Early Feasibility Study (EFS) IDEs

A Valuable Regulatory Tool for Medical Device Development

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CDRH Led Submission

• Submission may be given the informal designation of “Early Feasibility Study” or “First in Human”
  ➢ Similar to Phase 1 designation for drug development
  ➢ Intent of this designation is to acknowledge the unique purpose of this early stage clinical study

• CDER will provide consultation for the drug component
What is an EFS IDE?

IDE - Investigational Device Exemption
• Clinical study of an investigational device

EFS IDE - A standard IDE except...
• There are significant unknowns 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
  ➢ Initial indication of safety and/or effectiveness
  ➢ Proof of concept
Why the Focus?

- Clinical studies of novel technology are frequently conducted outside the US
- Devices may be approved outside the US only
- Device innovation may improve outside the US first

Goal of EFS Program
FDA is dedicated to enhancing patient access to beneficial technology and supporting innovation in the US
EFS Program Benefits

• Encourages **development of high quality products**
  - Allows for device and procedure changes early in the product development process

• Results in **high quality clinical data** that can...
  - demonstrate proof of concept which may be valuable to investors
  - allow for faster **US market approval** by building on EFS knowledge
  - be obtained for a device that has been used in **compassionate use** or **emergency use** cases and could support expanded device indications or a market application
  - And more!!
# Types of IDEs

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<th>EFS</th>
<th>Feasibility</th>
<th>Pivotal</th>
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<tr>
<td></td>
<td>Small number of patients, &lt; 15 (approximate)</td>
<td>More patients than EFS</td>
<td>Number of patients determined by statistical needs</td>
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<td></td>
<td><strong>There are fundamental questions about device performance &amp; safety</strong></td>
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<td>➢ Device design may change.</td>
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<td>➢ There may be limited nonclinical data available</td>
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<td><strong>Purpose of study can be...</strong></td>
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<td>➢ to demonstrate a proof of concept</td>
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<td></td>
<td>➢ get a very early look at safety/efficacy</td>
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<td>➢ examine human factors</td>
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<td>➢ determine what design or procedure changes could optimize the therapy</td>
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<td>➢ Determine patient characteristics that may impact device performance</td>
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<td><strong>Purpose of study can be...</strong></td>
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<td>➢ capture preliminary safety and effectiveness information and to adequately plan an appropriate pivotal study</td>
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<td><strong>Purpose of study can be...</strong></td>
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<td>➢ Demonstrate safety and effectiveness to support a marketing application</td>
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*note: not all of these are required for market approval*
Key Elements of the EFS Guidance

• **Doing the “Right Testing at the Right Time”**
  - Comprehensive testing during early phases of device development may add cost without significant return (some testing may be deferred)
  - 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
  - Informed consent recommendations
Key Elements of the EFS Guidance continued...

• Allows for timely device and clinical protocol changes
  - More changes can be made through 5-day notification rather than FDA approval
  - Contingent approval: approval of anticipate or proposed device changes can be obtained contingent on the completion of an agreed upon test plan and acceptance criteria

• Recommendations on pre-submission contents is provided
  - High quality submissions are important
Qualities of a Successful Submission
(for infrequent submitters in particular)

1. **Sponsor uses available resources:** Use FDA guidance documents & CDRH Learn Modules, communicates with FDA staff, seeks assistance with regulatory, nonclinical testing and clinical trial issues if needed

2. **Submissions are high quality**
   - Contents are well organized and navigable
   - High quality scientific discussion and evidence is provided
   - The sponsor is able to link together the information provided and tell the story of why an EFS is the right next step. (Why additional nonclinical testing will not be informative and a human clinical study is appropriate)
Qualities of a Successful Submission
Continued...

3. Submissions are well planned

- Sponsor reaches out to EFS rep or FDA team to discuss plan (informally)
  - Informational meeting may be useful (for novel ideas in particular)
- Initial pre-sub includes...
  - Design concept, clinical context & rationale for early feasibility study
  - Description of the risks and how they will be addressed
  - Investigational plan information – high level look (who will be treated, what type of information you want to collect...)
- Additional pre-subs as needed (ex: if test requirements are uncertain/discuss clinical protocol)
- IDE submission contains all required information
Note:

- Use of pre-submissions to discuss the test plan and the clinical protocol...
  - Can be useful when the nonclinical testing needed is unclear, can agree upon the test plan that will support an IDE submission with FDA
  - May avoid the need to re-do expensive and time consuming testing
  - May help determine appropriate clinical mitigations, reporting requirements and the patient population for whom the benefit-risk profile supports inclusion into the EFS

Planning in Advance is Key
Qualities of a Successful Submission

Continued...

4. The decision to start human clinical work is well supported and explained
   - There is a clear identification of potential risks & how they will be addressed
     - Nonclinical testing: Informative testing should be completed
     - Clinical mitigations strategies and appropriate reporting are proposed to protect patients - especially when nonclinical testing is uninformative
     - Rationale is provided for why the plan is sufficient: Explain what can/can not be learned from bench tests/animal models & why any information to be leveraged is directly applicable to the study
   - List which tests will be done to support the EFS versus which will be done to support a later study if applicable
We Would Like to Hear from You About your EFS Experience (good or bad)

- Test requirements do not seem appropriate for the EFS?
- Review team doing a great job?
- File progression is good/bad?

Contact me:

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Helpful Links

• Early Feasibility Study Guidance

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

• Pre-Submission Guidance

• IDE Submission Suggestions
  http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm046706.htm#reqele

• Design Controls Guidance
  http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070627.htm

• Electronic Submissions Guidance
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