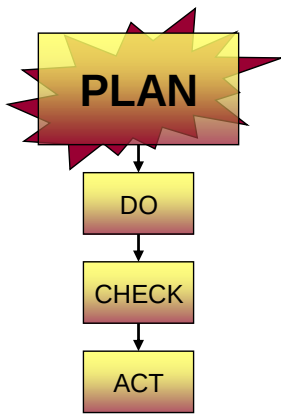
ISO 13485 Internal Auditor

PLAN: Determine the Requirements and Prepare for the Audit

"What Should Be"



Determine the Requirements

What Is ISO 13485:2016?

A set of quality management system requirements used in the medical device industry to *demonstrate* an organization's ability to *consistently* provide safe and effective product that meets customer and regulatory requirements.

Its intent is to facilitate global alignment of appropriate regulatory requirements for quality management systems applicable to organizations involved in one or more stages of the life-cycle of a medical device.

Reference: *ISO 13485:2016 Introduction, 0.4 Relationship with ISO 9001*

The Standard can be summarized in this common-sense approach:

- Develop a good understanding of your QMS processes
- Document QMS processes based on current best practices
- Deploy documented best practices throughout the organization
- Establish and deploy measurable objectives
- Ensure best practices are followed (Internal Audits)
- Identify opportunities to correct and prevent systemic problems from occurring or reoccurring
- Ensure Changes are Controlled
- Establish a strong foundation for maintaining effectiveness of your systems and processes

What Is ISO 13485:2016?

Background

- Medical QMS model can be used by an organization for the design and development, production, storage and distribution, installation and/or servicing of medical devices, and the design, development and provision of associated activities.
- 1st edition 1996, as companion to ISO 9001/02:1994
- 2nd edition 2003, as an unique individual Standard, aligned with ISO 9001:2000
- 3rd edition 2016 to align with ISO 9001:2008 and maintain consistency with latest cGMP/regulatory requirements.
- Can be used by internal and external parties, including certification bodies, to assess the organization's ability to meet customer and regulatory requirements.
- Internationally recognized and accepted
- Uses a process approach

Full title: *ISO 13485 Medical devices — Quality management systems — Requirements for regulatory purposes*

3rd edition 2016–03–01, Reference number ISO 13485:2016(E)

The associated regulation in the United States is *FDA Title 21 CFR Part 820: Quality System (QS) Regulation/Medical Device Good Manufacturing Practices*. The term “cGMP” gets used as well, and stands for Current Good Manufacturing Processes.

Other helpful documents:

- *ISO 13485:2016 - Medical devices — A Practical Guide (2017 Ed. 1),* replaces the former *ISO-TR 14969:2004 Medical devices — Quality management systems — Guidance on the application of ISO 13485:2003,* which was withdrawn.
- *ISO 14971:2007 Medical devices — Application of risk management to medical devices*

Guidance: Normative Reference

ISO 9000:2015 is a normative reference for definitions.

Additional Definitions in ISO 13485:2016:

1. Advisory Notice
2. Authorized Representative
3. Clinical Evaluation
4. Complaint
5. Distributor
6. Implantable Medical Device
7. Importer
8. Labelling
9. Life-Cycle
10. Manufacturer
11. Medical Device
12. Medical Device Family
13. Performance Evaluation
14. Post-Market Surveillance
15. Product
16. Purchased Product
17. Risk
18. Risk Management
19. Sterile Barrier System
20. Sterile Medical Device

Definitions increased from 8 in the 2003 version to 20 in the 2016 revision.

Product is defined as the "result of a process." Generic categories are given as services, software, hardware and processed materials along with the following text: *"Many products comprise elements belonging to different generic product categories. Whether the product is then called service, software, hardware or processed material depends on the dominant element."-3.15 ISO 13485:2016*. Additional examples and Notes are also provided.

The definition of "implantable medical device" now includes active implantable medical devices.

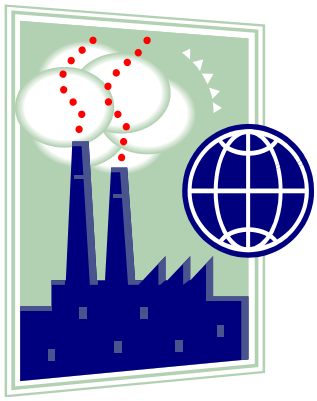
Guidance: “Appropriate”

- Always assumed to be appropriate
- When used in the Standard, exclusion must be justified
- *Meaning* — if it is necessary for:
  - product to meet requirements;
  - compliance with applicable regulatory requirements;
  - the organization to carry out corrective action;
  - the organization to manage risks.

ISO 13485:2016, *Introduction*, section *0.2 Clarification of concepts* was modified to add the criteria for regulatory requirements and risk management.

This section 0.2 also clarifies meanings regarding the use of the following terms: risk, documented, product, regulatory requirement, shall, should, may and can.

ISO 9001…The Commercial Model



CUSTOMER SATISFACTION
&
CONTINUAL IMPROVEMENT

ISO 13485…The Medical Regulatory Model

Safety and Efficacy

How Does It Differ from ISO 9001:2015?

- **Product Specific:** focus on maintaining the effectiveness of the QMS to consistently produce safe and effective products.
- **Regulatory**: emphasis on complying with regulatory requirements, and as such, customer satisfaction and continual improvement are not considered appropriate to include.
- **Documented**: Much greater emphasis on documented procedures and with detailed records requirements.
- Adds medical device-specific requirements in relation to:
  - Medical device file requirement
  - Risk Management – follows both ISO 14971 and ISO 31000
  - Controls for work environment and production processes related to contamination, cleanliness, sterilization and sterile barrier systems.
  - Nonconforming Material (rework of product)
  - Identification of product status, traceability, labeling and packaging
  - Installation activities
  - Design Control, stricter on documentation, records and validation
  - Feedback processes (as opposed to customer satisfaction)

ISO 13485:2016 contains 51 places where a specific documented procedure (including policies, objectives, plans, system, etc.) is required (some of these are "if applicable").

ISO 9001:2015 requires specific documents in just three places: scope of the QMS, quality policy and quality objectives.

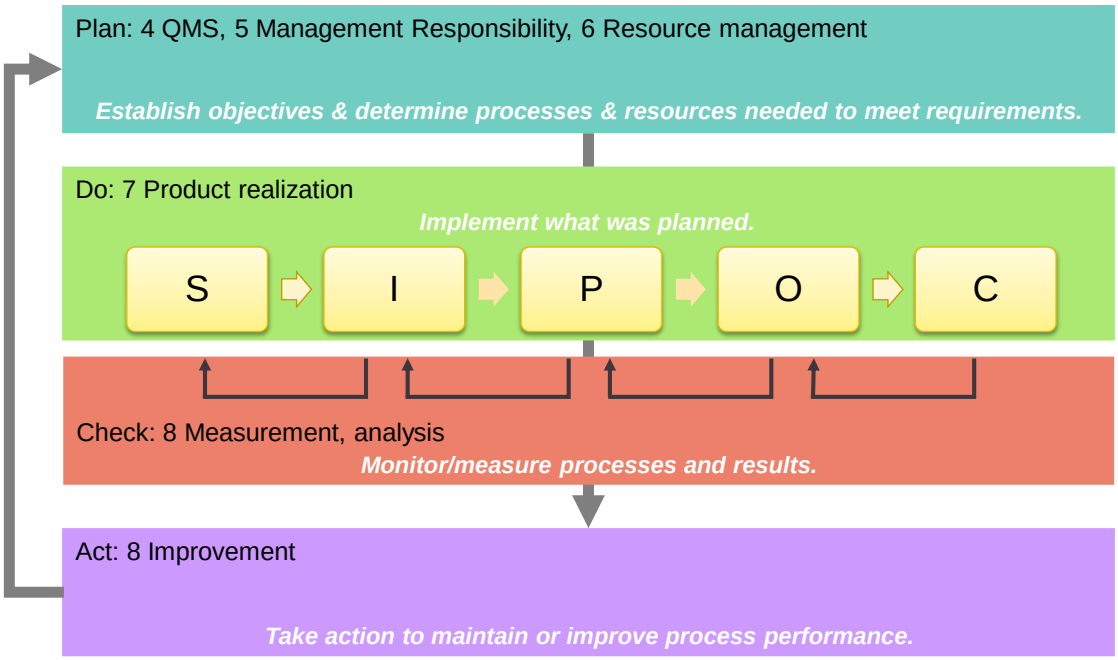
Both Standards contain many requirements for records.

ISO 13485:2016 did not adopt the new high-level Management System Structure for titles and numbers used in ISO 9001:2015; it does provide the correspondence between the current versions of ISO 13485 and ISO 9001 in Annex B.

ISO 14971 addresses risk related to product/patient safety (a regulatory compliance perspective).

ISO 31000 addresses risk to meeting organizational objectives (a business perspective).

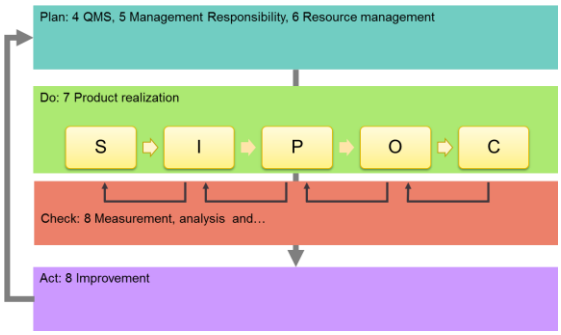
PDCA in ISO 13485



The Notes in this section will overview the changes to the Standard for each of the sections of the ISO 13485:2016 Standard.

The Standard has been modified throughout to refer to "applicable" regulatory requirements. The clarification in the *Introduction, section 0.2* states:
"When the term 'regulatory requirements' is used, it encompasses requirements contained in any law applicable to the user of this International Standard (e.g. statutes, regulations, ordinances or directives). The application of the term 'regulatory requirements' is limited to requirements for the quality management system and the safety or performance of the medical device."

Clause 4 Quality Management System



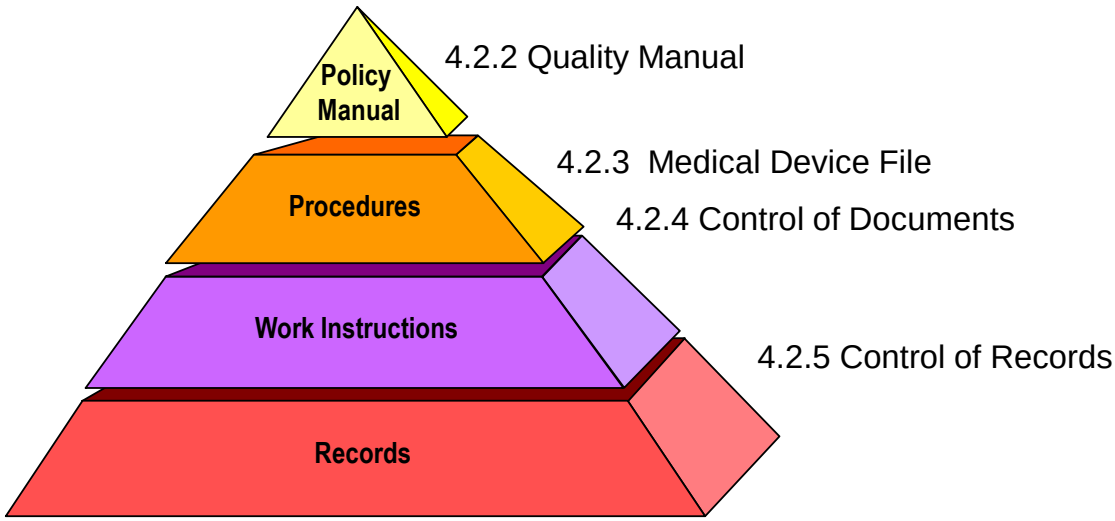
4.1 General Requirements

- 4.1.1* QMS and organization role
- 4.1.2 Determination of QMS processes and risk-based approach for control
- 4.1.3 Planning for the operation of QMS processes
- 4.1.4 Change management for QMS processes
- 4.1.5 Control of outsourced QMS processes
- 4.1.6 Validation of software used for the QMS

** These sub-heads are not in the Standard; they give descriptions of these untitled sub-clauses.*

- 4.1.1 has a new requirement to document the role undertaken by the organization under applicable regulatory requirements, and in 4.1.2 this role is to be taken into account when determining the processes needed for the QMS.
- 4.1.2 also adds that a risk-based approach is also to be applied to the control of appropriate QMS processes.
- 4.1.3 adds that records needed to demonstrate conformance to the Standard and compliance with regulations must be established and maintained.
- 4.1.4 requires that changes to QMS processes are evaluated for their impact on the QMS and the medical devices produced. Changes must be controlled per the Standard and regulations.
- 4.1.5 adds clarification of the organization's responsibility for outsourced processes and requirements for their control, including written quality agreements.
- 4.1.6 adds a requirement to document procedures for, and retain records of, the validation of the application of computer software used in the QMS. Specific S/W requirements related to production and support processes appear in later clauses of the Standard.

QMS Information Structure



Quality Policy & Manual

Document(s) stating organization's *policy* interpretation of external requirements/guidelines (e.g., International Standards, Regulations, Customer's Systems Requirements, Industry Standards, etc.) as applied to the organization. Says: *"What and why."* The Quality Policy and Manual provide the organization's philosophy and direction.

Procedures

Documents describing the organization's high-level processes (which may be listed in a Manual). They describe methods and responsibilities in more detail. Can make use of flow diagrams to simplify this task. Says: *"Who does what and when."*

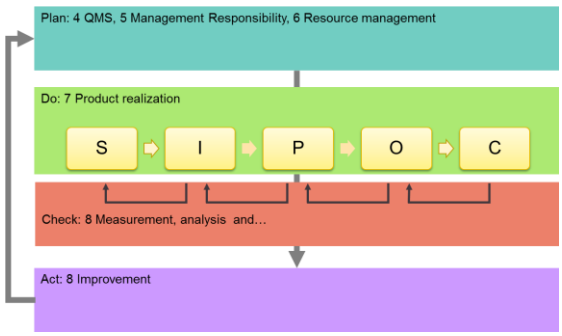
Work Instructions

Documents that provide detail to support the organization's procedures. They provide specific information on activities, tasks, and steps such as: how to build specific assemblies, how to load a program into a robot, keystrokes for order entry, etc. May also be forms, checklists, work standards/examples.
Says: *"How this part of the process is performed."*

Records

Records are the information and/or data that show a process has been performed. When a form (Work Instruction) has been filled out, it then becomes a record. Records can be such things as collected measurement/monitoring data, supplier information, computer data, test results, quality reports, etc. Records provide *"objective evidence"* that a process has been carried out.

Clause 4 Quality Management System

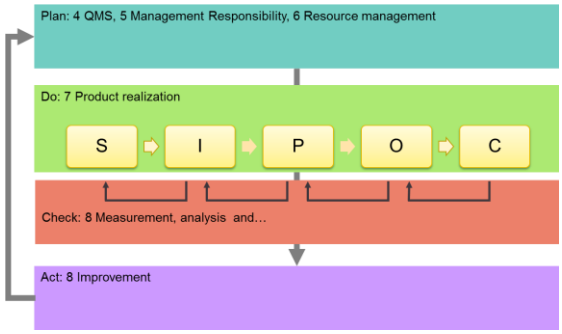


4.2 Documentation Requirements

- 4.2.1 General
- 4.2.2 Quality Manual
- 4.2.3 Medical device file
- 4.2.4 Control of documents
- 4.2.5 Control of records

- 4.2.3 is a new clause that pulls information from the 2003 version's 4.2.1 "General" clause and clarifies its application to each medical device type or family and lists what the contents should include, modifying some previous wording and adding a requirement for a "general description of the medical device, intended use/purpose, and labelling, including any instructions for use."
- 4.2.4 clarifies the application of documents of external origin and adds a requirement to prevent deterioration or loss of documents.
- 4.2.5 adds a requirement for protecting confidential health information contained in records. It also adds that changes to a record are to remain identifiable.

Clause 5 Management Responsibility



5.1 Management Commitment

5.2 Customer Focus

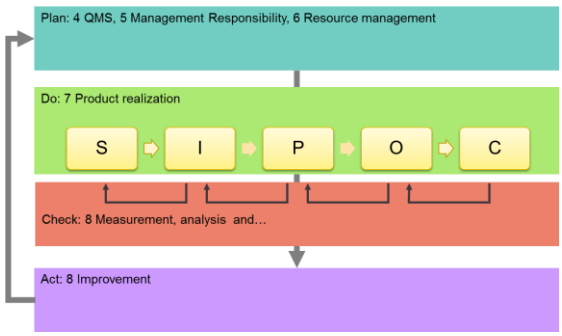
5.3 Quality Policy

5.4 Planning

- 5.4.1 Quality objectives
- 5.4.2 Quality management system planning

- 5.2 adds “applicable regulatory requirements” to requirements that top management must ensure are determined and met.
- 5.4.1 adds “applicable regulatory requirements” to the criteria for establishment of quality objectives.

Clause 5 Management Responsibility

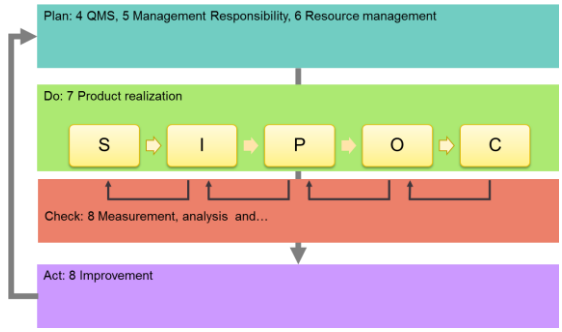


5.5 Responsibility, Authority, and Communication
- 5.5.1 Responsibility and authority
- 5.5.2 Management representative
- 5.5.3 Internal communication

5.6 Management Review
- 5.6.1 General
- 5.6.2 Review input
- 5.6.3 Review output

- 5.6.1 now requires documented procedure(s) for management review.
- 5.6.2 adds complaint handling and reporting to regulatory authorities to the list of review input.
- 5.6.3 adds that review output must include the input reviewed, and for the record of decisions and actions, “suitability” and “adequacy” are added to the list of improvements to the QMS, as are “changes needed to respond to applicable new or revised regulatory requirements.”

Clause 6 Resource Management



6.1 Provision of Resources

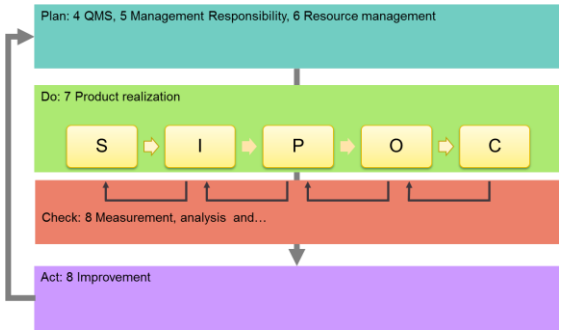
6.2 Human Resources

6.3 Infrastructure

6.4 Work Environment and contamination control

- 6.2 adds a requirement to document the process(es) for establishing competence, providing the training needed and ensuring awareness of personnel of their contribution to the QMS.
- 6.2 also has a guidance note that methods for checking effectiveness of training should be proportionate to the risk associated with the work.
- 6.3 adds that infrastructure requirements must be documented to ensure product conformity, prevent product mix-up and ensure orderly handling of product. Information systems are added to the list of supporting services, in alignment with the emphasis on software used in the QMS. This clause also adds clarification that maintenance requirements (as appropriate) also apply to equipment used for production, monitoring and measurement and work environment control.
- 6.4.1 adds that requirements for the work environment must be documented.
- 6.4.2 adds a sub-clause with specifics for contamination control for sterile medical devices, and again, requirements must be documented.

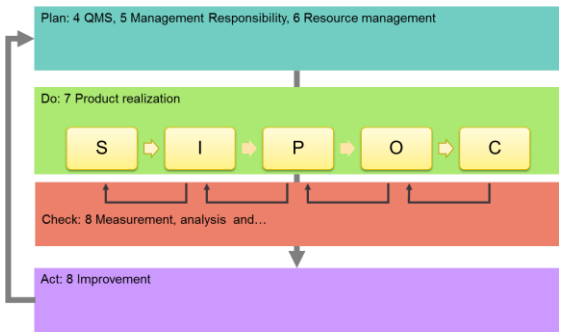
Clause 7 Product Realization



7.1 Planning of Product Realization

- 7.1 adds to and expands on some of the existing items in the list of planning considerations (related to infrastructure, work environment, measurement, handling, storage, distribution and traceability activities).

Clause 7 Product Realization



7.2 Customer–Related Processes

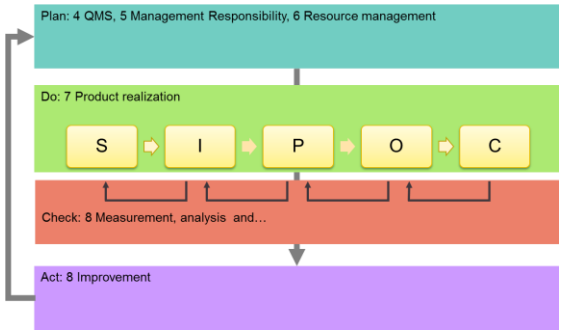
7.2.1 Determination of requirements related to product

7.2.2 Review of requirements related to product

7.2.3 Communication

- 7.2.1 adds determination of any needs for user training to ensure specified performance and safe use of the medical device.
- 7.2.2 adds to the review of requirements applicable regulatory requirements and any user training needs as identified in 7.2.1.
- 7.2.3 adds a requirement to document arrangements for communicating with customers, as well as to communicate with regulatory authorities per applicable requirements.

Clause 7 Product Realization

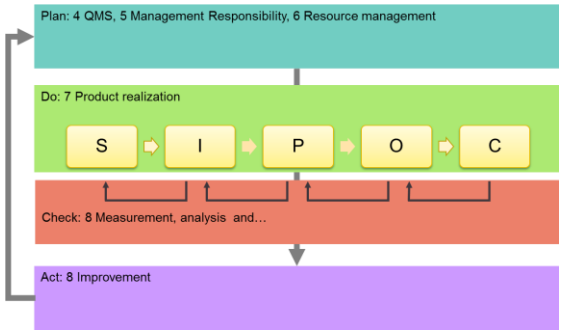


7.3 Design and Development

- 7.3.1 General
- 7.3.2 D & D planning
- 7.3.3 D & D inputs
- 7.3.4 D & D outputs
- 7.3.5 D & D review
- 7.3.6 D & D verification
- 7.3.7 D & D validation
- 7.3.8 D & D transfer
- 7.3.9 Control of D & D changes
- 7.3.10 D & D files

- 7.3.2 clarifies that D & D planning documents are to be maintained and that planning items shall be documented. Two items are added to the planning list: methods to ensure traceability of D & D outputs to inputs, and resource needs, including necessary competence of personnel. (The requirement to manage interfaces between different groups involved in D & D was eliminated).
- 7.3.3 expands on the wording of some D & D inputs and adds “usability” to the list of product-related inputs.
- 7.3.5 clarifies some specifics about documentation and record keeping for design reviews.
- 7.3.6 and 7.3.7 add documentation requirements for verification and validation plans and includes requirements for the samples to be used. Requirements are added for consideration of product interfaces with the medical device. Release and records requirements are also added.
- 7.3.8 is a new sub-clause that gives more specific requirements regarding the transfer of design outputs to manufacturing.
- 7.3.9 adds a requirement for a documented procedure for controlling D & D changes, and requirements for consideration of the effects of D & D changes in terms of risk, regulations and other product considerations.
- 7.3.10 is a new sub-clause that mirrors the earlier medical device file mentioned in 4.2.3, but is specific to D & D.

Clause 7 Product Realization

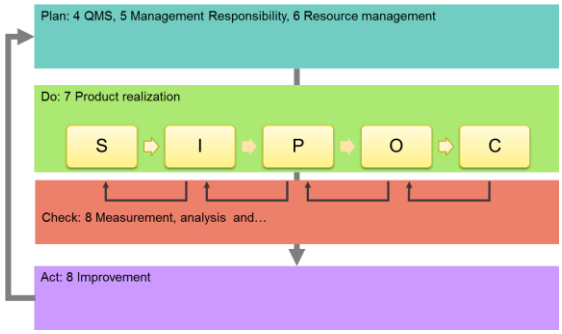


7.4 Purchasing
- 7.4.1 Purchasing process
- 7.4.2 Purchasing information
- 7.4.3 Verification of purchased product

7.5 Production and service provision
- 7.5.1 Control of production and service provision
- 7.5.2 Cleanliness of product
- 7.5.3 Installation activities
- 7.5.4 Servicing activities

- 7.4.1 adds consideration of associated risk to criteria for suppliers, including when requirements are not met. Also expands on the purpose of monitoring of supplier performance and how results should be used.
- 7.4.2 expands and clarifies purchasing information to be provided to the supplier, including written agreements regarding control of changes to purchased product prior to their implementation by the supplier.
- 7.4.3 carries through the added focus on risk in determining the extent of verification needed and adds requirements for the organization to assess risk when becoming aware of changes to the purchased product.
- 7.5.1 adds more details regarding controls for production.
- 7.5.2 adds contamination control to the previous cleanliness requirements.
- 7.5.4 adds requirements for the analysis of records of servicing activities for both complaint investigation and improvement.

Clause 7 Product Realization



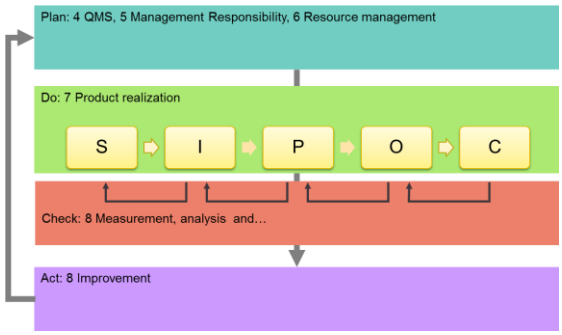
7.5 Production and Service Provision, *continued*

- 7.5.5 Particular requirements for sterile medical devices
- 7.5.6 Validation of processes for production and service provision
- 7.5.7 Particular requirements for validation of processes for sterilization and sterile barrier systems
- 7.5.8 Identification
- 7.5.9 Traceability
- 7.5.10 Customer property
- 7.5.11 Preservation of product

7.6 Control of Monitoring and Measuring Equipment

- 7.5.6 adds a requirement to document validation procedures and expands on the criteria, carrying through the emphasis on sample selection (from Design & Development) and approval of process changes. Details are added regarding required records of validation.
- 7.5.7 adds similar considerations for validation of processes for sterilization and sterile barrier systems.
- 7.5.8 brings identification of product status with respect to monitoring and measurement requirements under the sub-clause of Identification, with its requirement for documented procedures. A new requirement is added for a documented system for assignment of unique device ID, if required by applicable regulatory requirements.
- 7.5.9 has expanded descriptions of requirements and role responsibilities regarding traceability.
- 7.5.11 modifies wording used to describe preservation requirements.
- 7.6 adds requirements for documented procedures for calibration or verification, including validation of computer S/W used for monitoring and measurement, with S/W validation proportionate to risk associated with its use and the effect on product conformity. Records requirements for S/W validation are also added.

Clause 8 Measurement, Analysis & Improvement



8.1 General

8.2 Monitoring and Measurement

- 8.2.1 Feedback
- 8.2.2 Complaint handling
- 8.2.3 Reporting to regulatory authorities
- 8.2.4 Internal audit

- 8.2.1 clarifies that feedback should include data gathering from both production and post-production activities, and makes a stronger link to using this information as an input to risk management activities.
- 8.2.2 is a new sub-clause that expands on previous requirements regarding complaints handling and now requires a documented procedure.
- 8.2.3 is a new sub-clause that expands on previous requirements regarding reporting to regulatory authorities. In addition to the previous requirement for a documented procedure, it also requires the organization to maintain records of reporting to these authorities.

8.2.4 Internal Audit: "Must Do" Requirements

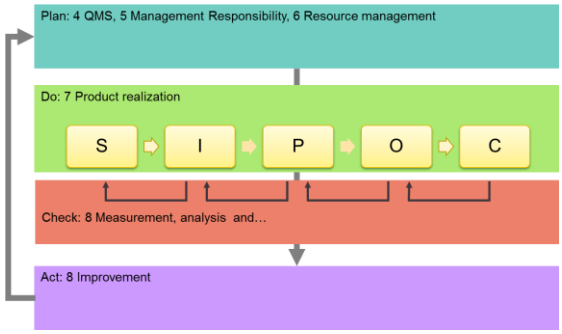
- Conduct audits at planned intervals
- Determine if QMS:
  - Conforms to:
    - Planned and documented arrangements (yours)
    - Requirements of the Standard
    - Requirements set by the organization (you)
    - Applicable regulatory requirements
  - Is effectively implemented & maintained
- Plan audits considering:
  - Status & importance of processes and areas
  - Prior results
- Define and record audit criteria, scope, interval and methods
- Audit records to include processes and areas audited and the conclusions

- 8.2.4 modifies wording to clarify that "arrangements" are those that are documented (as is seen in other parts of the Standard), along with some other wording modifications. More detail is given on what should be contained in the audit records, with an emphasis on providing evidence of both conformance and nonconformance.

8.2.4 Internal Audit: “Must Do” Requirements

- Ensure objectivity and impartiality in auditor selection and conduct
- Cannot audit own work
- Define responsibilities in documented procedure
  - Planning and conducting audits
  - Reporting results
  - Keeping records of audit results
- Management shall ensure necessary corrections and corrective actions are taken “without undue delay” to eliminate nonconformities and their cause(s)
- Must follow up to verify actions taken and reporting of results
- Audit results will be one input to management review (sub-clause 5.6.2)

Clause 8 Measurement, Analysis & Improvement



8.2 Monitoring and Measurement, continued

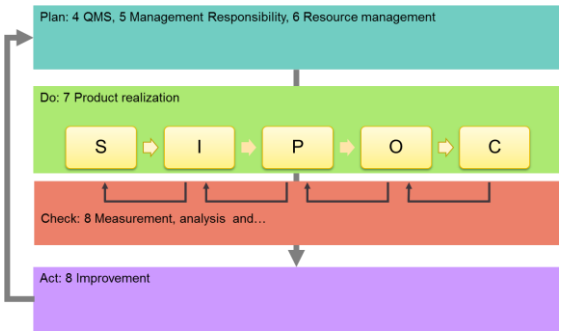
- 8.2.5 Monitoring and measurement of processes
- 8.2.6 Monitoring and measurement of product

8.3 Control of Nonconforming Product

- 8.3.1 General
- 8.3.2 Actions in response to nc product detected before delivery
- 8.3.3 Actions in response to nc product detected after delivery
- 8.3.4 Rework

- 8.2.6 adds, as appropriate, a requirement to record the ID of test equipment used to perform measurement activities.
- 8.3.1 adds more detail regarding evaluation and investigation, including notification of external parties and records of these activities, including rationale for decisions.
- 8.3.2 adds details to the requirements for concessions; this sub-clause covers actions in response to nonconformities detected before delivery.
- 8.3.3 addresses nonconformities found after delivery and adds records requirements related to issuance of advisory notices.

Clause 8 Measurement, Analysis & Improvement



8.4 Analysis of Data

8.5 Improvement

- 8.5.1 General
- 8.5.2 Corrective action
- 8.5.3 Preventive action

- 8.4 adds the same statement regarding determination of appropriate methods, including statistical techniques, that was previously and still is found in 8.1 under General requirements. Audits and service reports (as appropriate) are added to the list of inputs for analysis.
- 8.5.1 adds “adequacy” to the list of necessities for QMS improvements, along with medical device safety and performance and post-market surveillance.
- 8.5.2 adds a requirement that corrective action (CA) shall be taken without undue delay (as in 8.2.4). Also added is a requirement to verify that CA does not have an adverse affect on regulatory requirements or safety and performance of the medical device.
- 8.5.3 adds the same requirements as in 8.5.2 for updating documentation as needed as part of preventive action and the verification of no adverse effects.

Effective Use of the QMS