



MEDICAL DEVICE REGULATIONS

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Disclaimer

- The contents of this presentation are my own, and do not necessarily reflect the views and/or policies of the Food and Drug Administration or its staff. The Food and Drug Administration will not be bound by any of the comments or information contained in this presentation.



Purpose of Presentation

- This seminar is designed to give the audience some insight and guidance on FDA regulations you may need to observe in the development, manufacture and marketing of devices intended for human use.



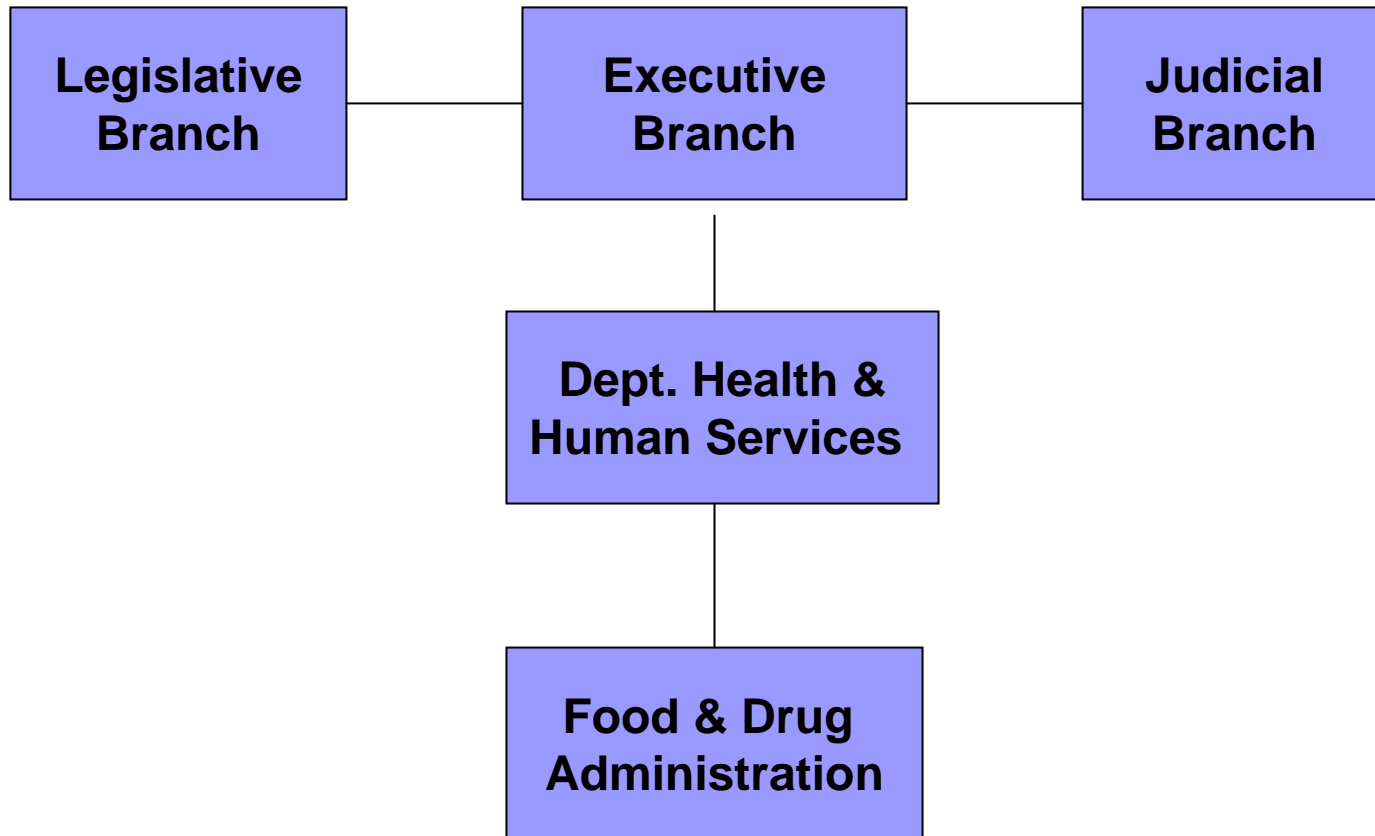
This Presentation Will Cover 3 Major Information Areas

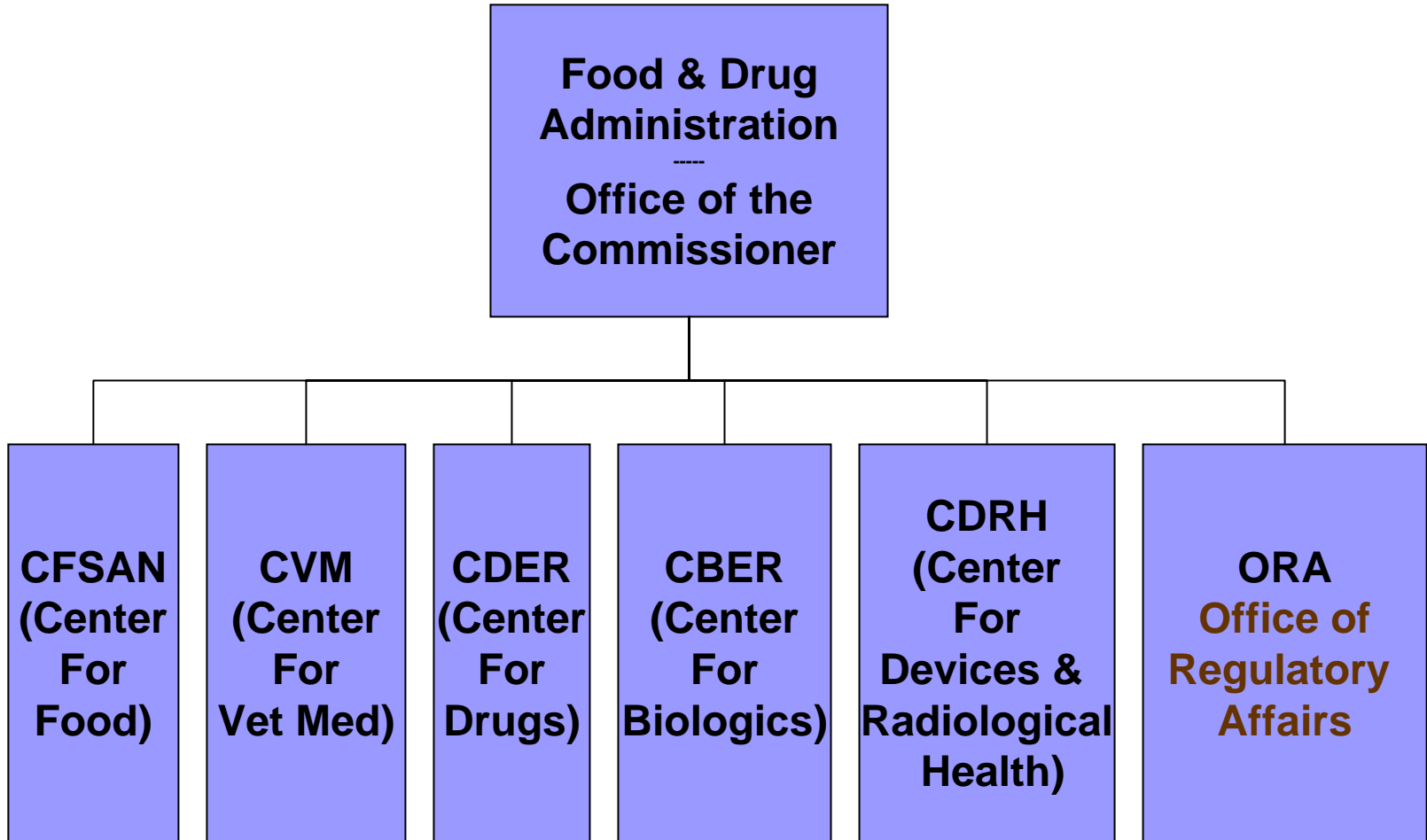
- For Regulatory & Clinical Affairs Personnel
- For Engineers re. Device Development
- For Engineers & for Regulatory Personnel re. Radiation Emitting Electronic Products



***Information for Regulatory &
Clinical Affairs Personnel***

U. S. Government & the FDA





What is a Medical Device?

- Federal Food Drug & Cosmetic Act, Section [201(h)] defines a medical device as: **“an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is ---**

Device Definition [201(h)], continued

- 1) recognized in the official **National Formulary, or the U.S. Pharmacopoeia**
- 2) intended for **use in diagnosis of disease or other conditions, or used in the cure, mitigation, treatment, or prevention of disease in man or other animals, or**
- 3) intended to affect the structure or any function of the body of man or other animals, **and ...**

Device Definition, continued

- **And which does not achieve its primary 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 its primary intended purposes.”**



Why the Need for FDA's Medical Device Regulations?

- To ensure that Medical Devices are Safe & Effective!
- To provide a means whereby unsafe and ineffective devices may be reported to FDA and removed from marketing channels!

Device Classifications [513] FFDCCA

- **Class I** – general controls - most, if not all, Class I devices are exempt from 510(k)
- **Class II** – general controls, special controls & 510(k) - Pre-Market Notification required, unless “Grandfathered” (marketed prior to 1976)
- **Class III** – general controls and Pre-Market Approval (PMA)

Examples of Class I Devices

- Inflatable Extremity Splint
- Oxygen Mask
- Line Isolation Monitor
- Intra-Oral Dental Drill
- Powered Toothbrush

Examples of Class II Devices

- Nebulizer
- Cardiac Monitor
- Hemodialysis System
- Electro-Surgical Cutting & Coagulation Device
- Surgical Laser for Dermatology Use

Examples of Class III Devices

- Cardiovascular Stent
- Intra-Aortic Ballon
- Implanted Urinary Continenence Device
- Implantable Diaphragmatic/Phrenic Nerve Stimulator
- Membrane Lung for Long Term Pulmonary Support

Device Product Codes

73 Anesthesiology	86 Ophthalmic
74 Cardiovascular	87 Orthopedic
75 Chemistry	88 Pathology (Diagnostic)
76 Dental	89 Physical Medicine
77 Ear, Nose, and Throat	90 Radiological
78 Gastroenterological and Urological	91 Toxicology
79 General and Plastic Surgery	92 (unassigned)
80 General Hospital and Personal Use	93 (unassigned)
81 Hematology (Diagnostic)	94 Ionizing (Rad. Health)
82 Immunology (Diagnostic)	95 Light Emitting (Rad. H)
83 Microbiology (Diagnostic)	96 Microwave, including RF
84 Neurological	97 Sound Emitting (Rad. H)
85 Obstetrical and Gynecological	92-97 = Non-Medical

Product Codes

- * **73-91** are for medical devices.
- * **92-97** are for non-medical devices
(i.e.: x-ray baggage screening machine,
laser light shows, microwave ovens).



Where Are the Medical Device Regulations?

ANS: Title 21 Code of Federal Regulations

- 21CFR 800-898 (Medical Device)
- 21CFR 900 (Mammography)
- 21CFR 1000-1050 (Radiological Health)



Device Development For Engineers

What Can You Do?

- As an engineer, you can work to design & develop products which are as safe and effective as possible. Become familiar with regulations, industry standards, guidance documents, and keep current in your field.
- As an employee, find a company with a work ethic of which you can be proud.
- As a individual, know your rights & your obligations (your duties & your responsibilities).



Designing a New Product?

**Let's Start with
Human Factors Engineering**

What is HFE?

- Human factors engineering (HFE) is the science and the methods used to make devices easier and safer to use.
- When applied to medical devices, HFE helps improve human performance and reduce the risks associated with use.

When to use HFE?

- HFE should take place early in the product development process. It should include tools such as analysis of critical tasks, use error hazard and risk analysis, and realistic use testing.

HFE Problems

- An Institute of Medicine report, [To Err Is Human - Building a Safer Health System](#), released in November 1999 estimated that as many as 98,000 people die each year from medical errors in hospitals. Medical devices are responsible for some of these deaths, due to:
 - Failure of the device
 - Actions of the user (or use-related errors)

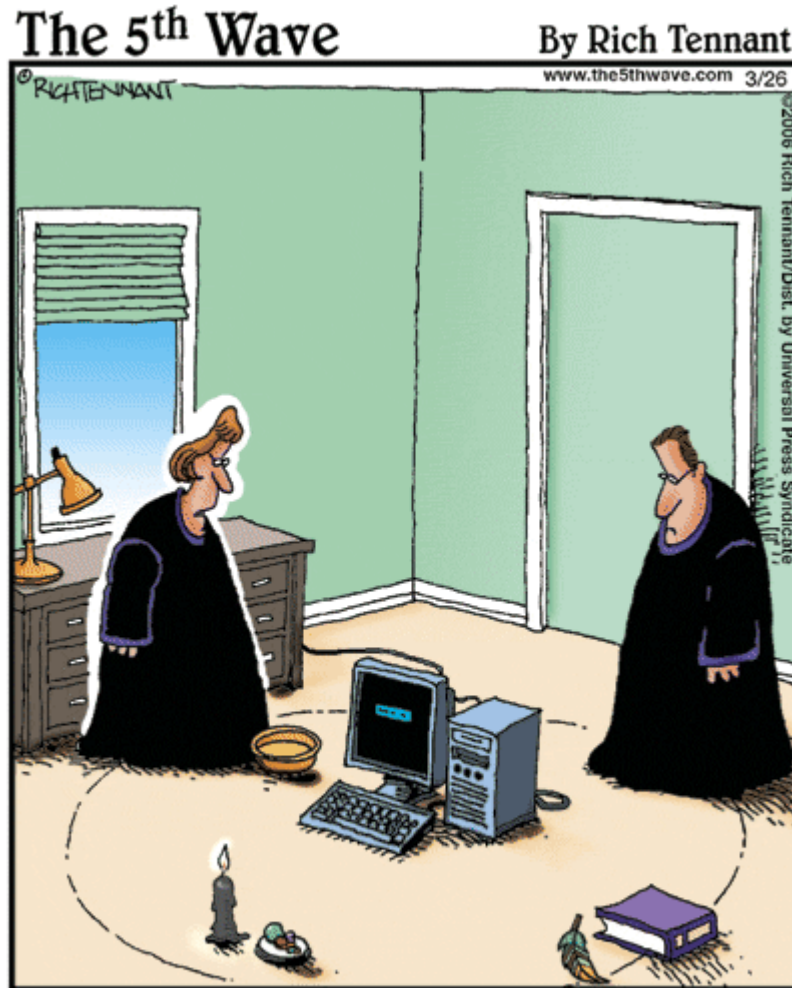
Use-Related Errors

- People blame repeated use errors on the user (i.e.: “User Errors”), rather than on poor product design or inadequate instructions for use (i.e.: “Use Errors”), so people don’t recognize the need for human factors.
- Medical devices can be complex;
- Medical devices are often used under stressful conditions;
- Users may think differently than device designers do;
- Consumers now use devices that were originally designed for experienced medical personnel.

What Are The Benefits of HFE?

- Reduced risk of device use error;
- Better understanding of device status and operation;
- Better understanding of a patient's current medical condition;
- Easier to use (or more intuitive) devices;
- Reduced need for training;
- Reduced reliance on user manuals;
- Easier to read controls and displays;
- Safer connections between devices (i.e. power cords, leads, tubes, etc.);
- More effective alarms; and
- Easier repair and maintenance.

The Most Common Problem



“We should cast a circle, invoke the elements and direct the energy. If that doesn’t work, we’ll read the manual.”



Related Topic

Quality System Regulation Design Controls

Design Controls, 21CFR 820.30

- The lack of design controls is one of the major causes of device recalls.
- IE: the “user errors” discussed above...

Design Controls, continued

- The intrinsic quality of devices, including their safety and effectiveness, is established during the design phase.
- A design plan/design history file is needed to document design requirements, specifications, intended use, and...

Design Control, continued

- Design Inputs
- Design Outputs
- Design Reviews
- Design Verification
- Design Validation
- Design Transfer
- Design History File

Design Input(s)

- **Human Factors Relevance:** Ensuring proper design of the user interface of a device is critical to address the user's needs. This is best done by systematic consideration of human factors in the development of the device user interface.
- The user interface includes all aspects of a device (including its labeling) that users see, feel and hear when operating the device.

Design Verification

- Human factors relevance: For both establishing the design input for the user interface, and carrying out design verification, manufacturers should conduct human factors activities throughout the design program.
- These activities can include task/function analyses, user studies, prototype tests and mock-up reviews.

Design Validation

- Human Factors Relevance: Design validation should be used to demonstrate that the potential for use error that can lead to patient injury has been minimized.
- Testing the device under actual or simulated use conditions is required. Realistic use conditions should be carried out by test participants who represent a range of typical intended users in terms of their ability to acquire information from, manipulate and maintain the device and understand the accompanying labeling.



Design Validation Shall Include Risk Analysis

- **Human Factors Relevance:** In addition to other hazards, risk analysis should include use error as well.
- A risk analysis is appropriate for any device where use error can lead to serious patient injury... or death.

Design Considerations

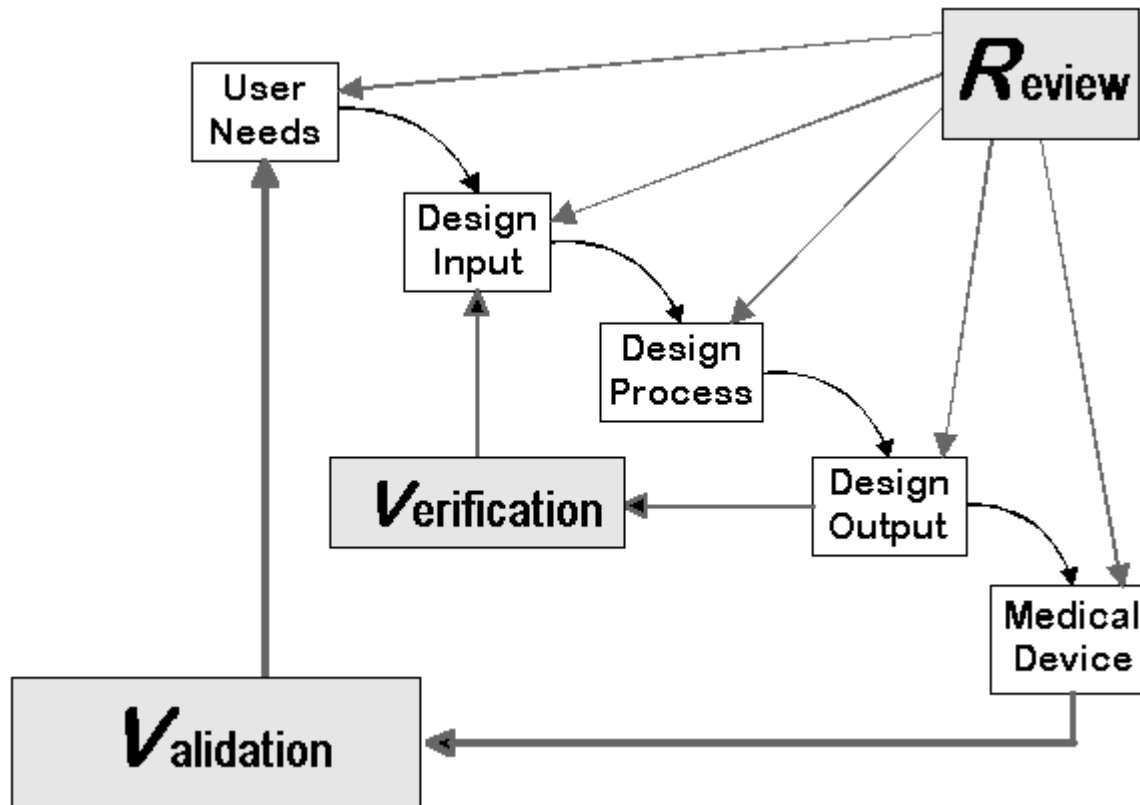
- Risk Management
- Materials Technology/Production/Mfg
- Engineering (software, reliability, durability, maintainability, serviceability, configuration)
- Regulatory Affairs & Quality Assurance
- Compliance w/Standards (EMI/EMC, etc.) and Regulatory Requirements

Design Considerations, continued

- The Device User (skill/education & worst case environmental conditions)
- Biocompatibility-Clinical Evaluations, etc.
- Potential Re-Use of Single-Use Devices
- Anticipating “device design improvements” and limitations on such improvements!

Figure 1 - Waterfall Design Method

(figure used with permission of Medical Devices Bureau, Health Canada)



Waterfall Design Method

- In a traditional waterfall development scenario, the engineering department completes the product design and formally transfers the design to production. Subsequently, other departments or organizations develop processes to manufacture and service the product.

Waterfall Design Method

- There has frequently been a divergence between the intent of the designer and the reality of the factory floor, resulting in such undesirable outcomes as low manufacturing yields, rework or redesign of the product, or unexpectedly high cost to service the product.

Waterfall Design Method

- Although the waterfall model is a useful tool for introducing design controls, its usefulness in practice is limited. The model does apply to the development of some simpler devices.
- For more complex devices, a concurrent engineering model is more representative of the design processes in use in the industry.

Concurrent Design Method

- One benefit of concurrent engineering is the involvement of production and service personnel throughout the design process, assuring the mutual optimization of the characteristics of a device and its related processes.
- While the primary motivations of concurrent engineering are shorter development time and reduced production cost, the practical result is often improved product quality.



***More
Information for Regulatory &
Clinical Affairs Personnel***

Other QSR Requirements in 21CFR 820

- Management Responsibility
- Document Controls
- Production & Process Controls
- Corrective & Preventive Actions
- Complaints & MDRs

Management Responsibility

- FDA court cases have confirmed that management with executive responsibility (usually the President) is ultimately responsible for the safety and effectiveness of the devices manufactured and distributed.
- This means the President can't blame a low level employee for failures in the quality system he (the President) was suppose to establish ...

MDR's-Medical Device Reports

- MDR's - when a manufacturer receives information indicating its device was involved in a death, serious injury/illness, or a malfunction, which, if repeated, could result in death or serious injury/illness, must submit a MDR to FDA.
- Inability to verify information is not an excuse for failure to report MDRs to FDA.



IDE – Investigational Device Exemption

*Investigations involving
Human Test Subjects to determine
the Safety & Efficacy of a Medical Device!*

- An **IDE**, with an **FDA number**, is required only when an IRB determines the research has the potential for **significant risk** (injury/death) to the human subjects.
- IRB = Investigational Review Board

Pre-Clinical Investigations

- Pre-Clinical Investigations (Bench Testing and or Animal Testing) may be warranted or recommended for a Class III device, before starting a Clinical Investigation.
- Confer with FDA's Office of Investigational Device Exemptions before finalizing the Pre-Clinical Investigational Test Protocol.

Types of Device Clinical Investigations

- IDE Feasibility Study (up to 3 subjects)
- IDE Pivotal Study (up to 12 subjects)
- IDE Study (typically over 50 subjects)
- Post-Market Study (this is becoming more and more common)

* *CDRH does not use the terms Phase I/II/III Studies.*

Investigational Device Exemptions

Consult FDA's IDE Office well before the Investigational Test Protocol is finalized, so that there is consensus re:

- The design of the protocol is acceptable and believed to achieve its intended purposes.
- The methods of statistical analyses are agreed upon, as well as the study end-point.

Who's Involved in IDE's?

- Sponsors (usually a manufacturer)
- IRB: Institutional Review Board
(usually a hospital IRB)
- Clinical Investigators (usually doctors)
- Monitors/Contract Research Organizations

Paperwork to be Filed Before Marketing* a Medical Device

- Establishment Registration (FDA-2891)
- Device Listing (FDA-2892)
- Application [510(k) or PMA] requesting authorization to market a medical device
- FDA, CDRH, HFZ-342, 9200 Corporate Blvd., Rockville, MD 20850

* Or otherwise distributing

510(k) Pre-Market Notifications

- Typically for a Class II device.
- Submitted 90 Days Prior to Marketing.
- It's an information package to demonstrate Substantial Equivalence (SE) to a legally marketed device (it is not a form).
- It constitutes Intellectual Property Rights

Pre-Market Approval (PMA)

- Typically for a Class III device.
(New Device, or New Use of an Old Device, which has the potential for significant risks).
- PMA is an information package with proof of Safety and Efficacy, including IDE clinical study data (it is not a form).
- Once submitted – FDA has 180 days to approve or deny application



Combination Products Requiring the Approval of 2 Centers

- Drug-Devices (CDER & CDRH)
 - a) Drug Eluting Cardiovascular Stents,
 - b) Use of a Laser to Photoactivate a Drug
- Biologic-Devices (CBER & CDRH)
 - a) Dental Bone Filling Device w/ Biologic Component to Encourage Bone Growth
 - b) Substitute Skin Made of Fibroblasts Human Cells on an Absorbable Mesh Material

What are IDE/510(k)/PMA #s?

- IDE: G081234
- 510(k): K081234
- PMA: P081234

- These are examples of the types of numbers which might be issued in 2008.



***Radiation Emitting Electronic
Products For Engineers and for
Regulatory Personnel***

Electronic Products which Emit Radiation

***(Ionizing or Non-Ionizing)
(Medical or Non-Medical)***

**fall under FDA Jurisdiction
per 21CFR 1000-1050**



Examples of Ionizing Radiation Emitting Electronic Products

- TVs and CRT Monitors
- X-Ray Tubes
- X-Ray Systems
- X-Ray Components (electron guns)

Examples of Non-Ionizing Radiation Emitting Electronic Products

- *RF Generating Equipment
- *Microwave Equipment
- *Laser Products
- *Sunlamp Products
- *Ultrasound Products
- *Ultraviolet Products, including High Intensity Mercury Vapor Discharge Lamps
- * Medical and or Non-Medical

Electronic Product Records & Reports

- Product Reports (describes the product)
- Annual Reports (qty marketed)
- Accidental Radiation Occurrences (AROs)

How About Products Which Are Both Medical Devices & Electronic Products?

- ANSWER: They require submission of both:
 - a 510(k)/PMA,
 - and a Product Report.

Accession Numbers

- CDRH issues a one page letter, bearing an accession number (document tracking number) ... if there are no questions with the submitted Report.
- Example of an Accession Number Issued During 2008: 0812345



Miscellaneous Information

Some Manufacturing Technologies Encountered By FDA

- Electronics, Software & Hardware
- Rubber, Plastic & Metal
- Purification, Sterilization & Time-Temperature Processes
- Radiation (UV, Ultrasound, Gamma)
- Bio-Engineering: mono/polyclonal antibodies, tissues, gene-probes, etc.

FDA Number Summary

- Device Establishment Registration #s
- Device Listing #s: products distributed
- 510(k) #s: authority to market class I/II device
- PMA #s: authority to market class III device
- IDE #s: authority to conduct clinical research
- Accession #: authority to market a radiation emitting electronic product (i.e.: x-ray or laser product)

Examples of Medical Device Citations (FDA-483 Inspectional Observations)

- Failure to establish adequate management controls to ensure that an effective quality system has been established and maintained, as required by 21CFR 820.20.
- Failure to follow procedures for conducting management reviews at defined intervals and frequency, as required by 21CFR 820.20(c).
- Failure to follow procedure for conducting quality audits, as required by 21CFR 820.22.

Examples of Medical Device Citations (FDA-483 Inspectional Observations)

- Failure to establish procedures for identifying training needs and ensuring that employee training is documented, as required by 21CFR 820.25.
- Failure to establish procedures to control the design process of a device to ensure that specified design requirements are met, as required by 21CFR 820.30(a).

Examples of Medical Device Citations (FDA-483 Inspectional Observations) - VALIDATION-

- Failure to adequately ensure that when the results of a process can not be fully verified by subsequent inspection and test, the process shall be validated with a high degree of assurance and approved according to established procedure, as required by 21CFR 820.75(a).

Examples of Medical Device Citations (FDA-483 Inspectional Observations)

- Failure to address in the “Corrective and Preventive Action” procedure what specific processes and work operations will be trended and how they will be trended to identify existing and potential causes of non-conforming product, or other quality problems; and what statistical methodology will be used as required by 21CFR 820.100(a)(1).

Examples of Medical Device Citations (FDA-483 Inspectional Observations)

- Failure to document corrective and preventive activities, investigations of causes of non-conformances, implementation of corrective and preventive actions, and verification that the corrective action is effective, as required by 21CFR 820.100(b).

FDA Websites

- CDRH: www.fda.gov/cdrh/index.html
- Human Factors:
www.fda.gov/cdrh/humanfactors/index.html
- Design Control:
www.fda.gov/cdrh/comp/designgd.html

FDA Forms

- <http://www.fda.gov/opacom/morechoices/fdaforms/CDRH.html>

Questions, contact industry support.

(Industry Assistance)

FDA Form #	Date	Title	Format	Paper Copy or Contact Info.
2579	07/02	Report of Assembly of a Diagnostic X-Ray System	Not Yet Electronic	PPF
2767	12/03	Notice of Availability of Sample Electronic Product	PDF WORD	Debbie Perrell 301-594-4654
2783	10/80	Mobile Radiographic Systems Field Test Record	PDF	PPF
2784	10/80	Above Table X-Ray Source Radiographic Systems	PDF	PPF
2785	05/82	Dental Radiographic Systems Field Test Record (2784.1-Pg1, 2784.2-Pg2, 2784.3-Pg3)	PDF	PPF
2786	05/82	Under Table X-Ray Source Fluoroscopic & Spot Film Systems Field Test Record	PDF	Stephen Toigo 301-827-2906
2877	12/03	Declaration of Products Subject to Radiation Control Standards	PDF WORD	Chris Colburn 301-827-7669
2891	03/02	Initial Registration of Medical Device Establishment THIS FORM MUST BE SUBMITTED IN TRIPLICATE	PDF	DSMA FAX 301-443-8818
2891a	03/02	Annual Registration of Medical Device Establishment	Not Yet Electronic	Bryan H. Benesch 301-594-4591 Ex151
2892	03/02	Medical Device Listing	PDF	DSMA FAX 301-443-8818

Thank You!

My thanks to Steve Baldwin, IEEE/PSES, for the opportunity to make this presentation.

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