Medical Device Quality Systems

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Some Background

- Visit FDA CDRH home page http://www.fda.gov/cdrh/
  - You should visit this site every few months for the rest of your careers.
  - It now contains a number of searchable databases of important documents.
  - My experience is that engineers don't make enough use of government resources like this website.

What is Quality?

- One definition is the degree to which a product or service meets the expectations of the customer.
- Who's the customer for medical devices?
  - Patients
  - Physicians, nurses, etc.
  - FDA
  - Other manufactures (for "components")

How can Quality be Assured?

- Old Approach – Final Inspections. This approach has the following problems:
  - It costs as much to produce a bad unit as a good one.
  - 100% inspection is costly, anything less is risky.
  - It is often impossible to evaluate all aspects of a product (for example, the effects of aging.

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"New" Approach

- Create a "system" that assures only quality units are produced. This could include:
  - Quality consideration during product design.
  - Quality consideration during manufacturing process design.
  - Quality evaluation of raw materials or raw material suppliers.
  - Quality evaluation of manufacturing process operation (control charts, etc.).

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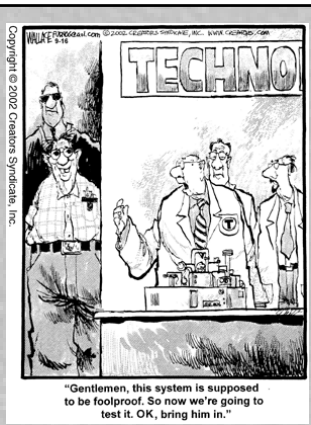
Idea is to create a foolproof quality system.



"Gentlemen, this system is supposed to be foolproof. So now we're going to test it. OK, bring him in."

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Some Comments

- These standards (the QSR and ISO 9000 series) are based on a lot of real world experience and can serve as a source of good ideas even if they are not legally required.
- I know the following slides are very wordy. My intention is to provide you with reference material as well as a lecture.

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Evaluating Quality

- The current approach is for the manufacturer or supplier to create their own quality system (generally based on some guidelines).
- "Auditors" (internal, external or regulatory) then evaluate this system for completeness, implementation and operation.
- The idea is, if the system is good, the product will be good.

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Currently Two Systems

- FDA's Quality System Regulation (QSR) – for medical devices only.
- The ISO 9000 series standards – for all types of products and services.
- The FDA QSR standards were based on the previous version of the ISO 9000 series standards.
- Companies making medical devices for distribution in the U.S. generally must comply with the FDA standard and may comply with the ISO standard.

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The Regulation

- The regulation described here is 21 CFR Parts 808, 812, and 820 (Medical Devices; Current Good Manufacturing Practice (CGMP) Final Rule; Quality System Regulation) published in the Federal Register, Vol. 61, No. 195 on October 7, 1996.
- The current GMP requirements was harmonized with the previous (1994) version of the ISO 9000 series quality standards.
- The FDA GMP requirements are slightly more extensive than the ISO 9000:1994 standards because they include extensive coverage of labeling, and complaint handling. The current GMP regulation was promulgated under section 520 of the Food, Drug and Cosmetic (FD&C) Act.

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Exemptions

- The Quality System (QS) regulation and the basic Good Manufacturing Practices (GMP) requirements apply to all manufacturers and distributors of medical devices, including medical device kits, trays or packs, for distribution in the United States.
- The QS regulation applies to finished devices intended to be commercially distributed for human use unless there is an approved exemption in effect.
- GMP exemptions are codified in the classification regulations 21 CFR 862 to 892. The exemption of most Class I devices from design controls is in section 820.30(a). Exemption from the GMP requirements does not exempt manufacturers of finished devices from keeping complaint files (820.198) or from general requirements concerning records (820.180). Sterile devices are never exempted from GMP requirements.

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“Components”

- A "component" is defined by 820.3(c) as "any raw material, substance, piece, part, software, firmware, labeling, or assembly that is intended to be included as part of the finished, packaged, and labeled device.“
- Component manufacturers are excluded from the QS regulation by 820.1(a)(i).
- Current FDA policy is to rely upon the finished device manufacturer to assure that components are acceptable for use.
- Component manufacturers are not routinely scheduled for GMP inspections. However, FDA encourages them to use the QS regulation as guidance for their quality system.

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Accessories

- Accessory devices [807.20(a)(5)] such as hemodialysis tubing or major diagnostic x-ray components, that are packaged, labeled, and distributed separately to a hospital, physician, etc., for health-related purposes are sometimes inappropriately referred to as components.
- However, FDA considers them finished devices because they are suitable for use or capable of functioning and are distributed for health-related purposes.
- The QS regulation applies to their manufacture.

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Custom Devices

- Section 520(b) of the FD&C Act and the IDE regulation (21 CFR Part 812) define a custom device.
- Custom devices are exempt from certain statutory requirements. For example, manufacturers of custom devices are not required to comply with premarket approval requirements (Section 515) and are exempt from premarket notification requirements [Section 510(k)].
- While custom devices are not exempt from the GMP requirements, current FDA policy is to not inspect manufacturers of custom devices.
- Manufacturers of custom devices should comply with the GMP considering the benefits it provides and flexibility it allows.
- A few years ago, this exemption was abused by some medical laser manufactures. The FDA has since been quite aggressive regarding what constitutes a custom device.

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Contract Manufacturing

- Specification developers provide specifications to contract manufacturers, who produce devices to meet the specifications. The contract manufacturer may package and label the device or the finished device may be shipped to the specification developer for packaging and labeling.
- Specification developers are manufacturers and are subject to the GMP requirements that apply to the activities they conduct, such as various design controls including correct transfer of the design information to a contract manufacturer [820.30(h)]. This activity, in turn, requires an adequate device master record [820.181] and adequate change control [820.40(b)].
- Further, if the product carries the specification developer's label, the developer is also responsible for maintaining a complaint file and processing complaints.

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Design Controls

- Each manufacturer is required by regulation to establish and maintain design control procedures for any class III or class II device, and a selected group of class I devices. The class I devices subject to design controls are devices automated with computer software and the following specific devices.

SECTION	DEVICE
868.6810	Catheter, Tracheobronchial Suction
878.4460	Glove, Surgeon's
880.6760	Restraint, Protective
892.5650	System, Applicator, Radionuclide, Manual
892.5740	Source, Radionuclide Teletherapy

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General Approach

- The Quality System regulation indicates the required end results rather than specifically prescribing how manufacturers are to comply with the regulation.
- It is the responsibility of the manufacturers to use good judgment when developing quality systems that appropriately applies the QS regulation to their specific products and operations.

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Management Responsibility

- One of the most important responsibilities of management when developing a quality system is to establish its policy and objectives for, and commitment to, quality.
- Management with executive responsibility must ensure that the quality policy is understood, implemented, and maintained at all levels of the organization.
- This means each manufacturer must establish the appropriate responsibility, authority, and interrelation of all personnel who manage, perform, and assess work effecting quality, and provide the independence and authority necessary to perform these tasks.

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Quality System Audits

- The quality system must be monitored through audits.
- The analysis and use of **feedback** data from product acceptance, audits, complaints, repairs and other sources are necessary parts of a self-correcting quality system.

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Specific FDA QSR Requirements…

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Design Controls

- The QS requires documentation and management of:
  - Interfaces among groups
  - Personnel training
  - Design planning
  - Development of specifications (design input)
  - Design review
  - Design output
  - Design verification (confirmation that the design output meets the design input requirements) and
  - Design Validation (confirmation by examination and provision of objective evidence that the particular requirements for the intended use can be consistently fulfilled).

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Process Validation

- The QSR requires establishing by objective evidence that a process consistently produces a result or product meeting its predetermined specifications.

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Personnel

- The QSR requires personnel involved in design, manufacturing, quality assurance, auditing, complaint processing, servicing, etc. be properly trained, both by education and experience.

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Buildings and Environment

- The QSR requires the buildings and environment in which components, devices and records are received, processed, built or stored be controlled so that finished devices will consistently meet the specifications established by the manufacturer.

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Equipment and Calibration

- The QSR requires each manufacturer develop, conduct, control and monitor production processes to ensure that production devices conform to their specifications.
- All equipment used to manufacture a device must be appropriately designed, constructed, placed and installed to facilitate maintenance, adjustment, cleaning and use.

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Device Master Record (DMR)

- The QSR requires all of the routine documentation required to manufacture devices that will consistently meet company requirements be kept in the DMR.
- A DMR is essentially the “recipe” for a device.
- A DMR is a compilation of records containing the procedures and specifications for a finished device.
- The *Design Output* is the basis of the DMR.
- Device master records should be technically correct, contain and/or reflect the approved device and process designs, **be under change control**, contain the release or other control date, contain an approval signature and be directed toward the intended users of the documents.

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Document & Change Control

- QSR requires formal procedures be established for changes to documents that make up the DMR. These change control procedures apply to:
  - The design
  - Device components, including software
  - Labeling and packaging
  - Device manufacturing processes
  - Production equipment
  - Manufacturing materials and all associated documentation such as quality system procedures, standard operating procedures, quality acceptance procedures, data forms and product-specific documentation.
- Change control should also be applied to any production aids such as labeled photographs and models or samples of assemblies and finished devices.

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Purchasing & Acceptance

- The QSR requires that the ability of component suppliers, consultants and contractors to meet specified requirements **be documented**.
- Possible appropriate methods of accomplishing this goal include audits, checking with other clients and previous performance data.
- If prior assessment is not possible, the manufacturer should assess the service as it is being performed.
- **Assessments must be documented**.
- Procedures for accepting incoming product must also be established and maintained. Various acceptance activities may include inspections, tests, and other forms of verification.

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Labeling

- The QSR requires devices be properly labeled.
- Proper labeling includes adequate directions for use (except for prescription devices), sterility information, etc.
- Labeling also must not be false or misleading in any particular.
- The wording and integrity of labels also must be appropriate for the intended use of the device.
- Labels also must be controlled to assure that they are correct, current and are applied to the correct devices.
- All written, printed or graphic matter on the device or any of its containers or wrappers, or accompanying the device is considered to be labeling.

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Product Evaluation

- The QSR requires documented evidence showing that a component, in-process unit, or finished device was manufactured according to the device master record (DMR) and meets all of the acceptance criteria/acceptance specifications in the DMR.

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Packaging

- The QSR requires medical device packaging protect devices during handling and shipping, and from the environment and microorganisms until the packaging is opened.
- This includes allowing for any necessary sterilization.
- Packaging may contain integral labeling and instructions for use or these instructions may be in a manual or package insert.
- Finally, when the consumer is ready to use this product, the package should be easy to open without compromising the quality of the device.

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Storage, Distribution & Installation

- The QSR requires controls be in place to assure that only correctly labeled, packaged and approved finished devices are distributed and, where appropriate, installed.
- Manufacturers should use a first-in, first-out (FIFO) distribution system when fitness for use of a device deteriorates over time.
- When a controlled environment is necessary to prevent abnormal deterioration of a product, the environment should be specified, controlled, and monitored according to specifications in the device master record.
- Installation requires verification that the device meets acceptance criteria.

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Complaints

- The QSR requires manufacturers to review, evaluate and, when appropriate, investigate complaints.
- Manufactures must establish and maintain written procedures describing the process used to perform these activities and designate a responsible individual or entity to perform these tasks.
- In Section 820.3(b) of the regulation, a complaint is defined as "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".
- Complaint files present a legal problem. Companies must maintain them but generally don't want them to be subject to subpoena.

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Servicing

- The QSR requires service be conducted by appropriately trained and experienced service personnel and verification that the serviced device meets acceptance criteria.
- The intent of the quality system regulation is to assure that servicing is correctly performed and verified according to company specified requirements such that the serviced device is suitable for the intended use and that service information is collected and analyzed to help correct any quality system problems and device design, manufacturing, labeling, or packaging problems.
- Special rules apply to 3rd parties the reprocess devices (see "Guidance for Industry and for FDA Staff Enforcement Priorities for Single-Use Devices Reprocessed by Third Parties and Hospitals" August 2000 and related documents).

Quality Systems Audits

- The QSR requires that a documented independent inspection and review of a quality system be performed on a periodic basis in accordance with written procedures.
- The objective is to verify, by examination and evaluation of objective evidence, the actual degree of compliance with those elements of the quality system under review.

Factory Inspections

- Section 704(a) of the *Food, Drug, and Cosmetic (FD&C) Act* gives the FDA the authority to conduct GMP inspections of medical device manufacturers.
- An FDA investigator examines facilities, manufacturing processes, records and corrective action programs during these inspections.
- The results provide information necessary to evaluate a manufacturer's compliance with the device QS regulation (21 CFR 820).

ISO 9000 Series Standards

- ISO 9000:1994
  - Obsolete
  - Less abstract (more easily understood and applied) than current version
- ISO 9000:2000
  - Current version
  - Intended to apply to everyone
  - Very (too?) abstract and general

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ISO 9000:2000 Standards

- ISO 9000 (QMS – Fundamentals and Vocabulary) describes the fundamentals and terminology of quality management systems.
- ISO 9001 (QMS – Requirements) specifies requirements for a quality management system.
- ISO 9004 (QMS – Guidelines for Performance Improvements) provides guidelines that consider the effectiveness and efficiency of quality management systems.
- ISO 19011 provides guidance on auditing quality and environmental management systems.

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Principles from ISO 9000

- Quality Management Principles from ISO 9000
- Customer Focus
- Leadership
- Involvement of People
- Process Approach to Activities
- System Approach to Management
- Continual Improvement
- Factual (Objective) Approach to Decision Making
- Mutually Beneficial Relationships

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ISO 9001 Overview

- ISO 9001 specifies the requirements for a quality management system that can be used for internal application by organizations, or for certification (formerly registration), or for contractual purposes.
- It focuses on the effectiveness of the quality management system in meeting customer requirements.

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ISO 9001 Sections

1. Scope
   1. General
   2. Application
2. Normative Reference
3. Terms and Definitions
4. Quality Management System
   1. General Requirements
   2. Documentation Requirements
   3. Management Responsibility
   4. Management Commitment
   5. Customer Focus
   6. Quality Policy
   7. Planning
   8. Responsibility, Authority and Communication
   9. Management Review

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Sections (continued)

5. Resource Management
   1. Provision of Resources
   2. Human Resources
   3. Infrastructure
   4. Work Environment
6. Product Realization
   1. Planning of Product Realization
   2. Customer-Related Processes
   3. Design and Development
   4. Purchasing
   5. Production and Service Prevision
   6. Control of Monitoring and Measuring Devices
7. Measurement, Analysis and Improvement
   1. General
   2. Monitoring and Measurement
   3. Control of Nonconforming Product
   4. Analysis of Data
   5. Improvement

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Sections (concluded)

- Annexes (Appendices)
  - A. Correspondence between ISO 9001:2000 and ISO 14001:1996 (an environmental management standard)
  - B. Correspondence between ISO 9001:2000 and ISO 9001:1994
- The ISO 9001:2000 Standard is 23 pages long (including the annexes).
- Organizations may request exemption from Section 7 requirements that do not apply to their operations.

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ISO 9004 Comments

- ISO 9004 gives guidance on a wider range of objectives for quality management systems than does ISO 9001.
- Its objectives include continual improvement of an organization's overall performance, efficiency and effectiveness.
- ISO 9004 is recommended as a guide for organizations wishing to move beyond the basic requirements of ISO 9001.
- It is not intended for certification or contractual purposes.
- The ISO 9004:2000 Standard is 57 pages long (including the annexes).

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References

- The FDA Website (www.fda.gov)
- The ISO 9000 series standards
- *Medical Device Quality Systems Manual: A Small Entity Compliance Guide, 1st edition* by Andrew Lowery, Judy Strojny, and Joseph Puleo of the FDA's Division of Small Manufacturers Assistance, Office of Health and Industry Programs (HSS Publication FDA 97-4179, December 1996)

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References (continued)

- ISO 9000 In Our Company. Jack Kanholm. Los Angeles: AQA Co. 1994 (ISBN 1-882711-03-3)
- ISO 9000 Explained (65 Requirements Checklist and Compliance Guide, 1994 Standards), 2nd ed. Jack Kanholm. Los Angeles: AQA Co. 1994 (ISBN 1-882711-06-8)
- Demystifying ISO 9000. Gerard W. Paradis, Fen Small and Information Mapping Team ISO. Reading, MA: Addison-Wesley Publishing Co. 1996 (ISBN 0-201-63490-2)