ISO 13485

DIVYA GANAPATHY

CONTENTS

ISO13485:2012, *Medical devices – Quality management systems – Requirements for regulatory purposes*

Focus on the following items:

- Section 4.0 - Quality Management System Requirements Section 5.0 - Management Responsibility
- Section 6.0 - Resource Management
- Section 7.0 - Product Realization
- Section 8.0 - Measurement, Analysis, and Improvement

QMS?

- A quality management system (QMS) is a formalized system that documents processes, procedures, and responsibilities for achieving quality policies and objectives.
- A QMS helps coordinate and direct an organization's activities to meet customer and regulatory requirements and improve its effectiveness and efficiency on a continuous basis.
- The purpose is to improve process, reduce waste and lower cost, engage staff, facilitate and identify training …

QMS

- The basic steps to implementing a quality management system are as follows:
- Design
- Build
- Deploy
- Control
- Measure
- Review
- Improve

Design and build

The design and build portions serve to develop the structure of a QMS, its processes, and plans for implementation. Senior management must oversee this portion to ensure the needs of the organization and the needs of its customers are a driving force behind the systems development.

Deploy

Deployment is best served in a granular fashion via breaking each process down into subprocesses, and educating staff on documentation, education, training tools, and metrics. Company intranets are increasingly being used to assist in the deployment of quality management systems.

Control and measure

Control and measurement are two areas of establishing a QMS that are largely accomplished through routine, systematic audits of the QMS.

Review and improve

Review and improvement deal with how the results of an audit are handled. The goals are to determine the effectiveness and efficiency of each process toward its objectives, to communicate these findings to the employees, and to develop new best practices and processes based on the data collected during the audit.

QMS

4.1 - General requirements

- Implementation and maintenance of an effective QMS to provide medical devices meeting customer and regulatory requirements.
- Ensure control of outsourced processes

4.2 - Documentation requirements **“control”.**

- what is to be done and by whom, when, where, and how it is to be done, what materials, equipment and documents are to be used,
- how an activity is to be monitored and measured, Design History File, Technical File, Complaint File, device records, etc.

QUALITY SYSTEM

MANAGEMENT RESPONSIBILITY

5.1 Management commitment

- Is demonstrated by actions ensuring processes operate as an effective network of interrelated processes

5.2 Customer focus

- ensure customer requirements are understood

5.3 Quality policy

- Establishes commitment to: quality; continuing effectiveness of the quality management system; meeting customer and regulatory requirements
- Should be reviewed periodically for continued applicability

MANAGEMENT RESPONSIBILITY

5.5 Responsibility, authority and communication

- Examples demonstrating Responsibility & Authority:
- documented position descriptions, including responsibilities and authorities
- organization charts can be included in documented procedures or flowcharts.
- Independence must be demonstrated for certain activities (e.g. internal audits, one design review participant; management representative)

- Above documents to be controlled.. (Section 4.2.3)

MANAGEMENT RESPONSIBILITY

- 5.5 Responsibility, authority and communication
- One management representative - designated by top management!
- Functions can be entirely related to quality management system activities or in conjunction with other functions and responsibilities within the organization.
- If responsibility for other functions, ensure no conflict of interest between the responsibilities!
- Within an effective quality management system communications must be:
  - Encouraged
  - clear and understandable
  - bi-directional
  - at all levels of the organization open and active
- **Examples:** Internal audits, external assessments, management reviews, bulletin boards, all employee meetings, suggestion boxes, etc.

MANAGEMENT RESPONSIBILITY

- 5.6 Management Review
  Periodic assessment of the QMS for continued suitability, adequacy and effectiveness.

Inputs include:

a) results of audits,
b) customer feedback,
c) process performance and product conformity,

d) status of preventive and corrective actions,

e) follow-up actions from previous management reviews,
f) changes that could affect the quality management system,
g) recommendations for improvement, and

h) new or revised regulatory requirements.

Outputs include:

a) agenda
b) attendance record
c) presentation materials
d) improvements needed to maintain the effectiveness of the quality management system and its processes
b) improvement of product related to customer requirements
c) resource needs
d) statement of conclusion the effectiveness of the quality management system

RESOURCE MANAGEMENT

6.1 Provision of resources

Resources can be:

people
infrastructure
work environment
information
suppliers and partners natural resources
financial resources

- **Adequate resources are prerequisite to an effective QMS**

6.2 Human Resources
Personnel performing work affecting product quality and device safety and effectiveness must be competent ....
Qualifications include: • Education
•Experience
•Skills
•EFFECTIVE Training (initial and refresher)
•Formal certification (e.g. welding, soldering)
Organization must be able to demonstrate this!

RESOURCE MANAGEMENT

6.3 Infrastructure

Includes:

Buildings

- Work space
- Utilities (water, electricity, waste management, etc.)
- Process equipment (software and hardware)
- Equipment maintenance activities & frequency
- Supporting services (cleaning, etc.)

If not considered and appropriately defined, the above examples can potentially affect conformance with product requirements!

6.4 Work Environment

The most significant factors within the work environment that can affect product quality are:

- process equipment,
- established work environment (controlled environments, clean rooms, etc.)

personnel – internal and ***external***! (health, cleanliness, protective equipment/gear, i.e. static dissipating wrist bands, hoods & gowning, etc.)

"Established" means defined, documented, implemented and maintained!

PRODUCT REALIZATION

7.1 Planning of product realization

“Product realization” describes the processes starting with planning

- determination of customer requirements customer
- Communication
- design and development (7.3),
- purchasing (7.4),
- production and servicing (7.5),
- control of monitoring and measuring devices (7.6)
- delivery of the medical device
- record keeping requirements

The organization shall determine :

- product quality objectives & requirements
- definition of medical device lifetime (record retention!)
- establishing processes & documents
- resource needs
- design and development (7.3),
- verification & validation
- monitoring and inspection
- test activities and product acceptance criteria
- **RISK MANAGEMENT**
- RECORDS

PRODUCT REALIZATION

7.2 Customer-related processes

Focus is on product and services to be supplied. This includes requirements related to the product:

- design input/output for new product development,
- customer delivery expectations vs. delivery schedules
- customer feedback & communications relative to orders placed or product delivered
- regulatory or legal requirements
- design related factors included in customer orders
- unspecified customer expectations.

Review of product requirements prior to committing to supply:

- product requirements defined & documented
- resolution of contract/order discrepancies
- ensure ability to meet defined requirements

Review of post-marketing product performance

- additional product information (e.g. service, additional applications, maintenance, upgrades)
- customer complaints
- advisory notices

PRODUCT REALIZATION

7.3 Design and development

Established procedures describing design processes and ALL Design activities

- goals and objectives of the design and development program (i.e. what is to be developed, timeline, etc.) the markets intended
- identification of organizational responsibilities with respect to assuring quality during the design and development phase, to include interface with any suppliers
- identification of the major tasks by phases of the design
- expected outputs (deliverables and records) from each phase
- identification of appropriate existing and anticipated measurement & monitoring devices for development of product specifications, verification, validation and production related activities
- the selection of reviewers & composition of review teams
- planning transfer to production
- risk management activities
- supplier selection

PRODUCT REALIZATION

Design inputs include:

- intended use of the device,
- Indications and contra-indications for use of the device,
- performance claims and performance requirements (including normal use, storage, handling and maintenance),
- user and patient requirements,
- physical characteristics,
- human factors/usability requirements,
- safety and reliability requirements,
- toxicity and biocompatibility requirements,
- electromagnetic compatibility requirements,
- limits/tolerances,
- measurement and monitoring instruments,
- risk management or risk reduction methods
- reportable adverse events, complaints, failures for previous products,
- other historical data,
- documentation for previous designs,
- compatibility requirements with respect to accessories and auxiliary devices,

PRODUCT REALIZATION

Design input

- compatibility requirements with respect to the environment of intended use,
- packaging and labeling (including considerations to deter foreseeable misuse),
- customer/user training requirements,
- regulatory and statutory requirements of intended markets,
- relevant voluntary standards (including industry standards, national, regional or international standards, “harmonized” and other consensus standards),
- manufacturing processes,
- economic and cost aspects,
- lifetime of the medical device requirements, and need for servicing.

PRODUCT REALIZATION

Design outputs may include:
specifications for raw materials, component parts and sub-assemblies,

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

PRODUCT REALIZATION

7.3 Design and development

Design reviews may address the following questions:

Do designs satisfy specified requirements for the product?

Is the input adequate to perform the design and development tasks?

Are product design and processing capabilities compatible?

- Have safety considerations been addressed?
- What is the potential impact of the product on the environment?

Do designs meet functional and operational requirements, for example, performance and dependability objectives?

- Have appropriate materials been selected?
- Have appropriate facilities been selected?
- Is there adequate compatibility of materials, components and/or service elements?

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

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

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

PRODUCT REALIZATION

7.3 Design and development

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

If computer software has been used in design computations, modeling or analyses, has the software been validated, authorized, verified and placed under configuration control?

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

Are the assumptions made during the design processes valid?

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

- tests (bench tests, lab tests, chemical analysis, etc.)
- alternative calculations,
- comparison with proven design,
- inspections, and
- document reviews (e.g. specifications, drawings, plans, reports).

PRODUCT REALIZATION

7.3 - Design and development

Design validation goes beyond the technical issues of verifying output met input. It is intended to ensure that the medical device meets user requirements and the intended use.

- actual or simulated conditions
- consider capability and knowledge of user
- operating instructions
- compatibility with other systems
- the environment in which it will be used
- any restriction on the use of the product
- performed on production or production equivalent unit(s)

PRODUCT REALIZATION

7.3 Design and development
Control of design and development changes
Product design may require change or modification for many reasons.
Change can happen during or after the design phase
Changes may result from:
design review
design verification or validation
omissions or errors during the design phase which have been identified afterwards

- difficulties in manufacturing, installation and/or servicing
- risk management activities,
- requests from the customer or supplier,
- changes required for corrective or preventive action
- changes needed to address safety, regulatory, or other requirements

improvements to function or performance

PRODUCT REALIZATION

7.3 Design and development

When changes are necessary, evaluate effects on:

- product requirements and specifications
- intended use
- current risk assessment
- different components of the product or system
- manufacture,
- installation or use
- Verification and validation
- the regulatory status of the product

PRODUCT REALIZATION

7.4 Purchasing

Purchasing information describes the product to be purchased in sufficient detail, such as:

- technical information and specifications,
- test and acceptance requirements,
- quality requirements for products, services, and outsourced processes,
- environmental requirements (in manufacturing, storage, transportation, etc.)
- regulatory requirements,
- certification requirements

PRODUCT REALIZATION

Purchasing information : May also include:

- requirements for product approval and subsequent changes
- procedures, processes & equipment
- qualification of personnel
- QMS requirements
- method of communication
- responsibilities (special instructions, traceability & test records, record retention & retrievability, etc.)

conditions for review & changes to purchasing agreement

Verification of purchased product to ensure specified requirements are met:

receiving Inspection (shipments are complete, properly identified, undamaged)

- product incoming inspection (100%, sampling, skip lot, etc.)
- certification of suppliers

certificates of conformance or acceptance test reports from supplier

PRODUCT REALIZATION

7.5 Production and service provision

Control of production and service requires ***controlled conditions*** and includes many aspects:

- infrastructure (see 6.3)
- documentation and records (procedures, specifications, work instructions, test results, etc.)

defined by *impact on quality & regulatory requirements* as well as *output from risk management activities*

- suitable equipment (process, measurement, monitoring)
- activities for release, delivery, and post delivery, including traceability

Process validation activities can be described in phases:
definition, review and approval of equipment specifications
installation qualification (IQ)
operational qualification (OQ)
performance qualification (PQ)

PRODUCT REALIZATION

Traceability means the ability to trace the history or location of a product or activity by recorded identification:
forward to customers (also known as “device tracking”)
backward to raw materials, components, processes used in manufacturing, calibration, etc.
Example: trace a nonconformity back to it’s source and determine location of the remainder of the affected batch/series.

Customer property within the context of the standard is defined as property or assets owned by the customer and under control of the organization.

Examples of such property are
raw materials or components supplied for inclusion in product (including packaging materials),
product supplied for repair, maintenance or upgrading, product supplied for further processing (e.g., packaging, sterilization or testing),
customer intellectual property

PRODUCT REALIZATION

Preservation of product applies throughout the product realization processes and includes storage, handling, transportation and delivery (may include installation).

- gloves, static-dissipative measure, gowning,
- temperature, humidity, dust (particle count),
- packaging
- method of transportation (air, sea, ground, environmentally controlled, etc.)

To avoid damage, deterioration or contamination during handling, storage, distribution.

Software used in the monitoring or measurement process must be validated!
Exempt from calibration may be: instruments used for indication only
(not quantitative!), volumetric measurement glassware, etc.

8. MEASUREMENT, ANALYSIS AND IMPROVEMENT

8.1 General

Monitoring and measurement processes are required to:

ensure product conformance

ensure conformance of the QMS maintain effectiveness of the QMS

These processes include measurement and analysis of products AND processes.

8.2 Monitoring and Measurement

Feedback as key performance indicators of the QMS include:

- customer related information, post-market surveillance, etc.
- internal & external audit results
- monitoring and measurement of processes (not limited to production processes but also QMS processes!)

monitoring and measurement of product (may extend to point of installation!)

8. MEASUREMENT, ANALYSIS AND IMPROVEMENT

8.3 Control of nonconforming product

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

- determine product(s) affected
- identify the nonconforming product (at supplier, inhouse, in transit, at customer)
- document the existence and root cause of the nonconformity
- evaluate the nature of the nonconformity

•determine and record disposition to be made,

- control (e.g. by physical segregation) the subsequent processing of the nonconforming product consistent with the disposition decision
- notify others as appropriate (regulatory authorities, customer, supplier, alternate manufacturing facilities, etc.)
- define and implement **corrective** and **preventive** actions
- assess the effectiveness of corrective and preventive actions

8. MEASUREMENT, ANALYSIS AND IMPROVEMENT

8.5 Improvement

Corrective action is intended to eliminate nonconformities with the intent to prevent recurrence. Nonconformities may be identified in the QMS

- on the product
- in manufacturing processes
- with training
- environmental conditions
- control of equipment
- with suppliers, etc.

8. MEASUREMENT, ANALYSIS AND IMPROVEMENT

***Effective* corrective action** includes the following:

- clear and accurate identification of the nonconformity
- affected process(es) or procedure(s)
- identification of affected device(s) and recipient(s)
- identification of the root cause of the nonconformity,
- action required to prevent recurrence
- required approvals prior to taking action
- records that corrective action was taken as identified
- Effectiveness checks (likely to prevent recurrence, no new risks introduced by the corrective action, etc.)

8. MEASUREMENT, ANALYSIS AND IMPROVEMENT

Preventive action is initiated to address ***potential*** nonconformities.
Sources to consider include information & data from:

- receiving and incoming inspection
- products requiring rework, reject or yield data
- customer feedback and warranty claims,
- process measurements,
- identification of results that are out-of-trend but not out-of-specification,
- suppliers performance
- service reports, and,
- concessions/deviations.

KEY RECORDS TO BE MAINTAINED

Management Review (5.6.1)
Education, training, skills and experience (6.2.2.e)
Product realization processes (7.1.d)
Product requirements review and action (7.2.2)
Product requirements inputs (7.3.2)
Design reviews and actions (7.3.4)
Design verification and actions (7.3.5)
Design validation and actions (7.3.6)
Design changes (7.3.7)
Design change reviews (7.3.7)
Supplier evaluation and actions (7.4.1)
Process validation (7.5.2)
Traceability (7.5.3)
Customer notification regarding damage to customer property (7.5.4)
Production or service delivery, as determined to be necessary for special processes (7.5.2)
Review of previous measuring results when measuring equipment is found not to conform to requirements (7.6)
Calibration or verification (7.6)
Internal audits (8.2.2)
Product release authorization (8.2.4)
Nonconformities and actions taken (8.3)
Corrective actions taken (8.5.2 e)
Preventive actions taken (8.5.3 d)