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Chapter 0: Introduction

ISO/ ISO 13485

- ISO: International Organization for Standardization.
- ISO 13485: Medical device Quality Management System (QMS) Requirements for Regulatory Purposes.
- ISO 13485 demonstrates a framework for management best-practices for organizations that:
  - Supply resources and services for medical devices;
  - Design and develop medical devices;
  - Manufacture/ produce medical devices;
  - Store, distribute devices;
  - Install, service, and dispose medical devices.

Process approach

- Process approach is used by ISO 13485 to implement effective QMS.
- Operations of the company must be observed as processes. This allows the company to monitor, measure, and improve the effectiveness and efficiency of each process. The best way to implement the process approach is to create a process map, which details the processes, their sequences, and their interconnections/ interactions.

Chapter 1: Scope

- ISO 13485 applies to organization with the roles listed above. One organization may be involved with one or more lifecycle stages of a medical device.
- Some requirements may be inapplicable to certain organization if the organization can provide documents to justify the exclusion.

Chapter 2: Normative references

Chapter 3: Terms and Definitions

Important terms include:

- Organization

- Context of the organization (internal and external factors that affect the purpose, objectives, performance, and sustainability of the organization)
- Interested party /stakeholder (customers, suppliers, contractors, community, governments, etc.)
- Product (four categories: services, software, hardware, processed materials)
- Process
- Procedure
- Quality
- Nonconformity (failure to meet a requirement)
- Risk (combination of probability of occurrence of harm and severity of harm).
- Effectiveness

Chapter 4: Quality management system (QMS)

General requirements for QMS (Section 4.1)

- The organization must define and document its role (manufacturer, authorized representative, importer, distributer, etc.) as well as any applicable requirements (by the International Standard, regulation authorities, etc.)
- The organization must establish and document a QMS, and commit to the implementation, maintenance of its effectiveness and continual improvements. Changes to the QMS must be evaluated for their impact on current QMS and its underlying medical devices , as well as for conformance to the standard and compliance with regulatory requirements.
- Process documentation involves determining:
    - Which process needs to be documented and with what methods, e.g., written instructions, control charts, flowcharts.,
    - Any order and interactions among processes
    - What necessary criteria for effective process execution and management using risk-based approach
    - What necessary resources and information and how to ensure their availability
    - How to monitor, measure, analyze the processes and improve them
    - Which necessary records to demonstrate conformance and compliance, and how to maintain them

Documentation requirements (Section 4.2)

General list of required documents:

i. Statements of quality policy and quality objectives
ii. A quality manual
iii. Any documented procedures and records required by the ISO 13485
iv. Documents, as determined by the organization, to be necessary for effective planning, operation, and controls of its processes
v. Other documents required by applicable regulations.

Quality Manual (Section 4.2.2)

- Quality Manual is required to be established and maintained by the ISO 13485.
- Quality Manual contains:
    - (required) Definition of the scope of the aforementioned QMS

  - (required) List of any requirement exclusions, their details and justification
  - (required) Description of involved processes (including responsibilities and authorities of process owner) and interactions among processes.
  - (required) Procedures or references to procedures.
  - Description of document structure
  - Description of the organization (definition of the organization, its mission and vision, milestones, organizational structure, responsibilities, authorities, etc.)

Medical device file (Section 4.2.3)

- Each medical device or family of medical devices needs its own medical device file to demonstrate conformity to regulations and effectively manage processes.
- Medical device file contains:
  - Description of each device/ family (intended use, usage instructions, etc.)
  - Certificate of Conformity to applicable regulatory requirements, or references to documents proves conformity.
  - Procedures for production and associated manufacturing processes (storage, packing, handling, and distribution, etc.)
  - Specifications of product (dimension, material, manufacturing, finishing, etc.) and inspection procedures for each specification.
  - Information regarding installation and servicing/ maintenance procedures.

Control of documents (Section 4.2.4)

- A documented procedure for control of documents is required by the ISO 13485.
- Documents must be approved (dated and signed) before use/ change reviewed periodically, and updated with new information.
- All changes must be identified and communicated to applicable users; Substantial change will result in publication of a new version of the document and archival of the obsolete version. These obsolete documents must be retained for at least the lifetime of the medical device, but not less than 2 years since its release by the organization.
- Documents must be available at points of use, legible, and readily identifiable.
  - Example of good practice: A Master Control List with details regarding the current version, effective date, changes made, and validity of the documents.

Control of records (Section 4.2.5)

- Records demonstrate conformity to applicable regulation and effectiveness of established QMS.
- Procedures related to the identification, storage, security, integrity, retrieval, retention time, and disposition of records must be documented.
- Procedures for protecting confidential health information in records (if any) must also be documented.
- Records must be retained for at least the lifetime of the medical device, but not less than 2 years since its release by the organization.

Chapter 5: Management responsibility

Management commitment and Customer focus (Section 5.1 and 5.2)

- Top-level management, must demonstrate evidence of commitment to the development, implementation, and maintenance of effective QMS by:
    - Communicating to the organization the importance of determining and meeting requirements from customers and applicable regulatory functions.
    - Establishing quality policy and quality objectives
    - Conducting management reviews
    - Ensuring availability of resources.

Quality Policy (Section 5.3)

- Quality Policy is a high-level document that:
    - Demonstrates commitment for compliance with regulatory requirements and maintenance of an effective QMS.
    - Provides framework to determine and review quality objectives
- Top management must ensure that the quality policy is:
    - Applicable to the purpose of the organization
    - Is communicated and understood by employees within the organization
    - Is continually reviewed and improved.

Planning (Section 5.4)

a. Quality Objectives (Section 5.4.1)

- Quality objectives are established at relevant departments/ levels, are measurable, timed, and consistent with quality policy.

b. QMS planning (Section 5.4.2)

- QMS planning must meet requirements listed in section 4.1 and in the quality objectives.
- Since quality objectives are changeable, top management must maintain the integrity of the QMS when changes are planned and implemented.

Responsibility, authority, and communication (Section 5.5)

- Responsibilities and authorities must be defined, documented, assigned, and communicated to all levels of the organization. Personnel(s) who manage, perform, verify work quality must have their interrelation documented, and be provided necessary independence and authority to complete such tasks.
- A management representative must be appointed by top management to, besides their regular duties, perform QMS related activities, such as:
    - Ensuring QMS processes documentation
    - Reporting on the effectiveness or current QMA and any necessary changes
    - Promoting the awareness of and compliance to established requirements within the organization.
- Communication processes, especially those regarding QMS, must be established by top management.
- Example of internal communication:

  - Top-down communication (from manager to employee) as in instructions, performance evaluation, etc.
  - Bottom-up communication (from employee to manager) as in reports, suggestion boxes

Management review (Section 5.6)

- Top management must review the QMS at planned intervals (typically, at least once a year). The review procedures and review records must be documented.
- The review process for QMS, quality policy and objectives, and involved processes is to ensure the following characters:
  - Suitability: are they still suitable/ relevant to the organization?
  - Adequacy: do they still comply with current standard/ requirements?
  - Effectiveness: do they deliver planned results?
- Review inputs include, but not limited to, feedbacks, complaints, audits, new and revised standard(s)' requirements, etc.
- Review outputs include any actions and decisions related to:
  - Changes/ improvements to the processes, the QMS, the policy and objectives to ensure the aforementioned characters
  - Change/ improvement to product
  - Necessary resources.

Chapter 6: Resource management

Provision of resources (Section 6.1)

- The organization must determine and provide resources (finance, personnel, infrastructure, etc.) necessary to implement and maintain effective and requirement compliant QMS.

Human resources (Section 6.2)

- The organization must:
  - Determine necessary competence for the positions
  - Provide training or take actions to reach and maintain determined competence.
  - Evaluate the effectiveness of the actions taken
  - Ensure awareness of current QMS in relation to their role
  - Retain appropriate records regarding the education, training, skill, and experience.

Infrastructure (Section 6.3)

- Infrastructure includes buildings, workspace, process equipment (software and hardware), and supporting services and utilities (transportation, information system, etc.)
- The organization must determine and document infrastructure requirements to ensure conformity and effective operation, as well as their associated maintenance (interval, procedures, adverse effects, etc.).

Work environment and contamination control (Section 6.4)

- The organization must document the work environment requirements (humidity, noise, temperature, etc.) necessary for conformity to established product and regulatory requirements.

  - If condition of work environment can adversely affect product quality and conformity, requirements as well as procedure to monitor and control them must be documented.
  - If interaction between personnel and the product/ work environment can adversely affect product quality and conformity, requirements regarding health, cleanliness, and clothing of personnel in contact with the product must also be documented.
  - If working under special environmental environment is required, personnel must be competent for the work or be supervised by a competent person.
- As appropriate, to prevent contamination of work environment, personnel, and product, the organization must document procedure(s) for control of (potentially) contaminated product.
  - In case of sterile medical devices, procedure(s) to control contamination of microorganism and particulate matter, and to maintain cleanliness of work environment must also be documented.

Chapter 7: Product realization

Planning of product realization (Section 7.1)

- Planning and developing processes for product realization is required by ISO 13485, must be in line with requirements established in the QMS, and must include records on any involved process(es) of risk management.
- The organization must determine and document:
  - Product quality objectives and requirements
  - Necessary resources and commitment to their arrangement
  - Criteria for verification, validation
  - Criteria for measurement, monitoring, inspection, handling, storage, distribution, and traceability.
  - Criteria for product acceptance
  - Evidence that product and involved processes comply with established requirements.

Customer-related processes (Section 7.2)

- The organization must establish and keep records of all product requirements, including:
  - Customers' requirements, including delivery (transport, deadlines, etc.) and post-delivery (install, maintenance, etc.)
  - Requirements specific to the intended use of product, even if not stated by the customers (safety requirements, etc.)
  - Applicable regulatory and legal requirements
  - Requirements for user training necessary for the safe and effective use of the product.
  - Additional requirements deemed necessary by the organization.
- The organization must review and ensure its ability to fulfill the above requirements priors to committing any delivery of product. Actions resulted from the review and changes must also be documented and communicated to relevant parties.
- The organization must establish and document necessary process(es) for communicating with customers (regarding product information, enquiries, customer feedback, or any relevant changes, etc.), as well as regulatory authorities as stated by regulatory requirements.

Design and development processes (Section 7.3)

- A design and development file containing evidence of conformity to relevant requirements, records of design and development processes, and records of changes must be maintained for each medical device type/ family.
- Design and development procedures include:
    - Planning
    - Inputs and outputs
    - Review, verification, validation, and transfer
- For the planning of design and development process, the organization must document:
    - Stages and necessary review(s) at each stage
    - Methods of verification, validation, and transfer at each stage
    - Responsibilities and authorities of involved personnel
    - Methods for traceability of each outputs to inputs
    - Necessary resources
- Design and development inputs must be complete and verifiable, reviewed and approved, and must include:
    - Requirements of product function, performance, usability, and safety
    - Requirements as stated by applicable regulatory and legal functions
    - Output(s) from relevant risk management
    - Information from previous similar product
    - Other requirements deemed necessary by the organization (market information, etc.)
- Design and development outputs must be verifiable against input, approved before releasing, and meet the following requirements:
    - Input requirements
    - Provision of appropriate information regarding purchase, production, and service
    - Inclusion or reference to product acceptance criteria
    - Specification of product characteristics necessary for safety and intended use.
- Reviews to ensure requirement compliance and necessary subsequent action must be documented (identification of reviewed design, involved participants, and review date), and include representatives of relevant functions and appropriate specialist(s).
- Plan for verification that outputs meet input requirements must include methods, acceptance criteria, and necessary statistics with appropriate sample size.
- Plan for validation that product meets the requirements for specified/ intended application must be completed prior to delivery of product, and must include:
    - Methods, acceptance criteria, and necessary statistics with appropriate sample size
    - Rationale for choice of representative product (initial production units, batches, or their equivalents)
    - Clinical evaluations/ performance evaluations according to applicable regulations.
- If product usage requires interfacing with other device(s), verification and validation must be done during their interaction.
- Transfer of final manufacturable specifications of outputs to manufacturing must ensure that product requirements can be satisfied by the production capability.
- Changes at any phase/ stage must be documented, reviewed, verified, validated, and approved prior to implementation.

Purchasing (Section 7.4)

- Procedures for purchasing products and services must be documented to ensure satisfaction of specified purchasing information.
- The organization must establish and document the criteria (based on supplier' ability and performance, effect of product/service on device quality, and associated risks) for evaluating and selecting suppliers, and the plan for monitoring and re-evaluating suppliers according to those criteria, as well as maintain records on all results and actions stemming from these processes.
- The organization must determine and document, prior to contacting a supplier, necessary purchasing information, including where applicable:
    - Product specifications and requirements for product acceptance
    - Requirements for relevant procedures, processes, and equipment
    - Requirements for qualified supplier personnel
    - Other QMS requirements
    - A written agreement of notification from the suppliers prior to any changes that can results in nonconformity to specified requirements.
    - A statement on intended verification at the suppliers' premises
- The organization must determine a plan for necessary inspection activities (and their extents) to ensure satisfaction of specified purchasing requirements. When aware of any changes to purchased product, the organization must identify their effect on quality of product and/or the product realization process.

Production and service provision (Section 7.5)

- Production and service provision controls must be documented for each medical device/ batch of devices, and include:
    - Procedures and methods for production controls
    - Qualification of infrastructure
    - Avaliablity and use of monitoring and measuring equipment
    - Details on controls of process parameters and product specifications
    - Details on product labeling and packaging
    - Details on product release, delivery, and post-delivery activities.
- Cleanliness of product or contamination controls must be documented if:
    - Product is cleaned by the organization
    - Cleanliness is significant to product usage (whether product is supplied non-sterile and needs further cleaning/ sterilization, product is used non-sterile, or product cannot be cleaned)
    - Removal of process agents sued during manufacturing is necessary.
- When medical device requires installation (either by the organization or by specified external party), requirements for installation and acceptance criteria for installation verification must be documented and provided to relevant parties. Records of installation and verification must be maintained.
- When medical device requires servicing (as part of specified requirements), serving procedures, necessary reference materials and measurements, and criteria for verification of requirements

conformity must be documented. Records of these activities must be maintained and analyzed to determine possible complaint status and to act as input in future improvement.

- For sterile medical devices, the sterilization process parameters for each batch must be recorded and such records must allow traceability.
- Validation of effective processes for production and service provision must be conducted if resulting deficiencies can only be identified after product is in use or post-delivery. Procedures for validation processes (including applicable software use) must be recorded and include:
    - Criteria of process review and approval
    - Qualification of equipment and personnel
    - Methods, procedures, acceptance criteria
    - Criteria for process revalidation and revalidation procedures.
    - Requirements for records
    - Approval of any changes
- Regarding processes for sterilization and sterile barrier systems, validation is required prior to implementation and after product/ process changes. Validation results and subsequent actions must be recorded.
- Procedures for product (status) identification throughout product realization, storage, installation, and servicing must be documented, such that only conforming products are released, and that non-conforming product can be identified and distinguished.
- Procedures for traceability must be documented and its extent must follow applicable regulatory requirements.
- For implantable medical devices,
    - records of any aspects that compromise device safety and performance (components, materials, work environment, etc.) must be documented.
    - Records of distribution by distributor /distribution services must also be documented and available for inspection.
    - Records of name and address of shipping package consignee must be documented.
- Customer provided property (materials, equipment, intellectual property, etc.) must be identified, verified, and protected (from loss, alteration, contamination, and damage) while such property is being used or under control of the organization. Required conditions (such as packaging, etc.) for such protection must be controlled and documented.

Control of monitoring and measuring equipment (Section 7.6)

- The organization must establish and document the monitoring and measurement activities necessary for conformity, as well as involved equipment (including software) and procedures. The involved equipment must be calibrated and/or verified according to documented procedures and fit for its purpose. Results of this calibration and verification must be documented. In case of nonconformity, the previous measuring results must be assessed/ validated, and the organization must document and take appropriate actions regarding the equipment and affected products.

Chapter 8: Measurement, analysis, and improvement

General (Section 8.1)

- Process for monitoring, measurement, analysis, and improvement must be implemented using appropriate methods (including statistical techniques) to demonstrate conformity of product and ensure conformity and effectiveness of established QMS.

Monitoring and measurement (Section 8.2)

- The organization must establish and document procedures for the feedback process (applicable to data from production and post-production activities) to gather and monitor information as to whether customer requirements were satisfied. This information must serve as input for risk management, product realization and improvement processes.
- Procedures for timely and regulation-conforming complaint handling must be documented and include the requirements and responsibilities for:
    - Receiving and recording information
    - Assessing if information constitutes a complaint
    - Investigating complaints; or providing justification for the lack thereof
    - Assessing the need/ regulatory requirements for reporting to regulatory authorities; if yes, procedures for notification must be documented and followed.
    - Handling complaint-related product
    - Assessing the need for corrections or corrective actions
    - Cooperate with involved external party if complaint concerns activities outside the organization.
- Internal audits must be conducted at planned interval to ensure effectiveness of QMS, as well as its conformity to established documentation, applicable regulatory and legal requirements, and those deemed necessary by the organization.
    - Procedures for planning and conducting audits, as well as recording and reporting audit results, along with responsibilities and requirements (audit criteria, scope, interval, methods, etc.) associated with the above activities must be documented. Auditor selection must ensure objectivity and impartiality.
    - Necessary corrections or corrective actions must be timely implemented, verified, and reported.
    - Records of audits, audit results, and follow-up verification, if any, must be maintained.
- Appropriate monitoring and measurement of processes must be conducted to ensure their effectiveness and allow for necessary corrections and/or corrective actions.
- Appropriate monitoring and measurement of products according to their established requirements at applicable stages must also be conducted to ensure conformity to acceptance criteria prior to product release and service delivery.
    - Evidence of conformity, identities of personnel authorizing release, test equipment (if applicable), and identities of personnel testing/inspecting product (in case of implantable devices) must be recorded.

Control of nonconforming product (Section 8.3)

- Nonconforming products must be identified and prevented from use or delivery. Procedures for controlling these products must be documented and include:

    - Identifying controls
    - Determining responsibilities and authorities for identification, documentation, separation, evaluation (including need for investigation and/or report to applicable regulatory authorities and relevant external parties, and its associated rationale), and subsequent disposition of these products.
- If nonconforming product is identified before delivery, the organization must take one or more of the actions:
    - Removing identified nonconformities
    - Precluding its intended use/ application
    - Authorizing, under concession, its use, release, or acceptance, and providing justification, approval, and assurance of regulatory requirements satisfaction. Records of such acceptance and identities of authorizing personnel must be maintained.
- If nonconforming product is identified after delivery, the organization must document and take actions corresponding to the immediate and potential effects of the nonconformities, including issuing advisory notices.
- Rework on nonconforming product must follow documented procedures, be subjected to compliance verification after completion, and be recorded.

Analysis of data (Section 8.4)

- Procedures for collecting and analyzing data necessary for ensuring suitability, adequacy, and effectiveness of established QMS, as well as their results, must be documented. The input for these procedures must include:
    - Data from monitoring and measurement procedures
    - Feedback and audits
    - Conformity of processes and products to requirements
    - Potential improvements
    - Data from suppliers and service reports (if applicable)
    - Other data deemed necessary by the organization.

Improvement (Section 8.5)

- The organization must commit to the maintenance/ improvement of established QMS and products through the use of:
    - Quality policy and objectives
    - Audit results, post-market surveillance, analysis of data
    - Corrective and preventative actions
    - Management review.
- Corrective actions (to prevent recurrence) and preventative actions (to prevent occurrence) of nonconformities must be taken and in timely manner. Procedures for these actions and their results must be documented. The procedures must define requirements for:
    - Reviewing (potential) nonconformities (including complaints) and their causes
    - Evaluating the need for corrective/ preventative actions
    - Planning, documenting, and implementing the actions
    - Verifying and review action effectiveness and product compliance to established requirements.