Regulatory Brief

21CFR Part 820

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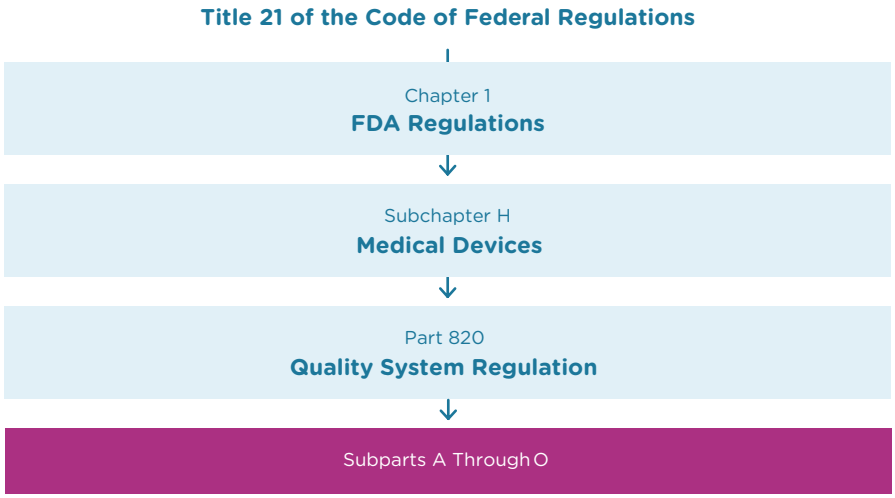
What is 21 CFR Part 820?

21 CFR 820 is the FDA federal regulation that pertains to quality systems for medical device manufacturers, and it is part of the agency's set of Current Good Manufacturing Practices (CGMP) for industry. Also referred to as the FDA's quality system regulation (QSR), the regulation defines design controls and quality processes at all stages of device development in order to ensure that all medical devices marketed in the United States are safe and effective.

21 CFR 820 consists of 15 subparts, which define quality system requirements for each stage and function within the medical device manufacturing process. We define each subpart below.

Federal regulations are organized as Title > Chapter > Subchapter > Part, which means that 21 CFR 820 is short-hand for:



21 CFR Part 820 Requirements

Part 820: General Controls (subpart A)

The General Controls subpart contains three sections providing general information about the regulation, including the scope and applicability along with key definitions.

Scope

The regulation defines current good manufacturing practice (CGMP) requirements governing the methods, facilities, and controls used for the "design, manufacture, packaging, labeling, storage, installation, and servicing of all finished devices intended for human use." Specifically, this subpart defines:

- Applicability:

  The requirements of this regulation are intended to ensure the safety and efficacy of all finished medical devices intended for human use that are manufactured in or imported into the United

States. Manufacturers that are involved in some, but not all, manufacturing operations should comply with those requirements that are applicable to the functions they are performing.

Exceptions:

- This regulation does not apply to manufacturers of medical device components, but such manufacturers are encouraged to use this regulation as guidance.
- Class I medical devices are exempt from the Design Controls defined in this regulation, except for those listed in § 820.30(a)(2).
- Manufacturers of blood and blood components are not subject to this regulation but are subject to Biologics good manufacturing practices as defined in Subchapter F, Part 606 of the regulation.

Definitions

This section of the regulation contains definitions for a number of terms used throughout the document. The following are the major definitions related to quality records:

- **Design history file** (DHF): A compilation of records that describes the design history of a finished device.
- **Design input:** The physical and performance requirements of a device that are used as a basis for device design.
- **Design output:** The results of a design effort at each design phase and at the end of the total design effort. The finished design output is the basis for the device master record. The total finished design output consists of the device, its packaging and labeling, and the device master record.
- **Device history record** (DHR): A compilation of records containing the production history of a finished device.
- **Device master record** (DMR): A compilation of records containing the procedures and specifications for a finished device.

Quality System

The section of the regulation sets the basic requirement for a quality system by stating that "Each manufacturer shall establish and maintain a quality system that is appropriate for the specific medical device(s) designed or manufactured, and that meets the requirements of this part."

The term "appropriate" is used throughout this regulation and can be open to interpretation. A manufacturer, however, should assume that all requirements are appropriate and applicable except in cases where non-implementation of the requirement can be shown to have no effect on the product's specified requirements or ability to carry out necessary corrective actions.

Quality system requirements (subpart B)

This section of the regulation defines the overall responsibilities and the resources required for the management of the quality system.

Management responsibilities

Executive management is responsible for establishing a quality policy and ensuring adequate resources to effectively maintain and manage the quality system. In addition, management is responsible for establishing a specific quality plan, consisting of relevant practices, resources, activities, and procedures.

Quality audit

Periodic audits of the quality system are required to be conducted by personnel not directly responsible for the activities being audited. The dates and results of each audit need to be documented, along with the results of the audit. It is expected that corrective actions and, when necessary, reaudits, be performed for any identified noncompliances.

Personnel

Manufacturers are responsible for assigning sufficient personnel with appropriate experience and training to perform all tasks required by the quality system plan.

Design controls (subpart C)

Manufacturers of all class II and class III medical devices, along with the specific class I devices listed in paragraph (a)(2) of this regulation, are required to establish design control procedures that ensure design requirements are met as specified.

Design controls shall define:

- **Design and development planning** - Plans that describe the design and development activities, and responsibilities for these activities and their implementation.
- **Design input** - Procedures that ensure design requirements are appropriate and address the intended use of the device.
- **Design output** - Procedures that document design output, including acceptance criteria, so that conformance to design input requirements can be adequately evaluated.
- **Design review** - Formal and documented reviews of the design results that include participation from representatives of all.
- **Design verification** - Procedures for verifying the device design that confirm that the design output meets the design input requirements.
- **Design validation** - Procedures for validating the device design, ensuring that devices conform to defined user needs and intended uses, and including testing of production units under actual or simulated conditions.
- **Design transfer** - Procedures to ensure that the device design is correctly translated into production specification.
- **Design changes** - Procedures for identifying, documenting, validating, and managing the verification and approval process of all design changes before they are implemented.
- **Design history file** - A design history file (DHF) is required for each type of device and should include or reference the records necessary to demonstrate that the design was developed in accordance with the approved design plan and device requirements.

Document controls (subpart D)

Medical device manufacturers are required to put in place document controls for all documents required in this regulation.

Document approval and distribution

One or more people must be assigned to review and approve documents prior to issuance. The approval must be documented, include a date and the signature of the approver, and be made available at all locations where applicable. Procedures must also be in place to ensure that obsolete documents are removed and/or prevented from being used.

Document changes

Similar to document approval procedures, changes to documents must be approved, reviewed, and documented. Records of all changes must be maintained.

Purchasing controls (subpart E)

Manufacturers must establish procedures that ensure all incoming products and services conform to defined requirements. Procedures shall include:

- Evaluation of suppliers, contractors, and consultants.
- Maintenance of purchasing data that describes specific requirements, including quality requirements, for all parts, along with supplier agreements and contracts.

Identification and Traceability (subpart F)

This subpart establishes the requirement for procedures that provide for the identification of products through all stages of receipt, distribution, and installation.

In addition, for any device that is intended for surgical implantation or to support or sustain life, procedures must be established to facilitate corrective action through the use of lot or batch control numbers for all finished devices. This identification must be documented in the design history file.

Production and process controls (subpart G)

Production and process controls

- **General** - Manufacturers are responsible for developing processes to ensure that a device conforms to its specifications and for maintaining and conducting all activities required in these processes. Process control procedures shall be put in place to ensure conformance to specifications where deviations occur. Where process controls are needed, they should include documented instructions, processes that control device characteristics during production, standards compliance, approval processes, and workmanship criteria and/or samples.
- **Production and process changes** - The establishment and maintenance of change procedures relative to specifications, methods, processes, or procedures.
- **Environmental control** - Required where environmental conditions could reasonably be expected to have an adverse effect on product quality, appropriate procedures need to be established to control such conditions.

- **Personnel** - Requirements for personnel that come into contact with the product or environment in any way that could reasonably be expected to have an effect on product quality (includes health, cleanliness, clothing, and other requirements).
- **Contamination control** - Procedures to prevent the contamination of equipment or product are required.
- **Buildings** - Buildings in which the product is stored or manufactured need to be sufficient to ensure quality procedures can be performed.
- **Equipment** - Manufacturers need to ensure that all equipment used in the manufacturing process meets all defined requirements and is maintained, inspected, and adjusted as needed.
- **Manufacturing material** - Procedures need to be in place to ensure that any manufacturing material that could adversely affect product quality is controlled, reduced, and, when possible, removed.
- **Automated processes** - Any software used as part of production needs to be validated for its intended use.

Inspection, measuring, and test equipment

Manufacturers are responsible for ensuring that all equipment used for inspecting, measuring, and testing is properly maintained and suitable for its intended purpose. Procedures for calibrating, inspecting, and maintaining such equipment shall be documented.

In particular, this part of the regulation defines specific requirements for equipment calibration, including the establishment of:

- Specific accuracy and precision limits
- Calibration standards
- Calibration records

Process validation

Manufacturers are responsible for establishing and maintaining procedures for validated processes used in monitoring and control of process parameters in order to ensure that specified requirements continue to be met.
Processes for which results cannot be fully verified through inspection and tests require a higher degree of control through established procedures. Process validation activities and results need to be fully documented.

Acceptance activities (subpart H)

Procedures for acceptance activities, including inspection and testing, need to be established and maintained for each of the following:

- Receiving and inspection activities
- In-process acceptance activities
- Final acceptance activities

In addition, the manufacturer shall document acceptance activities, including the activities performed along with the date of acceptance, results, equipment used (where appropriate), and signature(s) of the individual(s) conducting the acceptance activities. This documentation should be part of the device history file.

Nonconforming products (subpart I)

Manufacturers need to establish and maintain procedures for identifying and managing products that do not meet defined specifications. All evaluations and any investigations should be fully documented. Nonconformity review and disposition procedures should define:

- Responsibility for review and disposition of nonconforming product.
- Process for review and disposition activities.
- Rework, testing, and reevaluation of nonconforming product activities.

Corrective and Preventive action (subpart J)

Corrective and preventive action procedures shall be documented, and include requirements for:

- Processes used to analyze all sources of quality data, including audit reports and complaints, in order to identify the potential causes of non-conformance.
- Investigation of the cause of nonconformance.
- Identification of actions needed to correct and prevent recurrence of nonconformance issues.
- Ensuring that corrective and preventative actions are effective and do not have any adverse effects.
- Implementation and recording of changes to methods and procedures made to correct and prevent identified quality issues.
- Communication of information related to quality problems and nonconforming products to those directly responsible for quality assurance or prevention of identified problems.
- Submission of relevant information regarding quality problems to management for review.

Labeling and packaging control (subpart K)

Manufacturers are responsible for establishing and maintaining procedures to control labeling activities, including:

- **Label integrity** - Labels need to be legible and remain affixed to the product as intended during normal use.
- **Labeling inspection** - Labels need to be examined for accuracy of all information, including UDI, UPC, expiration date, control number, storage instructions, handling instructions, and any other relevant instructions. Label release shall be documented in the DHR.
- **Labeling storage** - Labels should be stored in a manner that allows for proper identification.
- **Labeling operations** - Labels used for each production unit, lot, or batch shall be documented in the DHR and controlled by procedures designed to prevent label mixups.
- **Control number** - Control numbers, when required by § 820.65, need to be on the device or accompany it throughout the distribution of the device.

In addition, manufacturers are responsible for ensuring the device packaging and shipping containers are sufficiently designed and constructed to protect the device during typical conditions found when the device is processed, stored, handled, or distributed.

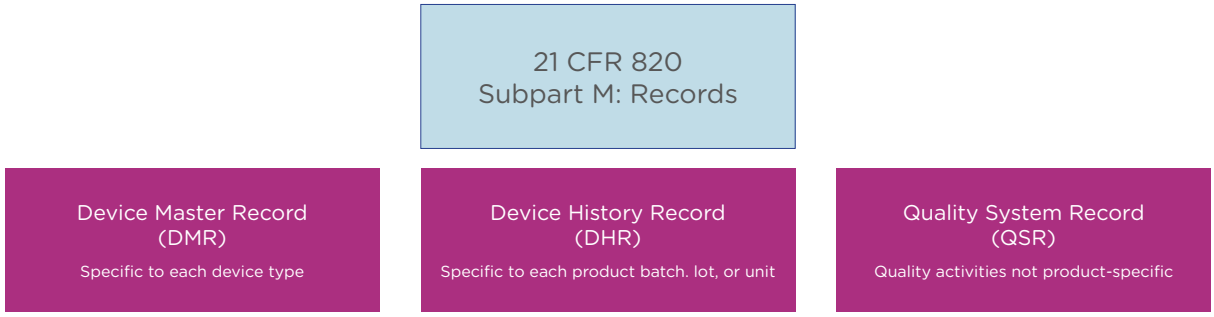
Handling, storage, distribution, and installation (subpart L)

Manufacturers are responsible for establishing, maintaining, and documenting procedures to ensure that the product is not adversely affected during handling, storage, distribution, and installation. This includes procedures for:

- Controlling storage areas and ensuring that no obsolete or rejected products are used or distributed.
- Controlling the distribution of finished devices and maintaining records that include consignee information, identification of devices shipped, ship dates, and any relevant control numbers.
- In cases where installation is required, installation and inspection instructions and procedures shall be provided to ensure that the device performs as intended.

Records (subpart M)

All records required by 21 CFR Part 820 shall be maintained at the manufacturing facility or otherwise be readily accessible to officials performing inspections. Records stored electronically need to be backed up appropriately and all records should be maintained for the expected life of the product and no less than 2 years from the date of the product's commercial release.



Device Master Record (DMR)

A DMR is required for each type of device and should include:

1. Device specifications
2. Production process specifications
3. Quality assurance procedures and specifications
4. Packaging and labeling specifications
5. Installation, maintenance, and servicing procedures and methods

Device History Record (DHR)

A DHR is required for each product batch, lot, or unit to demonstrate the device has been manufactured according to the Device Master Record and other requirements of Part 820. The DHR should include or reference:

1. Manufacture date
2. Manufacture quantity
3. Quantity released for distribution
4. Acceptance records that demonstrate the device has been manufactured in accordance with the DMR
5. Primary identification label and labeling used for each production unit
6. Any unique device identifier (UDI) or universal product code (UPC), and any other identification or control numbers used

Quality System Record (QSR)

The QSR includes procedures and documentation of activities that are not specific to a particular type of device, including those requirements defined in § 820.20.

Complaint files

Procedures need to be established to manage receiving, reviewing, and evaluating complaints. In addition to documenting all complaints, procedures should ensure that all complaints are processed in a uniform and timely manner. Complaint evaluations will determine:

1. If the complaint is related to an adverse event which is required to be reported under part 803 of this regulation. If so, the complaint must be promptly reviewed and the results recorded, including whether the device failed to meet specifications, whether the device was being used for treatment or diagnosis, and any relationship between the device and the reported incident or adverse event.
2. Whether an investigation is required. Any complaint involving the possible failure of a device, labeling, or packaging to meet specifications requires an investigation.

When an investigation is made, a record of the investigation is maintained and includes the following information:

- The name of the device
- The date the complaint was received
- Any device identifiers, including UDI or UPC
- Name, address, and phone number of complainant
- Nature and details of the complaint
- Dates and results of the investigation
- Any corrective actions taken
- Any reply made to the complainant

If the manufacturer's formally designated complaint unit is located separately from the manufacturing facility, the records associated with the investigation must be "reasonably accessible" at the

manufacturing facility. If the complaint unit is located outside of the United States, records required under this part shall be made available at a location in the U.S. where the manufacturer's records are regularly kept, or at the location of the initial distributor.

Servicing (subpart N)

Instructions and procedures for performing and verifying that servicing meets defined requirements must be established for devices where servicing is a requirement. In addition, manufacturers are responsible for:

- Analyzing service reports with "appropriate statistical methodology."
- Reporting any events received as part of a service report to the FDA under part 803 of this chapter.
- Including in all service reports:
  - The name of the device serviced.
  - The unique identifier, such as UDI or UPC, and any other device identification and control numbers used.
  - The date of service.
  - The individual(s) performing the service.
  - Details of the service performed.
  - Test and inspection data.

Statistical techniques (subpart O)

Each manufacturer shall establish and maintain procedures for identifying valid statistical techniques required for establishing, controlling, and verifying the acceptability of process capability and product characteristics.

Sampling plans, when used, shall be written and based on a valid statistical rationale. Each manufacturer shall establish and maintain procedures to ensure that sampling methods are adequate for their intended use and to ensure that when changes occur the sampling plans are reviewed.

21 CFR 820 and ISO 13485

While many countries have harmonized their quality standard with ISO 13485, the United States has not. That said, there are no requirements in 21 CFR Part 820 that conflict with ISO 13485, but manufacturers marketing devices in the U.S. along with other markets, including Europe, will need to comply with both Part 820 and with ISO 13485.

However, the FDA is moving towards harmonizing these standards and on February 22, 2022 issued a proposed rule to amend the QSR to align more closely with the international consensus standard for Quality Management Systems, primarily by incorporating reference to the ISO 13485 standard. The FDA has published FAQs about the proposed rule.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