THE
CERTIFIED MEDICAL DEVICE
AUDITOR PRIMER

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WITH A LITTLE HELP FROM MY FRIENDS.

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Acknowledgments

I thank my friends and professional associates for their assistance, particularly Tim Brenton and Wes Richardson who helped with this text.

We would appreciate any comments regarding improvement and errata. It is our concern to be accurate.

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First Edition - November, 2020

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CMDA Primer Contents

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Quality System Regulations

Quality System Regulations are presented in the following topic areas:

- **Quality System Regulation (QSR) Requirements (21 CFR 820)**
- **Post-market Surveillance (Guidance under Section 522 of FD&C Act)**

Quality System Regulation (QSR) Requirements (21 CFR 820)

Quality System Regulation (QSR) Requirements (21 CFR 820) are presented in the following key section areas:

- **Management Responsibility (20, 22, 25)**
- **Design Control System (30)**
- **Document (Part 40) and Record Control (180-186)**
- **Purchasing Controls and Acceptance Activities (50, 80, 86)**
- **Identification and Traceability (60, 65)**
- **Production and Process Controls (70, 72, 75)**
- **Nonconforming Product (90)**
- **Corrective and Preventive Action (CAPA) System (100)**
- **Product Handling, Storage, Distribution, and Installation (140-170)**
- **Servicing (200)**
- **Statistical Techniques (250)**

Additionally, General Provisions (1, 3, 5), Labeling and Packaging Control (120 and 130), and Complaint Files (198) will be discussed.

Often regulations overlap and must be understood together in order to avoid unacceptable gaps in a quality system. For example, 21 CFR 820.198 of the QSR establishes requirements for complaint files; this section must be understood and must also satisfy the requirements of 21 CFR 803, Medical Device Reports, 21 CFR 806, Reports of Removals and Corrections, 21 CFR 801, Labeling, where these apply to a complaint received.

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21 CFR 820 (Continued)

As an example, if a firm received a complaint reading, "Just a quick email to thank you for your prompt service! A patient received a minor burn because the label on the device stated that the dial should be set to 'Medium' but when it was set to medium it performed at the 'High' level. We called your service department and they came and replaced the unit with another one that worked fine."

This statement initially may not sound like a serious complaint. Yet it must not only be investigated as a device failure (under 21 CFR 820.198) but it also must be reported as an MDR (under 21 CFR 803), and as part of CAPA activities (under 21 CFR 820.100) similar devices may be subject to report as a recall (under 21 CFR 806), and it could have a labeling issue (under 21 CFR 801).

The section below will outline the Quality System Regulation (QSR) requirements, describe them in more detail, then will describe related regulatory requirements flowing from the statutes, and more details of the regulations related to, but not part of, the QSR (21 CFR 820).

Device Classifications

The FD&C Act created three classifications for devices: Class I, II, and III. Volume 8 of Title 21, contains parts 800 to 1299, and some of these parts describe specific devices and their classification, while others, such as Parts 801, 803, 807, and 820, among others, describe other regulatory requirements.

- **Class I devices are subject only to general controls because they are simple, present fewer risks and any risks are of lower severity than other device classes, so that general controls, including where stated, specific exemptions from portions of the good manufacturing practices (GMPs), are considered adequate to provide assurance of safety and effectiveness.**

- **Class II devices are more complex, than Class I devices, are subject to general controls, and, because general controls do not provide reasonable assurance of the devices' safety and effectiveness, Class II devices may also be subject to specific performance standards, postmarket surveillance, various guidance documents, and are subject to premarket notification ("510(k) filings").**

- **Class III devices cannot be classified as Class I or Class II because general and special controls do not provide reasonable assurance of their safety and effectiveness, the device is to be used in supporting or sustaining human life, and the device presents a potential for unreasonable risk of illness, injury, or death. Class III devices are subject to premarket approval ("PMA" review process and approval).**

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21 CFR 820 (Continued)

Device Classifications (Continued)

- **Predicate devices are devices which were legally marketed prior to May 28, 1976 which was the effective date of the Medical Device Amendment of 1976. Predicate devices are also used to clear a device that is similar in features to one cleared by a 510(k). These are the "me too devices" used to prove substantial equivalence for quick market entry.**

All Class I and Class II devices must have a predicate device identified for the regulatory approval process. All "new" devices, or devices without a predicate are designated as Class III devices. If such devices are cleared for sale, they may later be reclassified into Class I or Class II based on post market experience, including few adverse events.

The humble and well-known "tongue depressor" is in fact a medical device. Its full publication in the regulations is shown as:

[Code of Federal Regulations]
[Title 21, Volume 8]
[Revised as of April 1, 2012]
[CITE: 21CFR880.6230]

TITLE 21--FOOD AND DRUGS
CHAPTER I--FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUBCHAPTER H--MEDICAL DEVICES
PART 880 -- GENERAL HOSPITAL AND PERSONAL USE DEVICES

Subpart G--General Hospital and Personal Use Miscellaneous Devices

Sec. 880.6230 Tongue depressor.
(*a) Identificatio*n. A tongue depressor is a device intended to displace the tongue to facilitate examination of the surrounding organs and tissues.

***(b) Classification*. Class I (general controls). The device is exempt from the premarket notification procedures in subpart E of part 807 of this chapter, subject to the limitations in 880.9. If the device is not labeled or otherwise represented as sterile, it is also exempt from the current good manufacturing practice requirements of the quality system regulation in part 820 of this chapter, with the exception of 820.180, with respect to general requirements concerning records, and 820.198, with respect to complaint files.**

[45 FR 69682-69737, Oct. 21, 1980, as amended at 66 FR 38806, July 25, 2001]

A search for "tongue depressor" on http://www.fda.gov returns the reference above.

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21 CFR 820 (Continued)

Device Classifications (Continued)

The location within the regulations, the place and date of publication in the Federal Register ("FR" pages published on October 21, 1980 and amended on July 25, 2001), and the description (identification) and classification of the device are stated. Furthermore, in this case, (unless sterility is claimed) the tongue depressor can be manufactured in a facility exempt from "…good manufacturing requirements of the quality system regulation in part 820 of this chapter with the exception…" noted.

Quality System Regulation (QSR)

The "Quality System Regulation" is often cited simply as "QSR", as "CGMP", or as "cGMP", and is set forth in the Federal Code of Federal Regulations (CFR) as "Title 21 Code of Federal Regulations, Part 820" ("21 CFR 820").

The subparts of this regulation followed the ISO 9001 (1987) standard in structure, in support of "harmonization," and though the content of subsequent versions (1994, 2000, 2008) continued to apply (with the exception of a requirement in ISO 9001 for "continual improvement" that is absent from QSR or the medical device specific ISO 9000 family standard, ISO 13485), the QSR subparts do not follow the 1994 and later clauses of the ISO standards.

The Federal Register published on Monday, October 7, 1996, the "Final Rule" describing how the QSR was developed, FDA's thinking and response to comments on the proposed regulations over the six years since SMDA was passed in 1990. This document, called "the preamble," is important to understand. It can be obtained as a PDF by searching within the FDA website at http://www.fda.gov for "preamble."

QSR, 21 CFR 820 is only a small (though critical) portion of the regulations that must be followed by medical device designers, manufacturers, distributors, and marketers.

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21 CFR 820.20 / 820.22 / 820.25

Quality System Requirements

These citations include Management Responsibility, Quality Audit, and Personnel. It follows ISO 9001 and ISO 13485 requirements for:

- **Establishment of a quality policy;**
- **Quality planning: Although the ISO requirement for "continuous improvement" (later termed, "continual improvement") is not a part of the regulation, establishment of a quality plan that defines the quality resources and activities and describes how quality requirements will be achieved is required and must be documented;**
- **Quality audits conducted and documented to assure the quality system is in compliance with all requirement; Reports of these audits are reviewed with management in the affected areas, and reaudits are to be scheduled and conducted for deficiencies;**
- **Explicit definition of organizational structure (authority, responsibility, interactions);**
- **Provision of adequate resources (trained personnel, including qualified and trained internal quality auditing personnel) as well as appropriate infrastructure, tools, equipment, and facilities;**
- **Appointment of a management representative.**

21 CFR 820.20 Management Responsibility

The management representative must be appointed by executive management and must have the established authority, and responsibility for ensuring that quality system requirements are established and effective to satisfy the requirements of "this part" (i.e., the QSR compliance), and to report on the status of the quality system to top management ("management with executive responsibility").

The management representative's responsibility and authority are explicitly required to be "irrespective of other responsibilities" of his/her position. Management representatives who are figureheads while others in the organization exercise the true authority for quality related decisions may find that ISO auditors and FDA investigators quickly discern that the position is "pro forma."

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21 CFR 820.20 Management Responsibility (Continued)

Failure to conduct management review meetings, or lack of procedures describing what is to be covered in such meetings (whether held or not), and obviously failure to appoint a management representative all have been cited in FDA Warning Letters as serious deficiencies. Such observations usually prompt further review of the firm's quality system. Management responsibility is at the center and is the foundation of all other quality system controls/activities as shown in FDA's Quality System Inspection Technique ("QSIT") diagrammed earlier in Primer Section III.

Key points to remember about QSIT:

- **QSIT focuses on ensuring effective implementation of quality systems**
- **QSIT uses a top down approach**
- **4 major subsystems (management, design, CAPA, and production & process controls) as well as 3 other subsystems (facility & equipment controls, product controls, document, records, and change controls) of the Quality systems are audited**

21 CFR 820.22 Quality Audit

Each medical device manufacturer must establish procedures for quality audits and conduct such audits to assure that the quality system is in 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. Corrective action(s), including a reaudit of deficient matters, shall be taken when necessary. A report of the results of each quality audit, and reaudit(s) where taken, shall be made and such reports shall be reviewed by management having responsibility for the matters audited.

21 CFR 820.25 Personnel

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. Each manufacturer shall establish procedures for identifying training needs and ensure that all personnel are trained to adequately perform their assigned responsibilities. Training shall be documented. As part of their training, personnel shall be made aware of device defects which may occur from the improper performance of their specific jobs. 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.

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21 CFR 820.30 Design Controls

Each manufacturer of class II and class III devices shall establish and maintain procedures to control the design of the product in order to ensure that specified design requirements are met. Additionally, the following class I products are subject to design controls:

- **Devices automated with computer software**
- **The following identified items:**
    - **Tracheobronchial suction catheters**
    - **Surgeon's gloves**
    - **Protective restraints**
    - **Radionuclide teletherapy sources**
    - **Radionuclide manual applicators**

Definitions are also provided with this CFR regulation including:

- **Design and development planning**
- **Quality policy**
- **Quality system**
- **Remanufacturer**
- **Rework**
- **Specification**
- **Validation, both process and design**
- **Verification**

Design of medical devices can be a complex activity and the regulation of product design and development is likewise complicated.

FDA issued a guidance document, *Design Control Guidance for Medical Device Manufacturers*, on March 11, 1997 to assist firms that would be subject to 21 CFR 820.30 (Subpart C) when it became effective on June 1, 1997. The document can be obtained from FDA's website. It provides explanations of the reasons for the requirements of the design control regulations, and provides suggestions for complying with each requirement. Design controls are part of all regulatory regimes, and FDA states their support of global harmonization efforts, specifically citing the Global Harmonization Task Force ("GHTF") and the work of Study Group 3 ("SG3").

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21 CFR 820.30 Design Controls (Continued)

On June 29, 1999 the GHTF SG3 published the final document, *Guidance On Quality Systems For The Design And Manufacture Of Medical Devices*. This harmonized guidance document elaborates on much of FDA's 1997 guidance. Since the Global Harmonization Task Force completed its work, the taskforce website (www.ghtf.org) now directs users to the International Medical Device Regulators Forum (IMDRF), (http://www.imdrf.org).

The IMDRF Management Committee is made up of regulatory authority representatives from the following jurisdictions, with their associated regulatory authorities and websites noted:

- **Australia – Therapeutic Goods Administration (www.tga.gov.au)**
- **Brazil – National Health Surveillance Agency (Anvisa) (www.anvisa.gov.br/index.htm)**
- **Canada – Health Canada (www.hc-sc.gc.ca/index-eng.php)**
- **European Community – European Commission Directorate General Health and Consumers (www.ec.europa.eu/dgs/health_consumer/index_en.htm)**
- **Japan – Pharmaceuticals and Medical Devices Agency (www.pmda.go.jp/english/index.html) and Labour and Welfare (www.mhlw.go.jp/english/)**
- **United States of America – Food and Drug Administration (http://www.fda.gov)**

For development, manufacture, and distribution of medical devices in the United States, all Class II and Class III devices are subject to design controls under the QSR effective June 1, 1997.

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5.1. For a sterility assurance level (SAL) of 10^{-6} one would require a confidence level of?

a. 99.99%
b. 99.999%
c. 99.9%
d. 99.9999%

5.2. When complying with the requirements of 21 CFR Part 820, controls on a supplier that is a "sole source":

a. Are typically more relaxed because of past product performance
b. Require additional compliance with ISO 13485
c. May be more stringent than on other suppliers
d. Are required to be idential to all other suppliers of similar product categories

5.3. FDA's requirements under 820.100, Corrective and Preventive Actions, are applicable to?

a. Only nonconforming products that do not meet design specifications
b. Devices already in commerce within the United States
c. Devices suspected of having non conformities
d. CAPA procedures applying to devices in the warehouse with a potential for rejection

5.4. For Level 1 abbreviated QSIT inspection, which of the following combination of subsystems may be inspected?

a. Production and process control and CAPA
b. Production and process control and design control
c. CAPA plus facility control
d. Management and design control

5.5. Translation of device user (patient and/or operator) requirements into manufacturing specifications is an example of:

a. Design transfer
b. Design validation
c. Design verification
d. Design output testing

5.6. Which of the following fits best the definition of "design inputs"?

a. End-user convenience factors
b. Patient comments
c. Manufacturing needs/requirements
d. Feedback from post-market surveillance of similar devices

5.7. Which of the following items is part of the Device Master Record (DMR)?

a. Design verification and validation protocols
b. In-process inspection results
c. Receiving inspection specifications
d. Installation, operating, and performance qualification (IQ, OQ, and PQ) validation reports

5.8. Which of the following items is part of the Quality System Record?

a. Procedures specifying design verification and validation protocols
b. Incoming receiving inspection results
c. Final inspection specifications
d. Installation, operating, and performance qualification (IQ, OQ, and PQ) validation reports

5.9. Which of the following is a quality system requirement under QSR?

a. Continuous or continual improvement
b. Adequate management resources
c. Business viability (i.e., long-term profitability)
d. Outline of document structure per ISO requirements

5.10. Which of the following dispositions of nonconforming materials represents a concession?

a. Accept
b. Rework
c. Return
d. Use as-is

5.11. Which of the following statements is accurate regarding acceptance status?

a. Only authorized quality personnel can determine acceptance status.
b. Conforming product and/or components may be considered "acceptable".
c. "Status" in "acceptance status" relates to identification and control.
d. Acceptance status must be explicitly documented at all times.

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