GHTF Guidelines for Regulatory Auditing of Quality Systems - SG4.(99)28

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Focus of Guideline

- Regulatory auditing of manufacturers' quality systems
- Guidelines for auditing organizations
- Competence criteria for audit team
- Audit report requirements

4. Definitions

4.1 Audit

A systematic and independent examination to determine whether quality activities and related results comply with planned arrangements and whether these arrangements are being implemented effectively and are suitable to achieve objectives. *ISO 8402*

4.2 Auditee

Any organisation whose quality systems are to be audited for compliance with the relevant medical device regulatory requirements.

Note: this can be the manufacturer and/or their subcontractor(s).

4.3 Auditing Organization

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

4.4 Auditor

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

4.5 Lead Auditor

An auditor designated to manage an audit (also known as an audit team leader).

4.6 Manufacturer

The legal entity subject by regulation to quality system requirements.

4.7 Nonconformity

The non fulfillment of specified requirements within the planned arrangements.

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

4.8 Objective Evidence

Verifiable information or records pertaining to the quality of an item or service or to the existence and implementation of a quality system element, which is based on visual observation, measurement or test.

4.9 Quality Audit Observation

Statement of fact made during a quality audit and substantiated by objective evidence.

4.10 Quality System

The organizational structure, responsibilities, procedures, processes and resources for implementing quality management.

[ISO 8402]

4.11 Regulatory Requirements

For the purpose of these Guidelines any part of any law, ordinance, decree or other regulation which applies to quality systems of medical device manufacturers.

4.12 Subcontractor

An entity, separate from the manufacturer, that provides to the manufacturer either a material, product or sub-assembly (or a component) to a proprietary specification which is incorporated into or used in the manufacture of the finished medical device or a service (e.g. testing, sterilization) . . .

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4.12 Subcontractor

. . . to enable the medical device to meet defined requirements. If the separate entity is owned by the manufacturer, it may or may not be considered a subcontractor, depending upon the control exercised by the manufacturer.

5. General Principles for Auditing Organisations

5.1 Independence

Independence means being impartial and free from engagements and influences which could affect objectivity

5.1 Independence

Independence means **not** being:

- Involved in design, construction, marketing, installation, servicing or supply of device categories within the scope of the audit
- Involved in the design, construction, implementation or maintenance of the quality system being audited;
- An authorized representative of the manufacturer

5.1 Independence

Impartiality of the auditing organisation and auditors shall be established and documented.

5.2 Audit Objectives and Scope

- Clearly define and document audit objectives and scope
- Auditing organization, audit team and manufacturer should agree
- Scope and objectives may be modified based on quality audit observations

5.4 Resources

- Adequate resources for auditing include:
  - Competent staff
  - Financial support
  - Time to conduct effective audits
  - Access to technical information and expertise from external sources
- Adequate resources are required to ensure reliable audit results and conclusions

5.5 Competence of Audit Team

Team as a whole should possess education, skills and experience regarding:

- Regulatory requirements
- Device technologies
- Auditing

5.6 Consistency of Procedures

- Conduct audits according to defined and documented methodologies and techniques
- Provides consistency of approach and depth
- Manage audit activities according to documented, systematic procedures

5.7 Audit Documentation

Maintain sufficient documentation of audits to:

- Provide adequate information for pre-market approval or post market surveillance
- Ensure traceability and continuity between successive audits
- Provide basis for corrective action and quality improvement by manufacturer

5.8 Confidentiality, Due Professional Care & Code of Ethics

- Safeguard confidentiality of documents and information obtained in association with audit

- Do not disclose information to 3rd party without approval of the auditee (unless it is a regulatory requirement)

5.9 Audit Results and Conclusions

Audit results and conclusions should be consistent and accurate no matter who conducts the audit [subject to limitations of objective evidence collected]

6. Audit Objectives

6. Audit Objectives

- Does manufacturer's quality system meet regulatory requirements?

- Is quality system effective in meeting quality objectives, including regulatory requirements?

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6. Audit Objectives

- Audit quality system as manufacturer has defined it
- Ensure that corrective actions resulting from previous audit have been completed effectively

7. Audit Scope

7. Audit Scope

- What medical devices are controlled by quality system to be audited?
- What quality system requirements will quality system audited against?
- Type of audit
- Physical location of activities and documentation to be audited

8. Types of Audits

8. Types of Audits

- Initial audit
- Surveillance audit
- Special audit
- Unannounced audit

8.1 Initial Audit

- Conducted to confirm conformance with regulatory requirements
- Generally covers all elements of quality system

8.2 Surveillance Audit

- May be a full or partial audit of quality system

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8.2 Surveillance Audit

- Time interval between surveillance audits will depend on:
  - **Risk associated with intended use of medical device**
  - **Number of quality system elements to be examined**
  - **Nature of quality system elements to be examined**
  - **Scope and results of previous audits**
  - **Post market surveillance data available indicating possible deficiency in quality system** ***more . . .***

8.2 Surveillance Audit

- Time interval between surveillance audits should not be greater than:
  - 2 years for high risk devices
  - 3 years for other devices
- If partial audits - all elements of quality system should be audited within 5 years

8.3 Special Audit

- May be required when:
  - Post-market surveillance data indicates significant deficiency in quality system
  - Significant safety-related information becomes known to auditing organization
  - Significant changes occur to manufacturer which could affect decision on manufacturer's state of compliance

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Significant Changes That May Affect the Quality System

- New ownership
- Relocation to new site
- Modifications in management representative's defined authority
- New device category added
- Significant modifications to special processes

8.4 Unannounced Audits

May be necessary if auditing organization has justifiable concerns about:

- Implementation of corrective actions
- Compliance with regulatory requirements

9. Roles and Responsibilities

9.1 Auditing Organization - Audit ***Management***

- Comply with relevant regulatory requirement for audit management
- Comply with GHTF SG 4 guidelines
- Train, select and supervise auditors
- Establish methods to ensure consistency in interpretation of regulatory requirements

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9.1 Auditing Organization - Audit ***Management***

- Maintain means for providing prompt guidance to audit team during audit
- Safeguard confidentiality of all documents and information
- Establish and comply with code of ethics
- Inform appropriate authority on decisions taken

9.1 Responsibility for Quality Objectives

Responsibility for achieving quality objectives does NOT transfer from the manufacturer to the auditing organization as a result of an audit

9.1 Auditing Organization - Audit ***Performance***

- Comply with regulatory requirements for auditing
- Agree on scope of audit with manufacturer
- Plan, organise, evaluate and report on audit

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9.1 Auditing Organization - Audit ***Performance***

- Select auditors
- Agree to the language of the audit
- Make decisions about regulatory requirements applicable to nonconformities during the audit and later verification of corrective actions

9.2 Auditors

- Comply with applicable regulatory requirements for auditing
- Help manufacturer understand regulatory requirements
- Plan and carry out assigned responsibilities objectively, effectively and efficiently per audit scope and code of ethics

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9.2 Auditors

- Co-operate with and support lead auditor
- Collect, analyse and document objective evidence . . .
- Establish extent to which procedures, documents and other information . . . are known, available, understood and used by personnel

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9.2 Auditors

- Remain alert to indications or evidence that can influence audit results and require more extensive auditing
- Inform lead auditor of observations in a timely manner
- Assist lead auditor in preparing report

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9.2 Auditors

- Inform lead auditor of major obstacles encountered
- Safeguard confidentiality of documents and information
- Verify corrective actions have been taken and are effective

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9.2 Auditors

- Minimise disruption of auditee's personnel and processes
- Comply with any health, safety or other requirements of manufacturer

9.2.1 Lead Auditor

- Identify requirements of each audit assigned
- Assist with selection of other audit team members
- Preview manufacturer's quality system description for adequacy before on-site visit

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9.2.1 Lead Auditor

- Prepare audit plan and working documents and brief audit team
- Represent audit team with auditee's management
- Communicate any nonconformities to manufacturer ASAP and indicate effect on compliance

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9.2.1 Lead Auditor

- Report any major obstacles to manufacturer and auditing organization
- Prepare and present audit results clearly and conclusively to manufacturer at closing meeting
- Prepare and submit audit report to auditing organization in timely manner

9.3 Manufacturer

- Define scope of audit as permitted by regulatory requirements
- Determine method of complying with regulatory requirements
- Inform relevant employees about objectives and scope of audit

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9.3 Manufacturer

- Appoint responsible members of staff to accompany audit team members and ensure they are aware of health, safety and other requirements

- Provide all resources needed by audit team to ensure effective and efficient audit

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9.3 Manufacturer

- Provide access to facilities and evidential material per regulatory requirements and as requested by auditors
- Co-operate with auditors to permit audit objectives to be achieved
- Receive quality audit observations

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9.3 Manufacturer

- Determine follow-up corrective actions to take to address nonconformities and other observations
- Inform auditing organization of any significant changes to quality system
- Inform any other auditees of objectives, scope, and other relevant arrangements

10. Audit Team

10.1 Audit Team Composition

- Audit team should include team leader who:
  - Shall be in charge of audit team
  - Has capability and experience to manage audit

10.2 Audit Team Competence

10.2.3 Auditor Qualifications, Training and Experience

To be covered by Judy Strojny.

11. Audit Process

11.1 Preparation

11.1.1 Notification

The manufacturer shall be notified in advance that an audit is to be conducted, where permitted by regulatory requirements

11.1.2 Preview of Quality System Description

- As basis for planning audit, lead auditor may carry out preliminary review of manufacturer's quality manual or procedures
- Consider review part of audit
- Resolve any concerns about adequacy of system before expending further resources

11.1.3 Site Visit Audit Plan

- Have audit plan for site visit
- Communicate plan to manufacturer if permitted by regulatory requirements
- Design audit plan to be flexible to permit changes in emphasis and effective use of resources

11.1.3 Site Visit Audit Plan

Audit plan should identify:

- Audit scope and purpose
- Manufacturer's management team having responsibilities regarding audit scope and purpose
- Reference documents
- Audit team members

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11.1.3 Site Visit Audit Plan

Audit plan should identify:

- Language of the audit
- Date and place of site visit
- Date and place where any additional documentation is to be reviewed
- Manufacturer's organization units and other auditees to be audited

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11.1.3 Site Visit Audit Plan

Audit plan should identify:

- Expected time and duration for each major audit activity
- Schedule of meetings, including any necessary daily briefings, to be held with manufacturer's management
- Distribution of audit report distribution and expected date of issue

11.1.3 Site Visit Audit Plan

- Audit plan should address multiple premises covered by quality system
- Manufacturer should have documented procedures for purchased product/services from subcontractor
- Auditing subcontractor may be necessary

11.1.3.1 Audit Plan Changes

During audit, lead auditor:

- May change auditor's work assignments and audit plan to achieve audit objectives
- Should advise manufacturer of changes

11.1.4 Audit Team Assignments

- Lead auditor consults with each team member and assigns specific tasks
- Assignments should be appropriate to auditor's particular technical expertise

11.1.5 Working Documents

- Lead auditor prepares working documents
- Working documents should:
  - Facilitate collecting objective evidence and reporting audit results
  - Not restrict audit activities or investigations
- Samples of working documents should be made available to manufacturer

11.1.5 Working Documents

- Working documents may include:
  - Check-lists for evaluating quality system
  - Forms for reporting quality audit observations
  - Forms for documenting supporting evidence for conclusions

6.0 Audit Process

11.2 Audit Execution

11.2.1 Opening Meeting

- Purpose of opening meeting:
  - Introduce audit team members to manufacturer's management
  - Review scope and objectives of audit
  - Provide summary of methods and procedures to be used in conducting the audit

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11.2.1 Opening Meeting

- Purpose of opening meeting:
  - Establish official communication links between audit team and manufacturer
  - Confirm availability of resources and facilities needed by audit team
  - Confirm time and date for closing meeting and interim meetings
  - Clarify any unclear details of audit plan

11.2.2 Onsite Examination

- Purpose/goals:
  - Determine quality system compliance with regulatory requirements
  - Confirm implementation of manufacturer's procedures
  - Verify effectiveness of quality system

11.2.2.1 Depth of Audit

- Sample documents at all levels
- Chose sample documents based on:
  - Risks associated with intended use of device
  - Complexity of manufacturing technologies
  - Range of devices produced
  - Any available post market surveillance data

11.2.2.2 Collecting Objective Evidence

- Collect objective evidence through:
  - Interviews
  - Examination and collection of documents
  - Visual observation of activities and conditions
- Verify information
- Base quality audit observations on objective evidence

11.2.3 Quality Audit Observations

- Record all quality audit observations
  - Express in clear, concise manner
  - Support with objective evidence
  - Identify specific requirements not met
- Review all nonconformties and quality audit observations that may become nonconformities with manufacturer ASAP

11.2.4 Non-compliance with Regulatory Requirements

Major nonconformities:

- Failure to address applicable element of regulatory requirements for quality systems
- Failure to implement applicable element of regulatory requirements for quality systems
- Excessive number of minor nonconformities against a regulatory requirement

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11.2.4 Non-compliance with Regulatory Requirements

Major nonconformities:

- Failure to implement appropriate corrective and preventive action when investigation of post market data indicates pattern of product defects
- Introducing products to market which cause undue risk to patients or users when device is used according to manufacturer's instructions

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11.2.4 Non-compliance with Regulatory Requirements

Major nonconformities:

- Existence of products that clearly do not comply with manufacturer's specifications and/or regulatory requirements due to defective elements in quality system
- Repeated nonconformities from previous audits

11.2.5 Closing Meeting

- Main purpose: to present quality audit observations to management and ensure they are understood
- Lead auditor:
  - Presents quality audit observations
  - Identifies those which are nonconformities
  - Indicates relative severity in respect to regulatory requirements

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11.2.5 Closing Meeting

- Lead auditor presents written list of quality audit observations/nonconformities to management
- Management acknowledges receipt of nonconformities
- Agree on date for submission of corrective action plans to address nonconformities

11.3 Audit Report

11.3.1 Report Preparation

- Audit report provides:
  - Permanent record of audit
  - Information on which manufacturer can base corrective action and improve quality system
- Prepared under direction of lead auditor
- Lead auditor responsible for accuracy and completeness

11.3.2 Report Content

- Report should:
  - Accurately reflect content of audit
  - Be dated and signed by lead auditor

11.3.2 Report Content

Report should reference or contain:

- Scope, objectives, processes and product groups
- Details of audit plan, audit team members, manufacturer's representatives, audit dates, identification of specific organization audited
- Audit criteria against which audit was conducted
- Identification of nonconformities

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11.3.2 Report Content

Report should reference or contain:

- Effectiveness of quality system in meeting quality objectives
- Details of any corrective actions taken during audit
- Recommendations to auditing organization for follow-up action

11.3.2 Report Content

- Auditing organization provides manufacturer with confirmation of nonconformities and recommendations within 6 weeks
- If longer, inform manufacturer of cause of delay and revised issue date

11.3.3 Report Distribution

- Auditing organization should:
  - Make report available to manufacturer
  - Issue report ASAP within defined time period
  - Advise manufacturer of any delay, reason and revised issue date

11.4 Retention of Audit Records

Auditing organization retains auditing documents for time specified in regulatory requirements

12. Corrective Action Follow-up

12. Corrective Action Follow-up

- Manufacturer and auditing organization will agree on time period for corrective action and follow-up audit
- Auditing organization may request reports on corrective action from manufacturer
- Auditing organization should report results of review to manufacturer