

# Fundamentals of Cardiovascular Device Regulation

## *Meeting FDA's Mission and Making the Process Work*

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# Disclosures

**I have the following financial relationships to disclose: None**

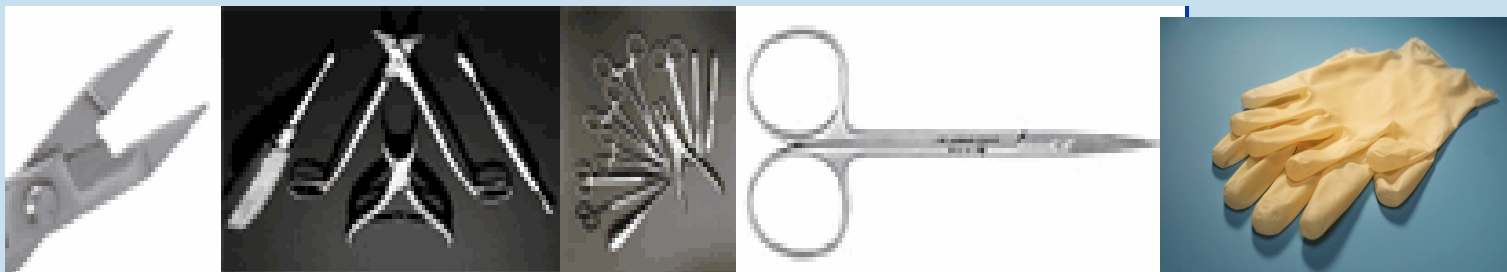
# FDA's Public Health Mission

- FDA's role: To assure that drugs and devices are **safe and effective for their intended uses** and that labeling and packaging is truthful, informative, and not deceptive
- CDRH is responsible for establishing a reasonable assurance of the safety and effectiveness of medical devices prior to marketing in the U.S.
- Regulation is a balancing act -
  - Get safe and effective devices to market as quickly as possible while ensuring that devices currently on the market remain safe and effective

# How The Process Works

## *FDA Uses a Risk-Based Paradigm*

- Class I: simple, low risk devices
  - General controls
    - E.g., registration, general record keeping, and compliance with Good Manufacturing Practice regulations (GMPs)
  - Vast majority exempt from premarket submission



# Risk-Based Paradigm

- Class II: more complex, higher risk
  - Subject to specific regulations or special controls
    - Labeling
    - Guidance
    - Device tracking
    - Design Controls
    - Postmarket Surveillance
  - *Path to marketing (clearance) is via a Premarket Notification [510(k)] submission*
    - 10-15% require clinical data



# What's a 510(k)?

- The 510(k) program is the regulatory pathway through which most medical devices go to market
- Manufacturer submits a “premarket notification” asserting the device is at least as safe and effective as one (“the predicate”) that’s already on the market
  - “Substantially equivalent”
- If FDA determines this is the case, the device can be marketed

# A 510(k) Device is *Not* Substantially Equivalent (NSE) if:

- There is no predicate device
- The device has a new intended use
- The device has different technological characteristics compared to the predicate device and raises new types of safety and effectiveness questions
- The device does not demonstrate that it is at least as safe and effective as the predicate

# A 510(k) Device is *Not* Substantially Equivalent (NSE) if:

- There is no predicate device
- The device has a new intended use
- The device has different technological characteristics compared to the predicate device and raises a novel type question of safety and effectiveness
- The device manufacturer does not demonstrate that it is at least as safe and effective as the predicate device

**For most devices for which there is no predicate, the path to marketing approval follows the PMA process**

# Risk-Based Paradigm

- Class III: Most complex, highest risk
  - Life-supporting, life-sustaining or important in preventing impairment of human health
  - Comprehensive bench, animal, and human studies required
  - Path to marketing is via a Premarket Application (PMA)
  - Post-approval study often required



# Basis for PMA Approval

Reasonable assurance that the device is safe and effective for the proposed intended use

# What is an Investigational Device Exemption (IDE)? - 21 CFR 812

- An IDE is issued by the FDA to allow the use investigational devices in human subjects in the US
- Within a clinical trial, the device is studied to collect data on safety and effectiveness to support a PMA or 510(k)
- Besides a study protocol, an IDE provides protection to human subjects (informed consent), outlines study monitoring, labeling, records/reports, & allows shipping of devices

# What is an Investigational Device Exemption (IDE)? 21 CFR 812

- An IDE *is required* when:
  - Using unapproved devices [i.e., devices with no 510(k) marketing clearance or Premarket Approval] OR
  - If seeking new indications for approved devices used in clinical trials *in the U.S.* OR
  - If performing clinical studies of off-label use of approved devices

# Working with CDRH

## *Start Early in Product Development*

- Informal: Pre-submission meetings highly recommended
  - Pre-IDE
  - Pre-PMA/Pre-510(k)
- Formal meetings
  - Determination meeting §513(a)(3)(D) – PMA/PDP
  - Agreement meeting §520(g)(7) – Class III or implant
- Similar mechanisms exist in CDER/CBER
  - Pre-IND, End-of-phase 2, pre-NDA meetings



# Informal Meetings

- Informal meetings can be requested at any time
  - In early product development
  - After bench and early animal data generated, but before clinical trial
  - Prior to starting a US or outside the US clinical trial/Between feasibility and pivotal clinical studies
  - Mid-clinical trial (if issues have arisen – to discuss changes in protocol, study design, etc.)
  - Prior to submitting the pre-marketing application (PMA) package
  - During review of marketing submission (to seek clarification of FDA questions)
- Can be by phone or face-to-face

# Planning Your Meeting With FDA

- In requesting a meeting, provide sufficient information regarding your objectives (so FDA can answer your questions)
- We read *all* of your materials
  - Clearly written & organized information submitted well in advance leads to effective meetings
- Reschedule the meeting rather than proceeding if you are not ready
  - If major design iterations are still occurring, it may be too early for a meeting
- Please share your long-range plans for product development

# Planning Your Meeting With FDA

- Do your homework
  - Be prepared with proposals for bench testing, animal studies, & clinical trials
    - FDA will not design your trial for you
  - Review publicly available information on similar products (FDA guidance documents, SSEDs for approved products, & recent Advisory Panel transcripts)

# Making the Most of FDA Meetings

- Focus your presentation on meeting objectives
  - FDA will be familiar with the clinical setting
  - Discuss unmet needs that your product hopes to address
  - A lengthy review of your corporate history is not needed
- Bring the right people
  - Have scientific experts available to answer questions & interact with FDA scientists, but don't bring the *entire* project team
  - Bring decision-makers to facilitate moving your program forward
- Have your questions ready as part of your meeting objectives

# Making the Most of FDA Meetings

- Respect FDA's feedback
  - Submissions subsequent to meetings should address feedback, i.e.,
    - “ABC company has incorporated FDA's suggestion that ...”
    - “ABC company has considered FDA's suggestion and has proposed an alternative for the following reasons ...”
  - Please ask if:
    - You don't understand our feedback
    - You want to explore an alternative approach
    - You have new/more information that might change FDA's recommendations

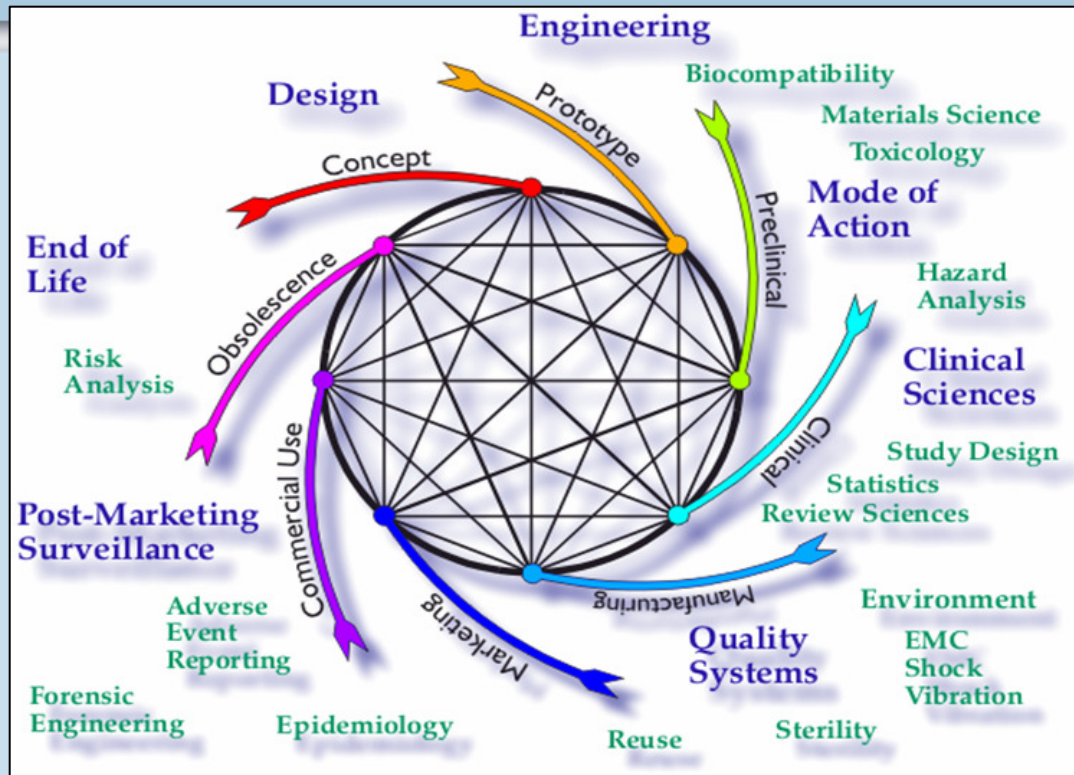
# Use of Data Collected Outside the United States (OUS)

- FDA is increasingly being asked to review global trials
- OUS studies often used to provide initial safety and effectiveness data to support initiation of a pivotal IDE study in the US
- Studies performed solely OUS may be considered for the PMA
  - Sponsor must show that the data generated about the new product are applicable to a US population

# Use of Data Collected Outside the United States (OUS)

- Be aware of potential problems and pitfalls with OUS studies
  - Protocols missing essential elements
    - Study endpoints
    - Detailed inclusion/exclusion criteria
    - Subject follow-up schedules
  - Lack of an independent clinical events committee (CEC), data safety monitoring board (DSMB), and/or core labs
  - Inadequate monitoring of source documentation and accounting of protocol deviations
  - Inadequate long-term follow-up beyond the primary endpoint

# FDA Interacts With Sponsors at All Stages of Product Development



We look forward to working with you  
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