Glisland® Training Series:

Overview of FDA Compliance for Medical Devices

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Description

This course provides a concise overview of how FDA regulates medical devices and what a medical device manufacturer needs to know about regulatory compliance. It is designed for those who are new to medical device industry, for who want to have a high level understanding of FDA regulatory requirements for medical devices, and for responsible executives who need to have background and knowledge necessary to understand the role of regulatory compliance unit in their organizations.

Definition of Medical Device

"an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:

a. recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,
b. intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
c. intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of it's primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes."

How FDA Regulates Medical Devices

1. Federal Food Drug & Cosmetic (FD&C) Act
2. FDA Center for Devices and Radiological Health (CDRH)
3. Code of Federal Regulations (CFR)
4. Title 21 CFR Parts 800-1299

Three Levels of Controls

1. General Controls:
    a. Adulteration provisions
    b. Misbranding provisions
    c. Establishment registration and device listing
    d. Compliance with QSR
    e. Submission of 510(k)
    f. Banned devices
    g. Notification and Repair, replacement, and refund provisions
    h. Records and reports
    i. Restricted devices

Three Levels of Controls

2. Special Controls:
    a. Special Labeling requirements
    b. Recommendation to follow FDA certain guidances
    c. Mandatory performance standards
    d. Human clinical trials
    e. Postmarket surveillance requirements
3. Premarket Approval

Device Classes and Regulatory Controls

1. Class I: General Controls
2. Class II: General Controls, Special Controls
3. Class III: General Controls, Special Controls, PMA

Marketing Requirements

1. Marketing Applications
   a. 510(k)
   b. PMA
   c. IDE
2. Premarket requirements
   a. Labeling
   b. Registration
   c. Listing
3. Postmarket requiremeent
   a. Quality System
   b. Medical Device Reporting
   c. Others

Additional Requirements for IVD

1. In vitro diagnostics (IVD)
2. Clinical Laboratory Improvement Act (CLIA) of 1988
3. IVD Labeling (21 CFR 809)
4. Manufacturer Certification Programs (not mandatory)

When a 510(k) submission is required

1. New class I or Class II device, unless exempted by regulation
2. Certain Class III devices on the market prior to 1 December 1990
3. Modification of legally marketed devices that could be expected to have a significant effect on the safety or effectiveness of the device
4. Significant change of the intended use or addition of a new intended use

510(k) for class III device - special case

1. Similar to preamendment Class III device (existed before 1976) for which PMA has not been called and substantial equivalence to pre amendment Class III devices has been established.
2. When 510(k) is submitted for a Class III device, the submission must include summary and certification.

Exemptions

1. Most of Class I and some Class II devices are exempted from 510(k)
2. New device that is substantially equivalent to preamendment Class III for which PMA has not been called is exempted from PMA but subject to 510(k)
3. Class I devices exempted from 510(k) are also exempted from QSR except for general records and complaint files.

Other 510(k) Exemptions

1. A custom device
2. A device that is not generally available in finished form
3. A device not offered through labeling or advertising for commercial distribution
4. A device is intended for use by a patient named in the physician's or dentist's order or is intended for use by a physician or dentist and is not generally available to other physicians of dentists
5. Distributors of a pre-amendment device
6. Distributors of legally marketed device submitted by another person

PMA (Premarket Approval)

1. Class III devices
   a. support or sustain human life
   b. substantial importance in preventing impairment of human health
   c. presenting a potential, unreasonable risk of illness or injury
2. PMA process (21 CFR 814)

IDE

1. Investigational device exemption (IDE)
2. Requirements:
   a. An IDE approved by an institutional review board (IRB). If the study involves a significant risk device, the IDE must also be approved by FDA
   b. Informed consent from all patients
   c. Labeling for investigational use only
   d. Monitoring of the study
   e. Required records and reports
3. The sponsor must be located in the United States
4. Exemption from IDE requirements

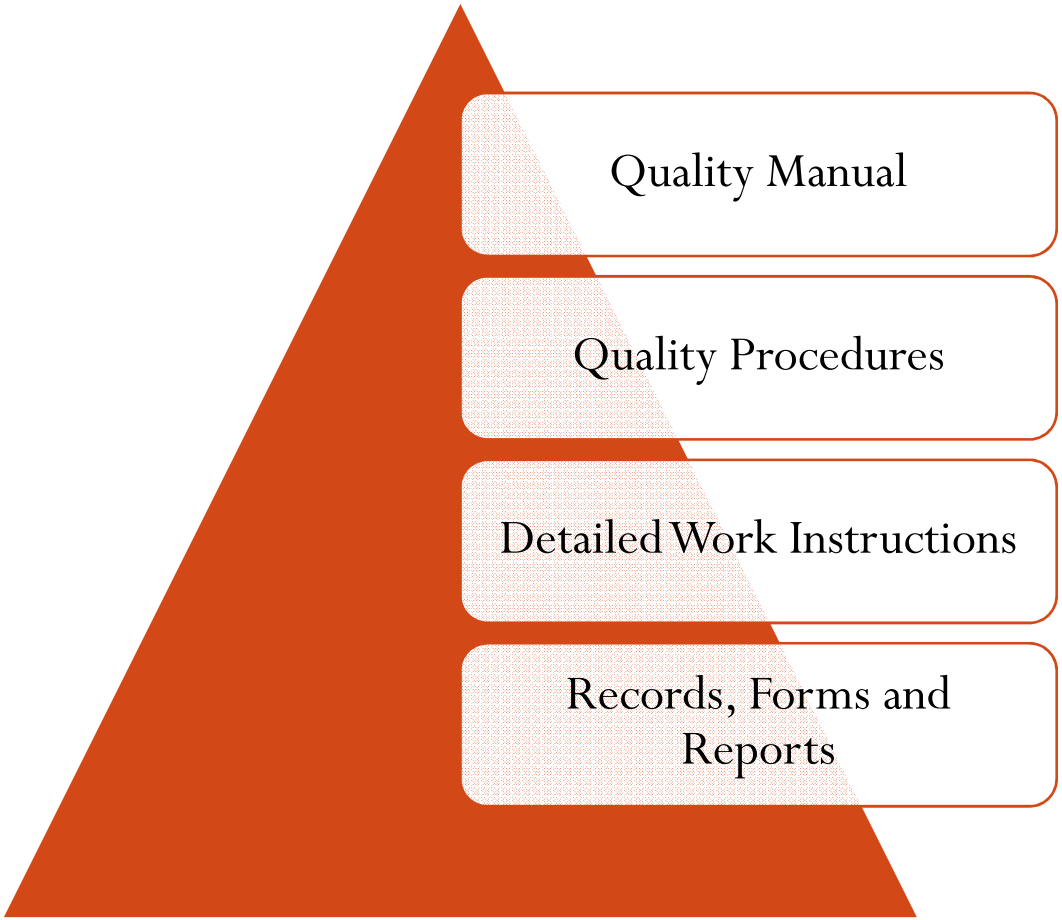
GMP Concept Outline

1. Adulteration provisions
2. Quality must be designed and built in
3. The quality system approach
4. Documentation

Medical Device GMP - Quality System Regulation (21 CFR 820)

1. Quality System Requirements
2. Design Controls
3. Document Controls
4. Purchasing Controls
5. Identification and Traceability
6. Production and Process Controls
7. Acceptance Activities
8. Nonconforming Product
9. Corrective and Preventive Action
10. Labeling and Packaging Control
11. Handling, Storage, Distribution, and Installation
12. Records
13. Servicing
14. Statistical Techniques

Quality System Pyramid



Regulatory Requirements in Development Phase

1. Good Laboratory Practice (GLP) - 21 CFR 58
2. Good Clinical Practice (GCP) - 21 CFR 812, 21 CFR 50, 21 CFR 54, 21 CFR 56
3. Design Control - 21 CFR 820.30

Design Control in Development Phase

1. Required for Class II and Class III and Class I devices automated by software
2. Define design process
3. Establish and maintain procedures to control the design
4. Establish and maintain design and development plans
5. Define responsibility for implementation
6. Design history file

Change or Modification to an Existing Device

1. Possible Changes:
   a. Labeling Changes
   b. Technology, engineering and performance changes
   c. Materials changes
   d. Manufacturing, sterilization, process, packaging
2. Change Impacts:
   a. Intended use, safety and effectiveness
   b. New 510(k)
3. PMA supplement

Electronic Records and Electronic Signatures

1. 21 CFR Part 11 and Final Guidance
2. Enforced rules and requirements:
   a. System access controls
   b. Enforce Sequence Steps
   c. Application Access Controls
   d. Device checks
   e. Competence of People
   f. Accountability
   g. System document control
   h. Controls for open systems
3. e-signature requirements

Medical Device Reporting
-the Final Rule

1. Medical device manufacturers, importers and distributors are no longer required to submit and annual certification statement (Form FDA 3381).
2. Domestic distributors no longer have to submit MDR reports, but they must continue to maintain records of adverse events.
3. Importers continue to be subject to the remaining requirements of the MDR regulation, 21 *CFR* 803.
4. User facilities now submit a report annually instead of semiannually.

MDR Requirements for Manufacturers

1. Thirty day reports (Form FDA 3500A)
   a. death, serious injuries and malfunctions
2. Five day reports (Form FDA 3500A)
   a. events that require remedial action to prevent and unreasonable risk of substantial harm to the public health and other types of events designated by FDA
3. Baseline reports (Form FDA 3417): stayed
4. Annual Certification (Form FDA 3381): repealed

Medical Device Corrections and Removals

1. 21 *CFR* 806: "*Medical Devices; Reports of Corrections and Removals*"
2. Recall definition: a correction or removal of a product that is defective, could be a risk to health or is in violation of FDA regulations.
3. Manufacturers and importers are required to report to FDA any correction or removal undertaken to reduce a risk to human health posed by use of the device
4. Manufacturers and importers are required to report to FDA action taken to remedy a violation of the act caused by the device.
5. FDA would take legal action if no voluntary correction action was taken.

MDR Baseline Report

1. Baseline report is triggered by MDR. If you have reportable adverse event, you are required to file baseline report and annual update.
2. 21 CFR 803.55 describes in what circumstance you need to submit baseline report information is required to the patient level.

MDR Requirements for User Facilities

1. 10-day death report to FDA and Manufacturer (Form FDA 3500A)
2. 10-day serious injury report to manufacturer (to FDA only if manufacturer unknown)
3. Annual reports of death and serious injury to FDA (Form FDA 3500A

MDR Requirements for Importers

1. 10-day death and serious injury report to FDA (Form FDA 3419)
2. 10-day death, serious injury and malfunction report to manufacturer

Medical Device Corrections and Removals

1. 21 *CFR* 806: "*Medical Devices; Reports of Corrections and Removals*"
2. Definition of recall:
3. "*A recall is a method of removing or correcting products that are in violation of laws administered by the Food and Drug Administration (FDA).* "
4. Report to FDA any correction or removal undertaken
5. Report to FDA action taken to remedy a violation of the act caused by the device
6. Voluntary correction action vs. FDA legal action

Device Tracking

1. Codified in 21 *CFR* 821 to implement *FD&C Act* 519(e)
2. Tracking requirements apply only to those who receive a tracking order from FDA
3. Tracking information at the patient level

Advertising and Promotional Materials

1. FDA - Drug, restricted device, biologics advertising
2. FTC - Nonrestricted medical device and cosmetics advertising
3. Memorandum of understanding (MOU) between FDA and FTC

FDA Advertising Regulations

1. True statement & summary
2. Fair Balance
3. Approved labeling
4. Promotional labeling must contain the full labeling.

FDA Enforcement

1. Establishment registration and product listing
2. Marketing clearance/approval
3. Reports
4. Inspections
5. Notice of Violations (FDA-483, Warning Letters…)
6. Recalls
7. Civil money penalties
8. Seizure
9. Injunction
10. Prosecution

Compliance with State Laws and Regulations

1. Manufacturing facility vs. commercial distribution in each state
2. Check each state laws and regulations
3. Example: California Sherman Food, Drug and Cosmetic Law