conformity with regulatory requirements and the effectiveness of the quality management system in meeting quality objectives.

If possible, any diverging opinions concerning the audit findings and conclusions should be resolved. Any unresolved issues should be documented.

A target date should be agreed upon for submission to the audit organization of corrective and preventive action plans necessary to address identified nonconformities and potential issues, taking into account the significance and criticality of the identified nonconformities or potential issues. Where a correction, or corrective action, has been implemented before the closing meeting, this action should be acknowledged and documented.

10.6.4 Audit report

10.6.4.1 Audit report preparation

An audit report should be written for each audit to provide the auditing organization with a permanent record of the audit conducted, and to provide the manufacturer with information on which to base corrective and preventive actions.

The lead auditor is responsible for the preparation, content, accuracy, and completeness of the audit report.

10.6.4.2 Report content

The audit report should accurately reflect the content of the audit. It should be dated and signed by the lead auditor and other team members as required by the auditing organization. At a minimum, the report should include or make reference to the following items:

a) the scope and objectives of the audit, including the processes and product groups involved

b) details of the audit plan, the identification of audit team members and auditee's representative(s), audit dates, and identification of the specific organization audited

c) identification of the audit criteria against which the audit was conducted

d) audit findings with a summary of the audit process, including any obstacles encountered that could compromise the reliability of the audit findings and conclusions

e) any areas not covered , although within the audit scope

f) identification of nonconformities, including:

   i. details of each nonconformity

   ii. the audit criterion or the specific regulatory requirement to which it applies

   iii. the relative significance with respect to regulatory requirements

   iv. the date for submission of any necessary corrective action plans

g) the effectiveness of the quality management system in meeting quality objectives

h) details of any corrections or corrective action(s) taken during the audit

i) recommendation to the auditing organization for follow up action including time schedule

j) audit conclusions

Any unresolved diverging opinions between the audit team and the auditee should be noted in the report. Confirmation of the nonconformities and recommendations given by the audit team as referred to under f), g) and i) should be provided to the manufacturer and/or auditee by the auditing organization as soon as possible.

Trade secrets and proprietary information should be identified in the report to ensure confidentiality.

Note: For further detailed guidance on report content for regulatory audits, consult the document GHTF/SG4/N33 Guidelines for regulatory auditing of quality systems of medical device manufacturers: Part 3 – Regulatory Audit Reports.

10.6.4.3 Report distribution

The audit report should be dated, reviewed, and approved in accordance with the procedures of the auditing organization.

The audit report should be transmitted or made available to the manufacturer and/or auditee by the auditing organization as soon as possible within a defined time period.

The audit report should be issued as soon as possible within a defined time period. If it cannot be issued within the defined time period, the reasons for the delay should be given to the manufacturer and/or auditee and a revised issue date should be established when permitted by the regulatory policies of the auditing organization.

10.6.5 Audit completion

The audit is completed when all activities listed in the audit plan have been completed and the final audit report has been submitted to the manufacturer and/or auditee.

10.6.6 Retention of audit records

Documents pertaining to the audit should be retained or destroyed by agreement between the participating parties and in accordance with applicable audit program procedures, contractual requirements, statutory, and regulatory requirements.

10.7 Adequacy of audit documentation

Documentation associated with each audit shall be maintained in accordance with applicable

regulatory requirements and be sufficient to:

a) demonstrate the implementation of the audit program and should include the records related to individual audits, auditees, results of audit program review and audit personnel.

b) provide adequate information to the appropriate regulatory authorities to be used, if necessary, in pre-market approval or post market surveillance activities

c) ensure traceability and continuity between the successive audits of the same quality management system

d) provide a basis for corrective and preventive action and opportunities for improvement for the auditee, if applicable

10.8 Follow-up activities

The conclusion of the audit may indicate the need for corrections, corrective, preventive or improvement actions, as applicable. Such actions are usually decided and undertaken by the manufacturer and/or auditee within an agreed upon timeframe and are not considered to be part of the audit. The status of these actions should be monitored by the manufacturer and/or auditee.

The auditing organization should review any corrections, corrective actions and/or preventive actions submitted. The completion and effectiveness of corrective actions should be verified. This verification may be part of a subsequent audit.

The audit program may specify follow-up by members of the audit team. In such cases, care should be taken to maintain independence in subsequent audit activities.