21CFR Part 820

Current good manufacturing practice (CGMP) requirements are set forth in this quality system regulation.

Basis for GMP Revision

- Safe Medical Devices Act
- Device GMP Advisory Committee
- Responses to FR notices
- Recall Data
- Experience with current GMP’s
- International Harmonization

New Sections

- Design Controls
- Purchasing Controls
- Servicing Controls
Changes

• Critical device requirements
• Failure investigations
• Complaints
• Specifications and process changes

Harmonization

• Reorganize structure
• Modify language
• ISO 9001 Quality Systems Part 1 -
  – Specifications for Design/Development, Production, Installation, and Servicing
• EN46001 Quality Systems -
  – Medical Devices - Particular Requirements for the Application of EN29001
• EN46002 Quality Standards -
  – Particular Requirements for the Application of EN29002

Sec. 820.1 Scope

• (A)(1) The provisions of this part shall be applicable to any finished device as defined in this part, intended for human use, that is manufactured, imported, or offered for import in any State or Territory of the United States, the District of Columbia, or the Commonwealth of Puerto Rico.
Sec. 820.1 (c) Authority
• Part 820 is established and issued under authority of sections 501, 502, 510, 513, 514, 515, 518, 519, 520, 522, 701, 704, 801, 803 of the act

Sec. 820.1 (c) Authority
• The failure to comply ... renders a device adulterated under section 501(h) of the act.

Sec. 820.3 Definitions
• (b) Complaint means any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device after it is released for distribution.
Sec. 820.3 Definitions

• (i) Device history record (DHR) means a compilation of records containing the production history of a finished device.
• (j) Device master record (DMR) means a compilation of records containing the procedures and specifications for a finished device.

Sec. 820.3 Definitions

• (l) Finished device means any device or accessory to any device that is suitable for use or capable of functioning, whether or not it is packaged, labeled, or sterilized.

Sec. 820.3 Definitions

• (o) Manufacturer means ... includes but is not limited to those who perform the functions of contract sterilization, installation, relabeling, remanufacturing, repacking, or specification development, and initial distributors of foreign entities performing these functions.
Sec. 820.3 Definitions

• (p) Manufacturing material means any material ... used in or used to facilitate the manufacturing process, ... which is present in or on the finished device as a residue or impurity not by design or intent of the manufacturer.

Sec. 820.3 Definitions

• (s) Quality means the totality of features and characteristics that bear on the ability of a device to satisfy fitness-for-use, including safety and performance.

Sec. 820.3 Definitions

• (t) Quality audit means a systematic, independent examination of a manufacturer's quality system ...
Sec. 820.3 Definitions

• (u) Quality policy means the overall intentions and direction of an organization with respect to quality, as established by management with executive responsibility.

Sec. 820.3 Definitions

• (v) Quality system means the organizational structure, responsibilities, procedures, processes, and resources for implementing quality management.

Sec. 820.3 Definitions

• (w) Remanufacturer means any person who processes, conditions, renovates, repackages, restores, or does any other act to a finished device that significantly changes the finished device's performance or safety specifications, or intended use.
Sec. 820.3 Definitions

• (x) Rework means action taken on a nonconforming product so that it will fulfill the specified DMR requirements before it is released for distribution.

Sec. 820.3 Definitions

• (z) Validation means confirmation by examination and provision of objective evidence that the particular requirements for a specific intended use can be consistently fulfilled.

Sec. 820.3 Definitions

• (aa) Verification means confirmation by examination and provision of objective evidence that specified requirements have been fulfilled.
Quality Control

• The process of
  – measuring actual quality performance,
  – comparing it with standards and
  – acting on the difference
• Standards = Design Specifications

Quality Assurance

• The overall program to assure and verify confidence in the quality of the process used to manufacture a finished device
• QC is part of QA

Sec. 820.20
Management responsibility

• (a) Quality policy. Management with executive responsibility shall establish its policy and objectives for, and commitment to, quality. Management ... shall ensure that the quality policy is understood, implemented, and maintained at all levels of the organization.
Sec. 820.20
Management responsibility

• (b) Organization. Each manufacturer shall establish and maintain an adequate organizational structure to ensure that devices are designed and produced in accordance with the requirements of this part.

Sec. 820.20
Management responsibility

• (c) Management with executive responsibility shall review the suitability and effectiveness of the quality system

Sec. 820.20
Management responsibility

• (d) Each manufacturer shall establish a quality plan...
  • The manufacturer shall establish how the requirements for quality will be met.
Sec. 820.20
Management responsibility
• (e) Each manufacturer shall establish quality system procedures and instructions.

Sec. 820.50
Purchasing controls
• Each manufacturer shall establish and maintain procedures to ensure that all purchased or otherwise received product and services conform to specified requirements.

Sec. 820.50
Purchasing controls
• (a) Each manufacturer shall establish and maintain the requirements, including quality requirements, that must be met by suppliers, contractors, and consultants.
Sec. 820.50
Purchasing controls
• (b) Each manufacturer shall establish and maintain data that clearly describe or reference the specified requirements, including quality requirements, for purchased or otherwise received product and services.

Sec. 820.70
Production and process controls.
• (a) Each manufacturer shall develop, conduct, control, and monitor production processes to ensure that a device conforms to its specifications.

Sec. 820.70
Production and process controls.
• Where process controls are needed they shall include:
  – (1) Documented instructions, standard operating procedures (SOP’s), and methods that define and control the manner of production;
  – (2) Monitoring and control of process parameters and component and device characteristics during production;
Sec. 820.70  
Production and process controls  
  • Where process controls are needed they shall include:  
    – (3) Compliance with specified reference standards or codes;  
    – (4) The approval of processes and process equipment; and  
    – (5) Criteria for workmanship which shall be expressed in documented standards or by means of identified and approved representative samples.

Sec. 820.70  
Production and process controls  
  • (b) Each manufacturer shall establish and maintain procedures for changes to a specification, method, process, or procedure.

Sec. 820.70  
Production and process controls  
  • (c) Where environmental conditions could reasonably be expected to have an adverse effect on product quality, the manufacturer shall establish and maintain procedures to adequately control these environmental conditions.
Sec. 820.70
Production and process controls

• (d) Each manufacturer shall establish and maintain requirements for the health, cleanliness, personal practices, and clothing of personnel if contact between such personnel and product or environment could reasonably be expected to have an adverse effect on product quality.

Sec. 820.70
Production and process controls

• (e) Each manufacturer shall establish and maintain procedures to prevent contamination of equipment or product by substances that could reasonably be expected to have an adverse effect on product quality.

Sec. 820.70
Production and process controls

• (f) Buildings shall be of suitable design and contain sufficient space to perform necessary operations, prevent mixups, and assure orderly handling.
Sec. 820.70
Production and process controls

• (g) Each manufacturer shall ensure that all equipment used in the manufacturing process meets specified requirements and is appropriately designed, constructed, placed, and installed to facilitate maintenance, adjustment, cleaning, and use.

Sec. 820.70
Production and process controls

• (h) Where a manufacturing material could reasonably be expected to have an adverse effect on product quality, the manufacturer shall establish and maintain procedures for the use and removal of such manufacturing material to ensure that it is removed or limited to an amount that does not adversely affect the device's quality.

Sec. 820.70
Production and process controls

• (i) When computers or automated data processing systems are used as part of production or the quality system, the manufacturer shall validate computer software for its intended use according to an established protocol.
Sec. 820.75
Process validation.

• (a) Where the results of a process cannot be fully verified by subsequent inspection and test, the process shall be validated ... and approved according to established procedures.

Sec. 820.75
Process validation.

• (b) Each manufacturer shall establish and maintain procedures for monitoring and control of process parameters for validated processes to ensure that the specified requirements continue to be met.

Sec. 820.75
Process validation.

• (c) When changes or process deviations occur, the manufacturer shall review and evaluate the process and perform revalidation where appropriate.
Sec. 820.60 Identification

- Each manufacturer shall establish and maintain procedures for identifying product during all stages of receipt, production, distribution, and installation to prevent mixups.

Sec. 820.65 Traceability

- Each manufacturer of a device that is intended for surgical implant into the body or to support or sustain life and whose failure to perform ... can be reasonably expected to result in a significant injury to the user shall establish and maintain procedures for identifying with a control number each unit, lot, or batch of finished devices ...

Sec. 820.72 Inspection, measuring, and test equipment

- (a) Each manufacturer shall ensure that all inspection, measuring, and test equipment, ... is suitable for its intended purposes and is capable of producing valid results.
- Each manufacturer shall establish and maintain procedures to ensure that equipment is routinely calibrated, inspected, checked, and maintained.
Sec. 820.72 Inspection, measuring, and test equipment

• (b) Calibration procedures shall include specific directions and limits for accuracy and precision.
• When accuracy and precision limits are not met, there shall be provisions for remedial action to reestablish the limits and to evaluate whether there was any adverse effect on the device's quality.

Sec. 820.80 - Receiving, in-process, and finished device acceptance

• (a) Each manufacturer shall establish and maintain procedures for acceptance activities.
• Acceptance activities include inspections, tests, or other verification activities.

Sec. 820.80 - Receiving, in-process, and finished device acceptance

• (b) Each manufacturer shall establish and maintain procedures for acceptance of incoming product.
• Incoming product shall be inspected, tested, or otherwise verified as conforming to specified requirements.
• Acceptance or rejection shall be documented.
Sec. 820.80 - Receiving, in-process, and finished device acceptance

• (c) Each manufacturer shall establish and maintain acceptance procedures, ... to ensure that specified requirements for in-process product are met.
• Such procedures shall ensure that in-process product is controlled until the required inspection and tests or other verification activities have been completed, or necessary approvals are received, and are documented.

Sec. 820.80 - Receiving, in-process, and finished device acceptance

• (d) Final acceptance activities. Each manufacturer shall establish and maintain procedures for finished device acceptance to ensure that each production run, lot, or batch of finished devices meets acceptance criteria.
• Finished devices shall be held in quarantine or otherwise adequately controlled until released.

Sec. 820.80 - Receiving, in-process, and finished device acceptance

• (e) Each manufacturer shall document acceptance activities required by this part. These records shall include:
  – (1) The acceptance activities performed;
  – (2) the dates acceptance activities are performed;
  – (3) the results;
  – (4) the signature of the individual(s) conducting the acceptance activities; and
  – (5) where appropriate the equipment used.
Sec. 820.86
Acceptance status

- Each manufacturer shall identify ... the acceptance status of product, to indicate the conformance or nonconformance of product with acceptance criteria.
- The identification of acceptance status shall be maintained throughout manufacturing, packaging, labeling, installation, and servicing of the product ...

Sec. 820.90
Nonconforming product

- (a) Each manufacturer shall establish and maintain procedures to control product that does not conform to specified requirements.

Sec. 820.90
Nonconforming product

- (b) (1) Each manufacturer shall establish and maintain procedures that define the responsibility for review and the authority for the disposition of nonconforming product.
- (2) Each manufacturer shall establish and maintain procedures for rework, to include retesting and evaluation ...
Sec. 820.100
Corrective and preventive action

• (a) Each manufacturer shall establish and maintain procedures for implementing corrective and preventive action. The procedures shall include requirements for:

Sec. 820.100
Corrective and preventive action

• (1) Analyzing processes, work operations, concessions, quality audit reports, quality records, service records, complaints, returned product, and other sources of quality data to identify existing and potential causes of nonconforming product, or other quality problems.

Sec. 820.100
Corrective and preventive action

• (2) Investigating the cause of nonconformities relating to product, processes, and the quality system;

• (3) Identifying the action(s) needed to correct and prevent recurrence of nonconforming product and other quality problems;
Sec. 820.100
Corrective and preventive action

• (4) Verifying or validating the corrective and preventive action to ensure that such action is effective and does not adversely affect the finished device;
• (5) Implementing and recording changes in methods and procedures needed to correct and prevent identified quality problems;

Sec. 820.100
Corrective and preventive action

• (6) Ensuring that information related to quality problems or nonconforming product is disseminated to those directly responsible for assuring the quality of such product or the prevention of such problems; and
• (7) Submitting relevant information on identified quality problems, as well as corrective and preventive actions, for management review.

Sec. 820.40
Document controls

• Each manufacturer shall establish and maintain procedures to control all documents that are required by this part. The procedures shall provide for the following:
  – (a) Document approval and distribution
  – (b) Document changes
Sec. 820.120
Device labeling

• Each manufacturer shall establish and maintain procedures to control labeling activities.
  – (a) Label integrity
  – (b) Labeling inspection
  – (c) Labeling storage
  – (d) Labeling operations
  – (e) Control number

Sec. 820.130
Device packaging

• Each manufacturer shall ensure that device packaging and shipping containers are designed and constructed to protect the device from alteration or damage during the customary conditions of processing, storage, handling, and distribution.

Sec. 820.140
Handling

• Each manufacturer shall establish and maintain procedures to ensure that mixups, damage, deterioration, contamination, or other adverse effects to product do not occur during handling.
Sec. 820.150
Storage
• (a) Each manufacturer shall establish and maintain procedures for the control of storage areas and stock rooms ...
• (b) Each manufacturer shall establish and maintain procedures that describe the methods for authorizing receipt from and dispatch to storage areas and stock rooms.

Sec. 820.160
Distribution
• (a) Each manufacturer shall establish and maintain procedures for control and distribution of finished devices ...

Sec. 820.160
Distribution
• (b) Each manufacturer shall maintain distribution records which include or refer to the location of:
  – (1) The name and address of the initial consignee;
  – (2) The identification and quantity of devices shipped;
  – (3) The date shipped; and
  – (4) Any control number(s) used.
Sec. 820.170
Installation
• (a) Each manufacturer of a device requiring installation shall establish and maintain adequate installation and inspection instructions, ...
• (b) The person installing the device shall ensure that the installation, inspection, and any required testing are performed in accordance with the manufacturer's instructions and procedures ...

Sec. 820.30
Design controls
• (a) (1) Each manufacturer of any class III or class II device, and the class I devices listed in paragraph (a)(2), shall establish and maintain procedures to control the design of the device in order to ensure that specified design requirements are met.
• (2) (i) Devices automated with computer software; and
• (ii) The devices listed in the following chart.
### Sec. 820.30
#### Design controls

<table>
<thead>
<tr>
<th>Section</th>
<th>Device</th>
</tr>
</thead>
<tbody>
<tr>
<td>868.6810</td>
<td>Catheter, Tracheobronchial Suction.</td>
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<tr>
<td>878.4460</td>
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</tr>
<tr>
<td>880.6760</td>
<td>Restraint, Protective.</td>
</tr>
<tr>
<td>892.5740</td>
<td>Source, Radionuclide Teletherapy.</td>
</tr>
</tbody>
</table>

(b) Each manufacturer shall establish and maintain plans that describe or reference the design and development activities and define responsibility for implementation. The plans shall identify and describe the interfaces with different groups or activities that provide, or result in, input to the design and development process.

(c) Each manufacturer shall establish and maintain procedures to ensure that the design requirements relating to a device are appropriate and address the intended use of the device, including the needs of the user and patient. The procedures shall include a mechanism for addressing incomplete, ambiguous, or conflicting requirements.
Sec. 820.30
Design controls

(d) Each manufacturer shall establish and maintain procedures for defining and documenting design output in terms that allow an adequate evaluation of conformance to design input requirements.

Design output procedures shall contain or make reference to acceptance criteria and shall ensure that those design outputs that are essential for the proper functioning of the device are identified.

Sec. 820.30
Design controls

(e) Each manufacturer shall establish and maintain procedures to ensure that formal documented reviews of the design results are planned and conducted at appropriate stages of the device's design development.

Sec. 820.30
Design controls

(f) Each manufacturer shall establish and maintain procedures for verifying the device design.

Design verification shall confirm that the design output meets the design input requirements.
Sec. 820.30
Design controls
• (g) Each manufacturer shall establish and maintain procedures for validating the device design.
  – Design validation shall be performed under defined operating conditions on initial production units, lots, or batches, or their equivalents.
  – Design validation shall ensure that devices conform to defined user needs and intended uses and shall include testing of production units under actual or simulated use conditions.

Sec. 820.30
Design controls
• (h) Each manufacturer shall establish and maintain procedures to ensure that the device design is correctly translated into production specifications.

Sec. 820.30
Design controls
• (i) Each manufacturer shall establish and maintain procedures for the identification, documentation, validation or where appropriate verification, review, and approval of design changes before their implementation.
Sec. 820.30
Design controls

• (j) Each manufacturer shall establish and maintain a DHF for each type of device.
• The DHF shall contain or reference the records necessary to demonstrate that the design was developed in accordance with the approved design plan and the requirements of this part.

Sec. 820.200
Servicing

• (a) Where servicing is a specified requirement, each manufacturer shall establish and maintain instructions and procedures for performing and verifying that the servicing meets the specified requirements.

Sec. 820.200
Servicing

• (b) Each manufacturer shall analyze service reports with appropriate statistical methodology in accordance with Sec. 820.100.
Sec. 820.200
Servicing

• (c) Each manufacturer who receives a service report that represents an event which must be reported to FDA under part 803 or 804 of this chapter shall automatically consider the report a complaint and shall process it in accordance with the requirements of Sec. 820.198.

• (d) Service reports shall be documented ...

Sec. 820.250
Statistical techniques

• (a) Where appropriate, 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.

• (b) 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. These activities shall be documented.
Sec. 820.181
Device master record

• Each manufacturer shall maintain device master records (DMR's).
• Each manufacturer shall ensure that each DMR is prepared and approved in accordance with Sec. 820.40.

Sec. 820.181
Device master record

• The DMR ... shall include, or refer to the location of, the following information:
  – (a) Device specifications ... 
  – (b) Production process specifications ...
  – (c) Quality assurance procedures and specs ...
  – (d) Packaging and labeling specifications, ...
  – (e) Installation, maintenance, and servicing procedures and methods.

Sec. 820.186
Quality system record

• Each manufacturer shall maintain a quality system record (QSR).
• The QSR shall include, or refer to the location of, procedures and the documentation of activities required by this part that are not specific to a particular type of device(s), ...
Sec. 820.184
Device history record

• Each manufacturer shall maintain device history records (DHR's).

• Each manufacturer shall establish and maintain procedures to ensure that DHR's for each batch, lot, or unit are maintained to demonstrate that the device is manufactured in accordance with the DMR and the requirements of this part.

Sec. 820.184
Device history record

• The DHR shall include, or refer to the location of, the following information:
  – (a) The dates of manufacture;
  – (b) The quantity manufactured;
  – (c) The quantity released for distribution;
  – (d) The acceptance records which demonstrate the device is manufactured in accordance with the DMR;

Sec. 820.184
Device history record

• The DHR shall include, or refer to the location of, the following information:
  – (e) The primary identification label and labeling used for each production unit; and
  – (f) Any device identification(s) and control number(s) used.
Sec. 820.180
General requirements

• All records required by this part shall be maintained at the manufacturing establishment or other location that is reasonably accessible to responsible officials of the manufacturer and to employees of FDA designated to perform inspections. ...

Sec. 820.180
General requirements

• (a) Records deemed confidential by the manufacturer may be marked to aid FDA in determining whether information may be disclosed under the public information regulation in part 20 of this chapter.

Sec. 820.180
General requirements

• (b) All records required by this part shall be retained for a period of time equivalent to the design and expected life of the device, but in no case less than 2 years from the date of release for commercial distribution by the manufacturer.
Sec. 820.180
General requirements

• (c) This section does not apply to the reports required by Sec. 820.20(c), Sec. 820.22, and supplier audit reports used to meet the requirements of Sec. 820.50(a), but does apply to procedures established under these provisions.

Sec. 820.198
Complaint files

• (a) Each manufacturer shall maintain complaint files. Each manufacturer shall establish and maintain procedures for receiving, reviewing, and evaluating complaints by a formally designated unit.

Sec. 820.198
Complaint files

• Such procedures shall ensure that:
  – (1) All complaints are processed in a uniform and timely manner;
  – (2) Oral complaints are documented upon receipt; and
  – (3) Complaints are evaluated to determine whether the complaint represents an event which is required to be reported to FDA under part 803 or 804 of this chapter, Medical Device Reporting.
• (b) Each manufacturer shall review and evaluate all complaints to determine whether an investigation is necessary.

• (c) Any complaint involving the possible failure of a device, labeling, or packaging to meet any of its specifications shall be reviewed, evaluated, and investigated, ...

• (d) Any complaint that represents an event which must be reported ... shall be promptly reviewed, evaluated, and investigated ...
  – (1) Whether the device failed to meet specifications;
  – (2) Whether the device was being used for treatment or diagnosis; and
  – (3) The relationship, if any, of the device to the reported incident or adverse event.

• (e) When an investigation is made under this section, a record of the investigation shall be maintained ...

  • The record of investigation shall include:
    – (1) The name of the device;
    – (2) The date the complaint was received;
    – (3) Any device identification(s) and control number(s) used;
Sec. 820.198
Complaint files

• The record of investigation shall include:
  – (4) The name, address, and phone number of the complainant;
  – (5) The nature and details of the complaint;
  – (6) The dates and results of the investigation;
  – (7) Any corrective action taken; and
  – (8) Any reply to the complainant.

Sec. 820.198
Complaint files

• (f) When the manufacturer's formally designated complaint unit is located at a site separate from the manufacturing establishment, the investigated complaint(s) and the record(s) of investigation shall be reasonably accessible to the manufacturing establishment.

Sec. 820.198
Complaint files

• (g) If a manufacturer's formally designated complaint unit is located outside of the United States, records required by this section shall be reasonably accessible in the United States at either:
  – (1) A location in the United States where the manufacturer's records are regularly kept; or
  – (2) The location of the initial distributor.
Sec. 820.22  
Quality audit

• Each manufacturer shall
  – establish procedures for quality audits and
  – conduct such audits to assure compliance
    with the established quality system
    requirements and to determine the effectiveness
    of the quality system.
• Quality audits shall be conducted by
  individuals who do not have direct
  responsibility for the matters being audited.

Sec. 820.25  
Personnel

• (a) Each manufacturer shall have sufficient
  personnel with the necessary education,
  background, training, and experience to
  assure that all activities required by this part
  are correctly performed.

• (b) Each manufacturer shall
  – establish procedures for identifying training
    needs and
  – ensure that all personnel are trained to
    adequately perform their assigned
    responsibilities.
Sec. 820.25  
Personnel

• (1) As part of their training, personnel shall be made aware of device defects which may occur from the improper performance of their specific jobs.

• (2) Personnel who perform verification and validation activities shall be made aware of defects and errors that may be encountered as part of their job functions.