Agenda

• IDE basics
• FIH and EFS Landscape
• EFS Process
• Tools to facilitate EFS
• EFS examples
Patients are at the Heart of What We Do

CDRH Vision: Patients in the U.S. have access to high-quality, safe, and effective medical devices of public health importance first in the world
Multiple Approaches to Supporting Device Innovation

Pre-Clinical Testing → Clinical Studies → Pre-Market Application → Post-Market

- Real World Evidence
- Breakthrough Devices Program
- Early Feasibility Studies
- Pre-/Post-Market Balance
- Patient Engagement
IDE BASICS
Investigational Device Exemption

• 21 CFR 812.1:
  “An approved *investigational device exemption (IDE)* permits a device that otherwise would be required to comply with a performance standard or to have premarket approval to be *shipped lawfully* for the purpose of *conducting investigations* of that device.”

• An IDE is a *regulatory submission* that permits clinical investigation of devices
When is an IDE needed?

- **Applicable Device Study**
  - Exempt
  - **Not Exempt**
    - **Significant Risk (SR)**
    - **Non-Significant Risk (NSR)**

- **Full requirements**
- **Abbreviated requirements**
Non-Exempt Device Studies

- **Significant Risk** – Study can not begin until IDE is approved by FDA
- **Non-Significant Risk** – no IDE submission to FDA needed
  - abbreviated requirements
    - Labeling (812.5)
    - IRB Approval (56)
    - Informed Consent (50)
    - Monitoring (812.46)
    - Records and Reports (812.140(b)(4) and (5), 812.150(b)(1) - (3) and (5) - (10))
      - Annual and Final Progress Reports are not required
    - Promotion (812.7)

- The risk determination is based on the proposed use of a device in an investigation
Non-Significant Risk Studies

• IRB serves as the FDA’s surrogate for review, approval, and continuing review of the NSR device studies

• An NSR device study may start at the institution as soon as the IRB reviews and approves the study
Significant Risk (SR) Study

- 21 CFR 812.3 (m) – A significant risk device presents a potential for serious risk to the health, safety, and welfare of a subject and is:
  - an implant; or
  - used in supporting or sustaining human life; or
  - of substantial importance in diagnosing, curing, mitigating, or treating disease or preventing impairment of human health
  - otherwise poses a risk

- Full IDE requirements apply
  - IDE application reviewed by FDA within 30 days
  - If approved, sponsor obtains IRB approval
  - After both FDA and IRB approve the investigation, study may begin
The IDE Application (812.20)

- Name and address of sponsor
- Report of prior investigations and investigational plan
- Manufacturing, processing, packing, and storage of device
- Investigator agreement (example, listing, certification)
- List of the name, address, and chairperson of each IRB
- Participating institutions
- Amount to be charged for device
- Environmental assessment
- Labeling
- Subject materials including informed consent
- Additional information requested by FDA
Submission & Review Basics

• IDE applications are submitted to CDRH Document Control Center
  – Refer to IDE Device Advice webpage

• FDA sends acknowledgement with IDE number: GYYxxxx (e.g. G180001)

• IDE sent to appropriate review division based on intended use

• Lead reviewer assembles team of experts to review the application and make decision with management concurrence within 30 days

• FDA issues a decision letter to the sponsor
EARLY FEASIBILITY STUDIES
Device Development to Clinical Studies

Feasibility
Pivotal
(FIH
EFS
(much more known about device, procedure, indication)
Early Feasibility Studies Program

• There was growing concern regarding the time lag in the availability of beneficial medical devices for US patients
  – Data requirements for initiating an IDE in the US contributed to this lag

• October 2013 → EFS Program: Voluntary, informal program that allows devices in an early stage of development to be evaluated in a small human clinical study in the US

Enhance patient access to beneficial technology
Support innovation
EFS Program Benefits

- Familiarity with the technology and regulatory considerations throughout product development
- Opportunity for smoother transitions between types of clinical studies
- New opportunity to address unmet clinical needs
- Early experience with innovative technology
- Encourages development of high quality medical products
- Early access to potentially beneficial medical devices
What is an EFS IDE?

EFS IDE - A standard IDE except...

• There may be a **greater level of uncertainty** about how the device will perform
  - Device is generally early in development or
  - Device has a new intended use

• **Small number of subjects** in the clinical investigation (<15)
  - Initial indication of safety and/or effectiveness
  - Proof of concept

• Described in FDA Guidance document: *Investigational Device Exemptions (IDEs) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies*
EFS Process

- **Contact the EFS Representatives (if needed)**
  - Prepare for working with the review team

- **Submit Initial “Pre-Submission”**
  - Educate the review team on the device and clinical context
  - Reach agreement on the information needed to support study initiation (risk analysis, non-clinical testing, clinical mitigations)
  - May be significant discussion of risks and how they will be mitigated

- **Submit additional Pre-Submissions**
  - Obtain feedback on test protocols, the clinical study plan, informed consent

- **Submit IDE**
  - Interact with the review team to address any concerns
  - May be significant discussion of risks and how they will be mitigated
Key Provisions in Guidance Document

• **Doing the “Right Testing at the Right Time”**
  - Comprehensive testing during early phases of device development may add cost without significant return
  - However, informative nonclinical testing should be completed

• **Unknowns and risk can be addressed by...**
  - Using clinical mitigations to provide patients with extra protection
  - The use of more frequent/detailed reporting

• **Allows for timely device and clinical protocol changes**
  - More changes can be made through 5-day notification rather than FDA approval

• **Provides tools for communicating available data to CDRH**
  - Device evaluation strategy (DES) and tables for leveraging data
  - Consolidates leveraged info, non-clinical testing & clinical mitigation per device attribute/ risk
How are we doing?

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<th>1st Round APPR or APCN</th>
<th>Currently Fully Approved</th>
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- **Submitted**
- **1st Round APPR or APCN**
- **Currently Fully Approved**
Why EFS Helps Start Up /Small Companies

• Nearly half of EFS IDEs submitted by small manufacturers
  ➢ Over 6,500 medical device companies in the U.S.
  ➢ 80% of them have fewer than 50 employees (MDIC)

• Regulatory and product development knowledge varies

• Enhanced opportunities for interaction often helps companies with limited regulatory and product development experience

• EFS can help address issues related to time and money (burn rate)
Examples of Early Feasibility Projects
1st EFS Device to Pivotal Trial

Bridge-Enhanced(TM) ACL Repair

- Experimental use of a bridging scaffold to repair the ACL
- Potential benefit: No need to harvest a tendon, addresses clinical need
- EFS is complete, currently in a pivotal trial

Angel® Catheter

- Retrievable, Inferior Vena Cava (IVC) filter, coupled with a triple lumen, central venous access catheter
- Benefits: Pulmonary embolism protection. Ability to remove filter.
- Small company
- EFS and pivotal studies complete. 510(k) cleared (K160747)

http://www.bio2medical.com/angel-catheter/
Morales JP & Farb A, JVIR 2017
Regulatory Approaches to Support Innovative Devices

Innovative devices are being developed for a wide variety of diseases. It all comes back to the patient.

We need to use our regulatory tools and pathways to support bringing innovative devices to market:
- Early Feasibility Studies
- Breakthrough Devices Program
- Real World Evidence
- Patient Perspectives/ Patient reported outcomes
Helpful Links

• IDEs
  https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/default.htm

• EFS Device Advice Webpage

• FDA Voice Blog on EFS

• Early Feasibility Study Guidance

• EFS CDRH Learn Modules
  http://www.accessdata.fda.gov/cdrh_docs/presentations/EFS/story.html

• Pre-Submission Guidance
EFS IDE Submissions by Division

FY17 EFS IDE Submissions - Division Breakdown

- DCD
- DNPMD
- DRGUD
- DAGRID
- DSD
- DOD
- DOED
- OIR
Exempt Studies (21 CFR 812.2(c))

No IDE Needed

- Commercial devices used in accordance with labeling
- Many diagnostic devices
- Testing of consumer preference, of a modification, or of a combination of devices
  - if not for the purpose of determining safety or effectiveness and not putting subjects at risk:
- Veterinary devices
- Research on/with laboratory animals
- Custom devices as defined in 812.3(b)