Quality Management Systems for Medical Devices

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What is a Quality Management System (QMS)?

- A QMS consists of an organization's structure together with the planning, processes, resources and documents or records that you use to achieve your quality objectives
  - For example, quality objectives can be meeting a customers' and applicable regulatory requirements, establishing and maintaining a QMS, or improving a product.

- Generic QMS requirements are defined in ISO 9001 and are intended to be applicable to any organization, regardless of its type or size, or the product it provides.
  - The requirements of ISO 13485 (which is based on ISO 9001) are intended to be applicable to any medical device organization regardless of size and activity as a basis for demonstrating and supporting compliance with applicable regulatory requirements.

Quality Management System

Medical device manufacturers are required to develop and implement an effective QMS. To do this, a manufacturer must:

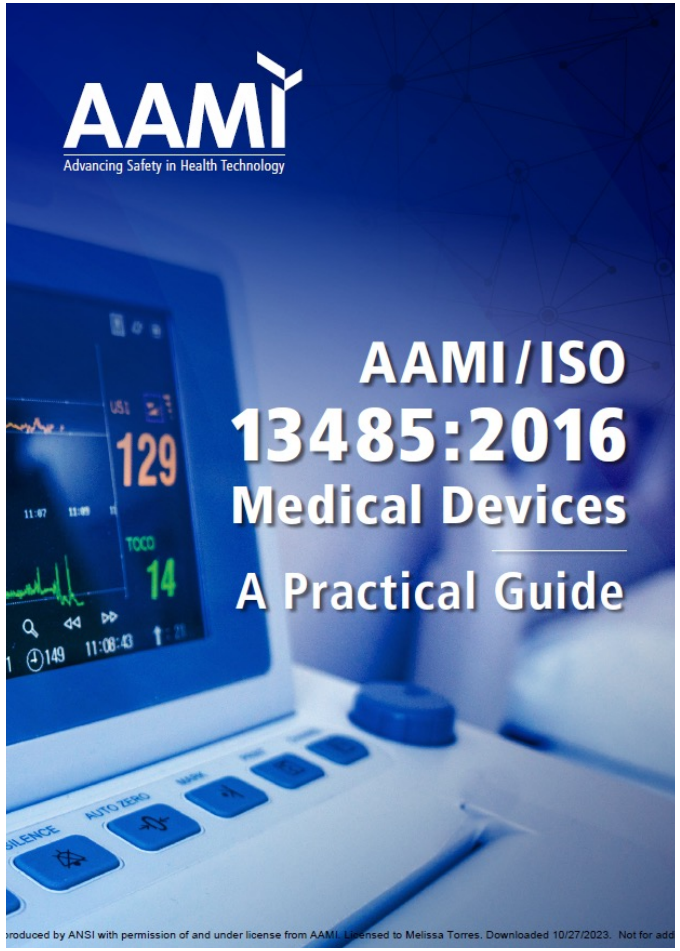
- Determine needs and expectations of customers
- Establish quality policy and quality objectives
- Determine needed processes and responsibilities
- Provide resources to attain quality objectives
- Establish methods for process measurement
- Determine process efficiency and effectiveness
- Determine means to prevent nonconformities
- Apply process for improvement of QMS
- Identify all applicable regulatory requirements

Flexibility of a Quality Management System

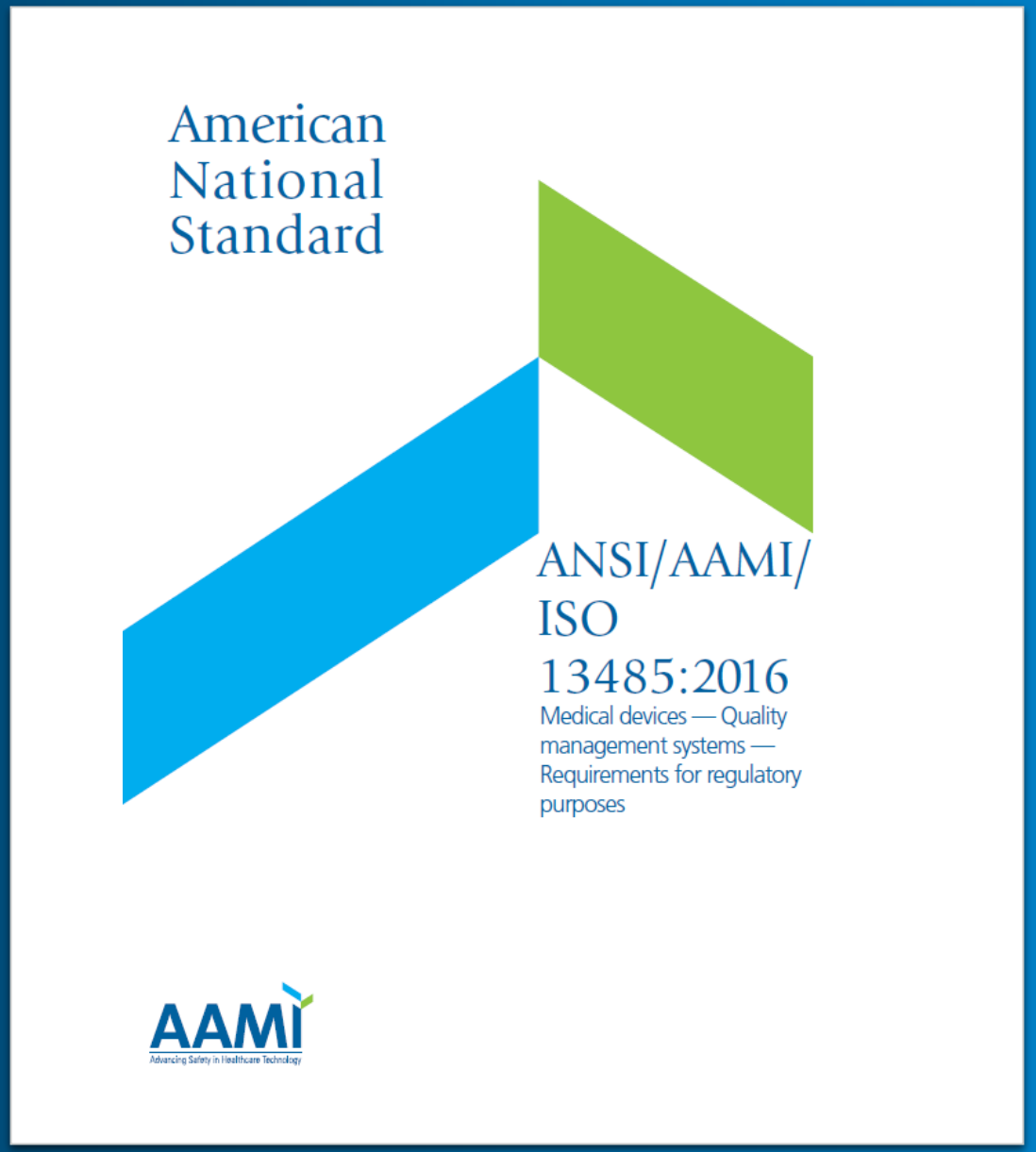
A manufacturer's Quality Management System depends on:

- The activities performed by the organization
- The size and structure of the organization
- The risk and complexity of their products and/or services
- The regulatory requirements for the countries in which they supply devices and/or services

ISO 13485 and ISO 13485 Handbook
Quality Management Systems for Medical Devices



Regulatory Authorities around the world require medical device manufacturers to meet the requirements in ISO 13485.



ISO 13485: 2016

FDA

Medical Devices – Quality Management Systems – Requirements for Regulatory Purposes

Establishes requirements for a Quality Management System (QMS) that can be used by an organization involved in one or more stages of the life-cycle of a medical device, including:

- design and development
- production
- storage
- distribution
- installation
- servicing and
- final decommissioning/disposal of medical devices

ISO 13485 employs a process-based approach

Regulatory use of ISO 13485

- ISO 13485 is used as a basis for QMS regulatory requirements by many Regulatory Authorities around the world.
  - Contains globally harmonized QMS requirements for medical device manufacturers/organizations.
  - US FDA has proposed legislation to incorporate ISO 13485 by reference into our regulations and replace our Quality System regulation.
- Global medical device manufacturers already comply with ISO 13485 to enter the market in many countries.
- ISO 13485 audits are routinely conducted globally of medical device manufacturers.

ISO 13485 Structure

1 Scope
2 Normative Reference
3 Terms and Definitions
4 Quality Management System
5 Management Responsibility
6 Resource Management
7 Product Realization
8 Measurement, Analysis and Improvement

Clause 4

Quality Management System

- 4.1 General Requirements
- 4.2 Documentation Requirements

Clause 4.1 General Requirements

An organization shall document a quality management system and maintain its effectiveness.

- All procedures, requirements, or activities that are required to meet the requirements of the standard and regulatory requirements shall be documented and controlled to ensure they are effective.
  - ***Documented*** = established, implemented and maintained.
- An organization has to ensure that resources and information are available to support the operation and monitoring of the processes.
  - Management is responsible for ensuring adequate resources.
- An organization is required to take a risk-based approach to the control of their QMS processes. This requires the organization to identify how their processes may directly or indirectly have an adverse impact to product safety or performance.

Sequence and interaction of the Processes

A quality management system is comprised of a series of interrelated processes, and the output of one process typically forms the input to another process.

To establish and maintain an effective QMS it is required that an organization determine the sequence and interaction of their applicable QMS processes.

Controlling changes to the QMS

Understanding the interactions of the QMS processes is crucial for evaluating the potential impact of a change to the QMS the medical devices produced under the QMS

Clause 4.1
Risk-Based Decision Making

ISO 13485:2016 Clause	Requirement
4.1.2	The organization shall apply a **risk based approach** to the control of the appropriate processes needed for the quality management system
4.1.4	Changes to be made to these (QMS) processes shall be: a) **evaluated for their impact** on the quality management system; b) **evaluated for their impact** on the medical devices produced under this quality management system
4.1.5	Outsourced QMS Activities - The controls shall be **proportionate to the risk involved** and the ability of the external party to meet the requirements in accordance with 7.4
4.1.6	The specific approach and activities associated with (QS) software validation and revalidation shall be **proportionate to the risk** associated with the use of the software

Clause 4.2
Documentation

Outlines the documents and records required by a QMS and how they should be controlled and documented

Documentation includes:

- quality policy
- quality objectives
- quality manual
- documented procedures and records to meet the requirements as well as those needed to ensure the effective planning, operation, and control of an organization's processes
- documentation specified by regulatory requirements
- medical device file

Clause 4.2.3
Medical Device File

General Description of the device including its intended use, labeling and IFU.

Product specifications

Specifications and procedures for manufacturing, packaging, storage, handling and distribution

Measuring and monitoring procedures

Installation and Servicing procedures if appropriate

Clause 4.2.4
Control of Documents

Procedures have to outline how to:

- review and approve documents for adequacy prior to issue;
- review, update as necessary and re-approve documents;
- ensure that the current revision status of and changes to documents are identified;
- ensure that relevant versions of applicable documents are available at points of use;
- ensure that documents remain legible and readily identifiable;
- ensure that documents of external origin, determined by the organization to be necessary for the planning and operation of the quality management system, are identified and their distribution controlled;
- prevent deterioration or loss of documents;
- prevent the unintended use of obsolete documents and apply suitable identification to them.

Many clauses in ISO 13485 reference this clause for how to document the various requirements in the standard

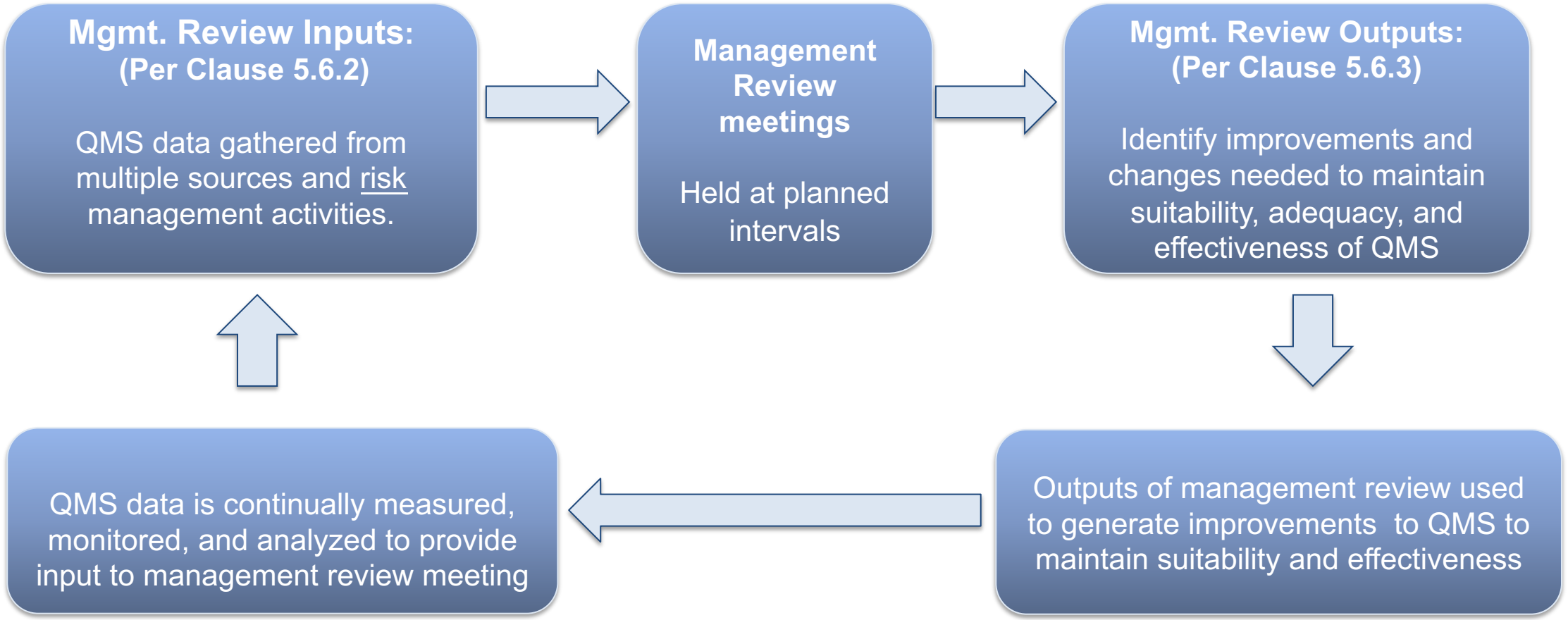
Clause 5

Management Responsibility

- 5.1 Management Commitment
- 5.2 Customer Focus
- 5.3 Quality Policy
- 5.4 Planning
- 5.5 Responsibility, Authority and Communication
- 5.6 Management Review

Top management has to demonstrate commitment to the development and implementation of the quality management system and maintenance of its effectiveness

Clause 5.6
Management reviews are an important tool for maintaining the suitability and effectiveness of a QMS



Clause 6

Resource Management

- 6.1 Provision of Resources
- 6.2 Human Resources
- 6.3 Infrastructure
- 6.4 Work Environment and Contamination Control

Clause 6
Resource Management - Summary

ISO 13485:2016 Clause	Requirement
6.1	An organization has to have the appropriate number of resources to implement the QMS, ensure the effectiveness, and meet customer and regulatory requirements.
6.2	Personnel have to be competent to perform duties and have the necessary education, training, skills and experience.
6.3	An organization has to have the appropriate infrastructure such as buildings, workspace, process equipment, and supporting services as well as maintenance activities.
6.4	An organization has to document procedures to ensure the work environment needed to achieve conformity to product requirements. The organization has to have procedures for control of contaminated or potentially contaminated product.

Clause 7

Product Realization

- 7.1 Planning of Product Realization
- 7.2 Customer-related Processes
- 7.3 Design and Development
- 7.4 Purchasing
- 7.5 Production and Service Provision
- 7.6 Control of Monitoring and Measuring Equipment

Clause 7.1
Planning of Product Realization

Product realization details the necessary controls, conditions, and risk management activities required to ensure that *product meets its specifications.*

The organization shall determine the following:

- quality objectives and requirements for the product;
- the need to establish processes and documents and to provide resources specific to the product, including infrastructure and work environment;
- required verification, validation, monitoring, measurement, inspection and test, handling, storage, distribution and traceability activities specific to the product together with the criteria for product acceptance; and
- records needed to provide evidence that the realization processes and resulting product meet requirements.

Clause 7.2
Customer-related Processes

- An organization shall:
  - determine the requirements related to the product such as customer and regulatory requirements as well as user training and any other identified requirements and
  - review those requirements related to the product.
- An organization shall document how they will relay information to the customer including:
  - product information;
  - enquiries, contracts or order handling, including amendments;
  - customer feedback, including complaints;
  - advisory notices.
- An organization has to have a process for communicating to regulatory authorities to ensure regulatory requirements are met.

Clauses of 7.3
Design and Development

7.3.1 General	7.3.2 Planning	**7.3.3 Inputs**	**7.3.4 Outputs**
7.3.5 Review	**7.3.6 Verification**	**7.3.7 Validation**	7.3.8 Transfer
	7.3.9 Changes	7.3.10 Files	

Clauses 7.3.3 and 7.3.4
Design Input and Design Output

- Design Input requirements form the basis for the device design, and ensure that the finished device is safe, effective, and meets its user needs and intended use.
  - Examples: Functions, features/options, safety requirements, software requirements, biocompatibility, manufacturability, use environment, applicable regulatory requirements and standards, etc.

- Design Outputs provide evidence of activities performed during the design process and are traceable to the design inputs
  - Examples: drawings, labeling, packaging, manufacturing procedures, test procedures, purchasing specifications, schematics, etc.

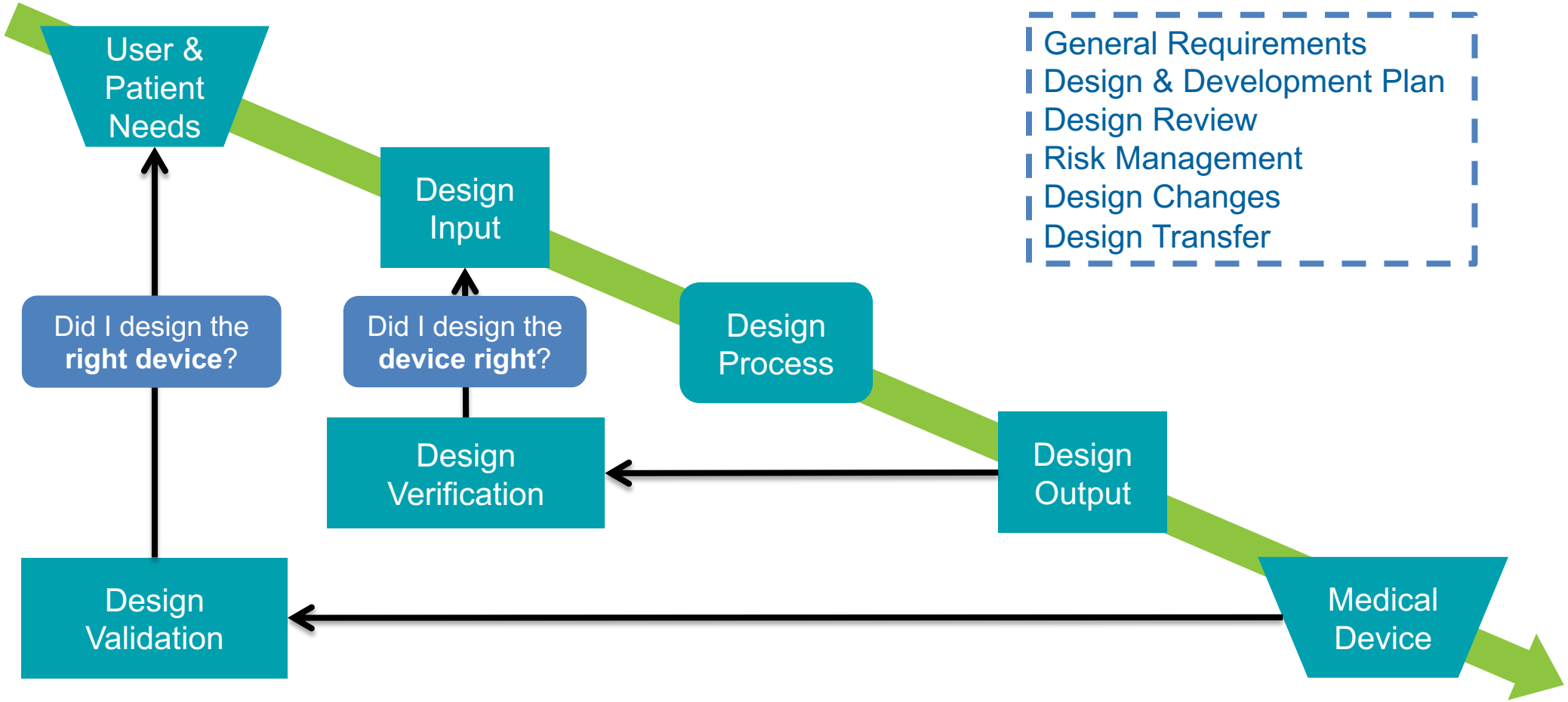
Clauses 7.3.6 and 7.3.7
Design Verification and Design Validation

- Design Verification ensures that the design and development outputs have met the design and development input requirements

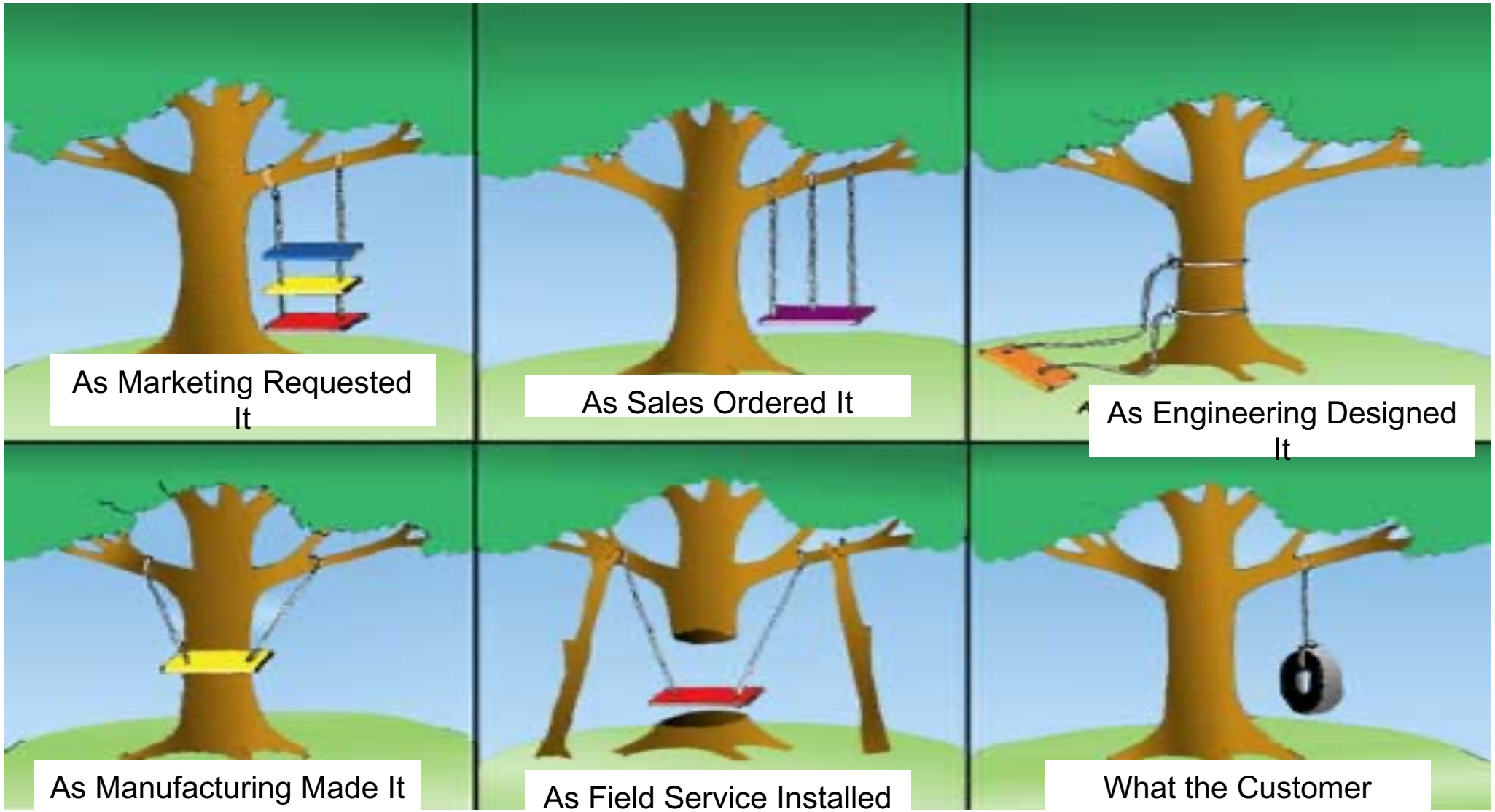
- Design validation ensures that device meets user needs and intended use.

- For both verification and validation activities the methods, acceptance criteria and, as appropriate, statistical techniques with rationale for sample size have to be documented.

Clause 7.3
Design and Development Activities



Why are Design and Development activities so important?



Clause 7.4
Purchasing

The evaluation and selection of suppliers is proportionate to the risk associated with the medical device

Manufacturers shall **evaluate** and **select** suppliers using a risk-based approach that considers:

- Can the supplier provide product that meets its requirements?
- Is there any data regarding the performance of the supplier?
- What is the effect of the purchased product on the quality of the medical device?

Purchasing information is maintained in documents and records.

Once a supplier has been established the company uses a risk-based approach of monitoring suppliers to ensure they consistently provide product which meets all requirements.

What is unique about medical devices and why is purchasing based on risk?

- Wide range in type of supplied products and services
  - Raw materials, Components, Software, Drugs, etc.
  - Laboratories, Sterilizers, Calibration, Installers and Service Providers, Auditors, Consultants
- Wide range in complexity in supplied products
  - From components up to finished devices
- Wide range in risk associated with supplied products and services
  - Same supplied product or service may have different risks based on use.
  - Same supplier may have different risks for different supplied product or service.

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Why should a Regulator be concerned about purchasing controls?

- Increasing outsourcing of critical components, and manufacturing of entire devices.

- Increasing recalls and product problems associated with purchased components.

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Risk Management in Purchasing (Clause 7.4 of ISO 13485)

- Manufacturing processes can be the source of hazards or hazardous situations, or the control measure for a hazard/hazardous situation.
- Analysis usually starts with the materials or services that are supplied
  - Finished devices
  - Raw material or component
  - Sterilization
  - Testing
  - Pest Control
- The criticality of what is supplied to the product or associated processes based on solid assessment will dictate the amount of supplier control required.

Risk Management in Purchasing (Clause 7.4 of ISO 13485)

- Based on the overall risk of the supplier, risk control measures may be implemented such as:
  - Supplier Audits
  - Quality Management System certificates
    - ISO 13485 or MDSAP certificates
  - Verification testing of materials received
  - Certificates of analysis
  - Test method validations
  - Statistical process control
  - Batch sizes

Clause 7.5
Production and Service Provision

- **Clause 7.5.1 Control of production and service provision**
- Clause 7.5.2 Cleanliness of product
- Clause 7.5.3 Installation activities
- Clause 7.5.4 Servicing activities
- Clause 7.5.5 Particular requirements for sterile medical devices
- **Clause 7.5.6 Validation of processes for production and service provision**
- Clause 7.5.7 Particular requirements for validation of processes for sterilization and sterile barrier systems
- Clause 7.5.8 Identification
- Clause 7.5.9 Traceability
- Clause 7.5.10 Customer property
- Clause 7.5.11 Preservation of product

Clause 7.5.1
Control of production and service provision

As appropriate, production controls shall include but are not limited to:

Documentation of procedures and methods for the control of production

Qualification of infrastructure

Implementation of monitoring and measurement of process parameters and product characteristics

Availability and use of monitoring and measuring equipment

Implementation of defined operations for labelling and packaging

Implementation of product release, delivery and post-delivery activities

Clause 7.5.6
Validation of Processes and Service Provision

- The organization shall validate any processes for production and service provision where the resulting output cannot be or is not verified by subsequent monitoring or measurement and, as a consequence, deficiencies become apparent only after the product is in use or the service has been delivered.

- Validation shall demonstrate the ability of these processes to achieve planned results consistently

Examples of processes that typically require validation

Welding	Injection Molding	Sterilization
Plastic Bonding	Sterilization	Sterile Package Sealing
Filling	Extrusion	Cleaning
Welding	Heat Treating	Plating
Aseptic Processing	Lyophilization	Clean room conditions

Risk Management in Production (Clause 7.5 of ISO 13485)

- Manufacturing processes can be the source of hazards or a hazardous situations and may include
  - Materials
  - Equipment
  - Personnel
  - Environment
  - Processes

- Risk assessment methods are used to identify, evaluate and determine the appropriate level of control for hazards and hazardous situations in manufacturing processes.
- Risk control measures may include validated test methods and validated processes.

Clause 7.6
Control of Monitoring and Measuring Equipment

Inspection, measuring, and test equipment is used to evaluate whether product is conforming or nonconforming during design activities, process validation, and routinely in production. It is important that the results are valid.

Determine monitoring and measurement to be undertaken and the equipment needed to provide evidence of conformity to product or process requirements.

Document procedures to ensure equipment is routinely checked, maintained, verified, or calibrated. (Includes handling, storage, and preservation.)

Records of all calibration and verification shall be maintained.

Clause 8

Measurement, Analysis and Improvement

- 8.1 General
- 8.2 Monitoring and Measurement
- 8.3 Control of Nonconforming Product
- 8.4 Analysis of Data
- 8.5 Improvement

Clause 8.2
Monitoring and Measurement

Clause	Title	Summary
8.2.1	Feedback	Gather and monitor information relating to whether the organization has met customer requirements
8.2.2	Complaint handling	Organization shall document procedures for timely complaint handling in accordance with applicable regulatory requirements
8.2.3	Reporting to regulatory authorities	The organization shall document procedures for providing notification to appropriate regulatory authorities (i.e., reporting adverse events or issuing advisory notices)
8.2.4	Internal audit	Organization shall conduct internal audits to determine whether the QMS conforms to requirements, is effectively implemented, and is maintained
8.2.5	Monitoring and measurement of processes	Organization monitors and measures the QMS processes
8.2.6	Monitoring and measurement of product	Organization monitors and measures product characteristics to verify requirements have been met.

Clause 8.3
Control of Nonconforming Product

The organization must have documented procedures and related responsibilities and authorities for the:

"Nonconforming" means that the product or service does not meet its requirements.

The requirements of Clause 8.3 ensure that nonconforming product is **not** used in production or distributed.

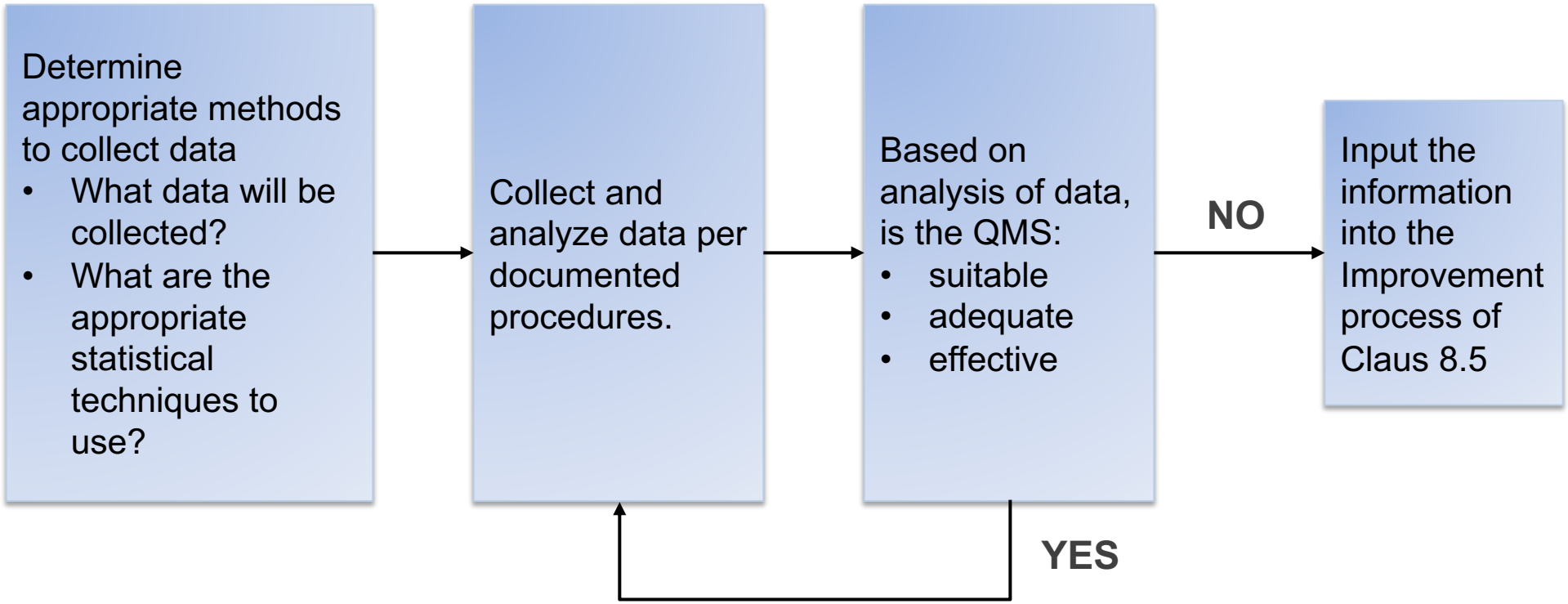
- Identification
  - Identify product that does not meet specification (i.e., dimension out of tolerance).
- Documentation
  - Forms used to document the nonconformance, investigations, test results, dispositions, etc.
- Evaluation
  - What happened, and do we need to **investigate** the cause of the nonconformity?
  - Do we need to notify external party of the nonconformity
- Segregation, and
  - Isolate the nonconforming product to ensure it is not used, installed, or distributed.
- Disposition of nonconforming product.
  - What happened to the nonconforming product?
    - (i.e., reworked, scrapped, use as is, returned to vendor)

Records must be maintained to document the nature of the nonconformity, the evaluation, any investigations performed, and rationale for decisions.

Clause 8.4
Analysis of Data

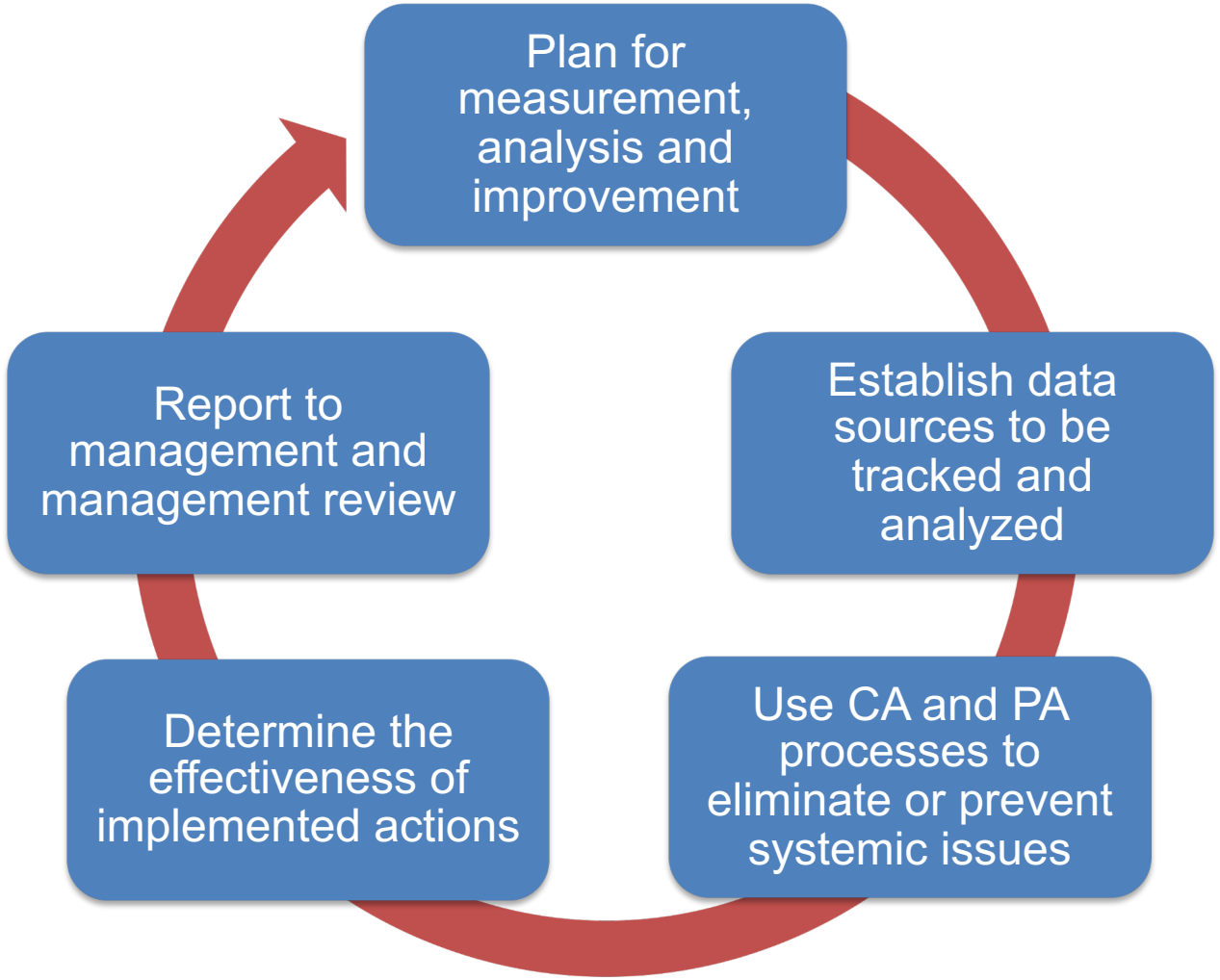
The analysis of data process is used to provide warnings of quality problems so that a firm may implement appropriate actions (Improvements) to resolve them.

Analysis of data is another process that ensures the QMS is maintained.



Clause 8.5 Improvement

The Improvement process is a closed feedback loop system that requires involvement from top management.



Clauses 8.5.2 and 8.5.3
Corrective Action/Preventive Action

The corrective/preventive action processes are used to identify and resolve systemic issues that impact:

- Products
- Manufacturing processes
- The QMS

The goal of the corrective/preventive action system is to improve the QMS:

- Use data to identify and resolve existing and potential problems.
- Determine the root cause(s) of the problem.
- Eliminate the cause of the problem or prevent a problem from occurring.

Corrective Action: *action taken to eliminate the cause of a detected nonconformity and to prevent recurrence.*

Preventive Action: *action taken to eliminate the cause of a potential nonconformity or other potential undesirable situations.*

Risk Management in Corrective Action/Preventive Action (Clause 8.5 of ISO 13485)

- Predetermined risk acceptability levels identified in the risk management plan can be used to determine when to:
  - Initiate an investigation
  - Perform a correction
  - Determine a corrective action
  - Identify a preventive action

- Risk analysis tools are used for investigation to root cause
  - Failure Modes and Effects analysis (FMEA)
  - Fault Tree Analysis (FTA)

Risk Management in Corrective Action/Preventive Action (Clause 8.5 of ISO 13485)

- Corrective Action and/or Preventive Action may be a control measure, or it may **cause new hazards or hazardous situations**
  - Design changes – software, material, etc
  - Process changes
  - Supplier changes
  - Specification changes

Summary

- A QMS documents the procedures and processes implemented throughout the lifecycle of a medical device and is essential for ensuring products are safe and effective for their intended use.
  - A QMS includes all aspects of design and development, manufacturing, supplier management, risk management, complaint handling, clinical data, storage, distribution, product labeling, and other areas.
- ISO 13485:2016 facilitates global alignment of appropriate regulatory requirements for QMS applicable to organizations involved in one or more stages of the lifecycle of a medical device.
- Many Regulatory Authorities around the world utilize ISO 13485 as a part of their regulatory requirements for medical devices.
- Utilization of ISO 13485:2016 certificates is a way of ensuring that the design and manufacturing of a medical device is done in a way to ensure that the product meets specifications.

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Resources

URL
ISO 13485:2016 - Medical devices — Quality management systems — Requirements for regulatory purposes (for purchase from standards organization)
ISO - ISO 13485:2016 - Medical devices - A practical guide (for purchase from standards organization)


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