Miscellaneous FDA Activities

• **MedWatch** -- FDA provides safety information on drugs and other FDA-regulated products, and allows for adverse event reporting.

• **Recalls** -- FDA posts significant product actions of the last 60 days.

• **Inspections** - FDA inspects processing plants and other agency-regulated facilities.

• **Advisory Committees** - FDA convenes public meetings with outside experts for advice on making key public health decisions.
Let’s look at the website for today

Main Page
http://www.fda.gov/MedicalDevices/default.htm

Recently Approved Devices in 2018
https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/Recently-ApprovedDevices/ucm596872.htm

List of Recalls in 2018
https://www.fda.gov/MedicalDevices/Safety/ListofRecalls/ucm590900.htm
Case Study: Shiley Heart Valves, U.S. Food and Drug Administration approved for sale in 1979, were discontinued in 1986.
During the manufacturing process, the Shiley was redesigned from a 60 degree opening heart valve to 70 degree.
An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory

1. Recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them, or

2. 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

3. Intended to affect the structure or any function of the body of man or other animals, and which does not achieve its 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 its primary intended purposes
Device class and Regulatory controls fall into 3 categories of risk

1. **Class I** (low risk)—deemed to be low risk and are therefore subject to the least regulatory controls. For example, dental floss, stethoscopes, bandaids;

2. **Class II** (moderate risk)—higher risk devices than Class I and require greater regulatory controls to provide reasonable assurance of the device’s safety and effectiveness. For example, condoms
   
   Most imaging devices such as CT, MRI and US scanners

3. **Class III** (high risk)—generally the highest risk devices and are therefore subject to the highest level of regulatory control. Class III devices must typically be approved by FDA before they are marketed. For example, replacement heart valves, pacemakers.
   
   Other devices may be Class III because:
   
   – Used in conjunction with Class III devices
   – Has a large potential effect on the public health
   – Scientific principles of the device are not well-known

Class III will require a PMA unless it is a pre-amendment device (on the market prior to passage of medical device amendments in 1976 or substantially equivalent to such a device)
Obtaining Market Clearance

- Make sure it is a medical device
  Drug? Electronic radiation emitting product?
- Classify Device
  - Identifies level of regulatory control to assure safety and effectiveness
  - Determines marketing process for FDA approval
    - Premarket notification [510(k)]
    - Premarket approval (PMA)
- Obtain data/information (clinical data) to submit marketing application
510(k)

A device is substantially equivalent if, compared to a predicate it:

– has the **SAME INTENDED USE** as the predicate; **AND**

– has the **SAME TECHNOLOGICAL CHARACTERISTICS** as the predicate;

OR
510(k)

has the **SAME INTENDED USE** as the predicate device; AND

Has different technological characteristics (e.g., change in material, design, energy source, software) AND the information submitted to FDA:

1. Does not raise different (i.e., new) types of questions of safety and effectiveness; AND

2. Demonstrates that the device is as safe and effective as the predicate device.
A 510(k) is Required to get most devices on the market

1. Introducing a device into commercial distribution (marketing) for the first time.

2. You propose a different intended use for a device which you already have in commercial distribution.

3. There is a change or modification of a legally marketed device and that change could significantly affect its safety or effectiveness.

A new 510(k) submission is required for changes or modifications to an existing device, where the modifications could significantly affect the safety or effectiveness of the device or the device is to be marketed for a new or different indication for use.

Some devices are exempted from 510(k) by regulation?

A list of the Class I and II exempted devices can be found on http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpcd/315.cfm
How long it has historically taken the FDA to clear 510(k) submissions?

![Bar chart showing average calendar days for all 510(k) clearances (Traditional, Special, and Abbreviated) from 1976-1980 to 2011-2015. The average days range from 39 days in 1976-1980 to 173 days in 1991-1995.](chart.png)
Types of devices cleared through 510K and time to approval

Average calendar days from submission to clearance for Traditional FDA 510(k) by FDA INTERNAL REVIEWERS ONLY in 2015

<table>
<thead>
<tr>
<th>Category</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dental</td>
<td>192</td>
</tr>
<tr>
<td>Surgery</td>
<td>187</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>176</td>
</tr>
<tr>
<td>Orthopedic</td>
<td>143</td>
</tr>
<tr>
<td>Radiology</td>
<td>124</td>
</tr>
<tr>
<td>All Devices</td>
<td>172</td>
</tr>
</tbody>
</table>
Obtaining Market Clearance
CDRH

- Make sure it is a medical device
  Drug? Electronic radiation emitting product?
- Classify Device
  - Identifies level of regulatory control to assure safety and effectiveness
  - Determines marketing process for FDA approval
    - Premarket notification [510(k)]
    - Premarket approval (PMA)
- Obtain data/information (clinical data) to submit marketing application
Premarket Approval is required if the FDA needs to evaluate the safety and effectiveness, especially of Class III medical devices

Class III devices are those that:

1. support or sustain human life
2. are of substantial importance in preventing impairment of human health
3. present a potential, unreasonable risk of illness or injury

Approval is based on a determination by FDA that the PMA contains sufficient valid scientific evidence to assure that the device is safe and effective for its intended use(s)
Premarket Approval (PMA) requires both non-clinical and clinical data

1. Non-clinical Laboratory Studies' Section:
   
   Non-clinical laboratory studies' section includes information on microbiology, toxicology, immunology, biocompatibility, stress, wear, shelf life, and other laboratory or animal tests.

2. Clinical Investigations' Section:
   
   Clinical investigations' section includes study protocols, safety and effectiveness data, adverse reactions and complications, device failures and replacements, patient information, patient complaints, tabulations of data from all individual subjects, results of statistical analyses, and any other information from the clinical investigations.
The review of a premarket approval application (PMA) is a four-step review process consisting of:

1. Administrative and limited scientific review by FDA staff to determine completeness (filing review)
2. In-depth scientific, regulatory, and Quality System review by appropriate FDA personnel
3. Review and recommendation by the appropriate advisory committee (panel review)
4. Final deliberations, documentation, and notification of the FDA decision
The timetable for IDE and PMA approvals shows a 30% reduction in time to approval for PMA new, novel devices whose type has not previously been classified.

**Investigational Device Exemption (IDE)** allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data.
Contact Lenses: Is it a medical device? If so, what class?

- A soft (hydrophilic) contact lens is a device intended to be worn directly against the cornea and adjacent limbal and scleral areas of the eye to correct vision conditions or act as a therapeutic bandage.
- The device is made of various polymer materials the main polymer molecules of which absorb or attract a certain volume (percentage) of water.
Surgical Drape: Is it a medical device? If so, what class?

A surgical drape and drape accessories is a device made of natural or synthetic materials intended to be used as a protective patient covering, such as to isolate a site of surgical incision from microbial and other contamination.

The device includes a plastic wound protector that may adhere to the skin around a surgical incision or be placed in a wound to cover its exposed edges, and a latex drape.
Infusion Pump: Is it a medical device? If so, what class?

How does the insulin get into your body?

1. Insulin pump
2. Flexible tubing delivers insulin from the pump reservoir to the infusion set
3. A tiny tube called a cannula is inserted under your skin to deliver insulin
4. Insulin in the blood
Components of Insulin Pump Therapy

1. **Insulin Pump**
   A small durable medical device that has:
   - Buttons to program your insulin
   - LCD screen to show what you are programming
   - Battery compartment to hold 1 AAA alkaline battery
   - Reservoir compartment that holds insulin

2. **Reservoir**
   A plastic cartridge that holds the insulin that is locked into the insulin pump. It comes with a transfer guard (blue piece at the top that is removed before inserting the reservoir into the pump) that assists with pulling the insulin from a vial into the reservoir. A reservoir can hold up to 300 units of insulin and is changed every two to three days.

3. **Infusion Set**
   An infusion set includes a thin tube that goes from the reservoir to the infusion site on your body. The cannula is inserted with a small needle that is removed after it is in place. It goes into sites (areas) on your body similar to where you give insulin injections. The infusion set is changed every two to three days.

4. **Infusion Set Insertion Device**
   An infusion set is placed into the insertion device and with a push of a button the infusion set is inserted quickly and easily.
On FDA website, use the identified product code to obtain information.

Product Code: LZG
Intended Use: Sec. 880.5725 Infusion pump

a. Identification: An infusion pump is a device used in a health care facility to pump fluids into a patient in a controlled manner. The device may use a piston pump, a roller pump, or a peristaltic pump and may be powered electrically or mechanically. The device may also operate using a constant force to propel the fluid through a narrow tube which determines the flow rate. The device may include means to detect a fault condition, such as air in, or blockage of, the infusion line, and to activate an alarm.

b. Classification: Class II (performance standards)
510K is likely, we need to prepare the general controls documents

General Controls include
Establishment Registration,
Medical Device Listing,
Manufacturing of Medical Devices in accordance with Current Good Manufacturing Practices (CGMP 21 CFR Part 820), and
Labeling Medical Devices in accordance with labeling regulations in 21 FR art 801 or 809.

Special Controls include special labeling requirements, mandatory performance standards, and post-market surveillance, e.g., biocompatibility, ensuring compatibility with the tubing and the insulin infusion, human factors testing.
Premarket notification or 510(k) requires the demonstration of substantial equivalence of a medical device to a predicate(s); therefore, consider assessing the following:

a. Intended use
   i. Deviation(s) from predicate device

b. Technological characteristics affecting user requirements or device performance but not different types of safety and effectiveness questions. Provide the data to demonstrate that this device performs substantially equivalent to the predicate.
   i. Materials used (e.g., biocompatibility, local or foreign source)
   ii. Energy employed (e.g., electrical, mechanical, or chemical)
   iii. Information processed e.g., software controlled, dosage accuracy
   iv. Performance/storage environment defined

c. Usability factors affecting device performance
   i. Target population
   ii. User friendliness
   iii. Environmental specs (transport, storage)
   iv. Instructions for use
## How much does this cost?

<table>
<thead>
<tr>
<th>510k Standard fees</th>
<th>PMA Fees</th>
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<tbody>
<tr>
<td>$4,960</td>
<td>Report filing $248,000</td>
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<tr>
<td></td>
<td>Panel submission $186,000</td>
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<tr>
<td></td>
<td>Biologics Efficacy Supplement $248,000</td>
</tr>
<tr>
<td></td>
<td>180 day supplement $37,200</td>
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</tbody>
</table>
Brainstorm and put in design notebook

– What kind of device are you designing?
– Will you need a 501k or premarket approval?
– What testing data might the FDA need?