Introduction to the FDA

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Historical Context

- In the early 1900's people were being ripped off, made sick and even killed by bad food, "patent" medicines and cosmetics with dangerous ingredients (like lead and arsenic).
- The federal congress passed the Food, Drug and Cosmetics Act in 1938 to protected the public. This act created the FDA.

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Changes over Time

- The Medical Device Amendments of 1976 extended and revised requirements for medical devices.
- The Safe Medical Devices Act of 1990 further refined the requirements for medical devices.
- The Medical Device Amendments of 1992 made further changes.
- All these laws were passed based on concerns for the public welfare.

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Hierarchy of Federal Oversight

- Laws
- Regulations
- Guidance Documents

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Laws

- Are passed by congress.
- Are often rather general.
- Represent the intentions of the congress and often lead to the creations of agencies (FDA, EPA, etc.).
- These agencies then write and enforce specific regulations.
- Laws are part of the United States Code (USC)

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Regulations

- Are generally more specific than laws.
- Are written by agencies under authority grated by congress.
- General done with extensive “public” input.
- Become part of the Code of Federal Regulations (CFR).
- Regulations are enforced by the agencies.

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Guidance Documents

- Are prepared by agencies.
- Are intended to help the "public" understand and comply with regulations and laws.
- Are often very useful to engineers working in regulatory compliance areas.
- Many agencies also offer training either free or at very reasonable costs.

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The Federal Register

- Where essentially all federal government actions are publicized.
- Contains draft and final text of laws and regulations.
- Contains requests of proposals and bids.
- Published every business day by the U.S. Government Printing Office (GPO).
- Available from http://www.access.gpo.gov/su_docs/index.html (free) or http://fr.cos.com/.

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About the FDA

- Regulates Foods, Drugs, Medical Devices, Cosmetic, Biologics and Radiation Emitting Devices.
- Website at http://www.fda.gov.
- Biomedical engineers often deal with their Center for Devices and Radiologic Health (CDRH).
- CDRH website: http://www.fda.gov/cdrh/index.html

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FDA Mandate

- The FDA requires that medical devices (and drugs) be proven to be safe and effective for specific medical conditions before they can be marketed in interstate commerce.

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What is a 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: (see next slide)

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What is a Device (continued)

- Is recognized in the official National Formulary (NF), or the United States Pharmacopoeia (USP), or any supplement to them,
- Is 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

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What is a Device (continued)

- Is 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."
- See FDA Device Advice webpage at: http://www.fda.gov/cdrh/devadvice/

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Medical Device Classes

- Class I – Lowest Risk
  - Subject to General Controls
  - Exempt from premarket notification unless "reserved".
  - Some exempt from QSR/GMP except for record keeping and complaint files.
- Class II
  - Subject to General and Special Controls
  - Require 510(k) premarket notification unless exempt.
- Class III – Highest Risk
  - Subject to General and Special controls
  - Require Premarket Approval Application (PMA) unless a preamendment device.

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Class I Devices

- Generally external devices (surgical scissors, manual stethoscopes, *in vitro* test kits, etc.)
- Subject to general controls only such as QSR/GMP (quality assurance and labeling). Some even exempted from some of these.

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Class II Devices

- More invasive than Class I devices (x-ray machines, ultrasound devices, etc.)
- Subject to general controls and special controls, such as compliance with performance standards, postmarket surveillance (tracking), and additional preclinical and clinical performance data as the FDA deems necessary.

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Class III Devices

- Life supporting and life sustaining devices (heart valves, VAD's, etc.).
- Subject to general and special controls.
- Require formal premarket approval.

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FDA Applications

- In general, medical devices must be proven to be safe and effective for a particular condition before they can be distributed in the U.S.
- An Investigational Device Exemption (IDE) must be obtained in order to distribute devices for clinical trials.
- Results of the clinical trials are used to produce a Premarket Approval Application (PMA) for Class III devices.

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Exception to PMA Requirement

- Devices that are "Substantially similar" to devices marketed before 1976 "only" require the filing of a 510(k) application
- The 510(k) application formally claims substantial similarity.
- I understand that some well understood devices can now be approved under 510(k) rules even if they were not marketed before 1976.

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Requirement to Start Clinical Trials

- Risk/Benefit analysis based on objective criteria.
  - Bench and animal data often used.
- Informed consent must be obtained from all patients
- Local Institutional Review Board [for use of Human Subjects] (IRB and FDA must approval "protocol").

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Issues Involved in "Clinicals"

- A clear hypothesis must be stated (A is better than B).
- Study must be designed to test (support or refute) the hypothesis.
- Clear entry criteria must be established and enforced.
- Data analysis should be ongoing to uncover possible problems (with the device or the study).
- A control group should be used.

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Types of Control Groups

- Prospective randomized groups (double blind if possible). Based scientific/statistical approach. Most expensive and time consuming.
- Non-randomized groups (possibly patients at different centers). Possibly more practical and ethical.
- Patients used as own controls. What would have happened without "treatment?"
- Historical data used as controls. What has changed?

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Other Issues

- Device classifications can be changed and additional applications required.
- Device Tracking
  - Required for all class III and some class II devices.
  - Mandated by SMDA of 1990.
- "Manufacturing" Controls
  - Quality System Regulation (QSR), formally Good Manufacturing Practices (GMP).
  - A lot like ISO 9000. Covers design and mandates design reviews and documentation.

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Current FDA Issues

- Third Party Review of 510(k)'s (http://www.fda.gov/cdrh/thirdparty/) – Pay a recognized "third party" for faster service. Limited to "eligible" devices.
- Mutual Recognition (http://www.fda.gov/cdrh/mra/) – Approval by conformity assessment bodies (CAB's) accepted by FDA. Limited to certain 510(k)'s and QSR inspections.

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Other Current FDA Issues

- Unapproved but widely marketed drugs (for Guaifenesin SR). See http://www.fda.gov/bbs/topics/NEWS/2003/NEW00962.html.
- Drug Import & Repackaging Issues (See, for example, http://www.fda.gov/bbs/topics/NEWS/2003/NEW00945.html).
- Decorative Contact Lens (See http://www.fda.gov/bbs/topics/NEWS/2003/NEW00955.html).

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