



Investigational Device Exemptions (IDEs) for Early Feasibility Medical Device Clinical Studies

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Opportunities Associated with US Early Feasibility Studies (EFS)

- Contact between inventors, developers, investigators, and regulators
 - Geographically closer
 - More collaborative
- Access to promising novel technology
 - Earlier
 - Continuous
 - Expanded

Goals

1. Providing the earliest and broadest patient access to beneficial medical devices
2. Maintaining or regaining US leadership in innovation

Prevailing Currents

- Initial clinical testing of novel devices has been moving to non-US sites
- Device innovation may follow overseas
- Devices are being developed exclusively for non-US markets

Consequences

- Palpable time lag in the availability of some beneficial medical devices for US patients
- Human costs associated with delaying access to new technology (particularly in the context of the limitations of current treatment alternatives)

Barriers to Innovating in the US

- **Insufficient predictability** of what information is needed to allow for the initiation of clinical studies
 - Data requirements can be difficult to identify
 - Increasingly complex devices
 - No established guidance or standards for innovative devices
 - No generally accepted method for justifying data requirements
- **Ineffective communication** between CDRH and industry
- **Poor-quality submissions** that do not include or coherently describe relevant information

FDA Commitment

- The FDA recognizes the value of encouraging medical device innovation to address clinical needs and improve patient care
- FDA is committed to improving U.S. patient access to new devices by strengthening and streamlining the clinical trial enterprise
- FDA has focused efforts on promoting public health

New Framework

- The core principle is the application of **benefit/risk principles** throughout regulatory decision-making
 - Keep the clinical context at the forefront
- Allows regulators to consider:
 - The totality of the benefit/risk profile for the device, for example:
 - Disease condition (e.g., life-limiting, life-threatening)
 - Limitations of and risks associated with currently available therapies
 - Patient tolerance for risk & perspective on benefits
 - Risk mitigation strategies when balancing risks and benefits



Early Feasibility Study (EFS) Guidance

- Intended to facilitate the clinical evaluation of medical devices in the US under the Investigational Device Exemptions (IDE) regulations, using risk mitigation strategies that appropriately protect study subjects
- Elements that define an early feasibility study:
 - Small number of subjects
 - Device intended for a specific indication that may be early in development, typically before the device design has been finalized
 - Does not necessarily involve the first clinical use of a device

Guidance Provisions: a Regulatory Toolkit

Enables sponsors and regulators to think in new ways about:

- Device development
- The appropriate evidence needed to move from bench to clinical study
- The implementation of timely device and clinical protocol modifications

Key Principle of the Guidance

Approval of an early feasibility study IDE may be based on less nonclinical data

- For some new devices, exhaustive nonclinical testing would not likely provide the information needed to further device development
- In these cases, early clinical use of the device in a limited number of subjects is needed to:
 - provide initial insights into clinical safety and device function;
 - inform subsequent clinical and non-clinical testing; and/or
 - improve device performance through iteration before finalizing the design



Just-In-Time (JIT) Testing:

A guiding principle of the EFS Guidance

- Applies to the type and timing of nonclinical testing needed to justify study initiation
 - Departs from the custom of expecting exhaustive nonclinical testing prior to *any* clinical use
 - Recognizes that comprehensive testing during early phases of device development may add cost without return
 - Testing could have limited future applicability if the device is modified
 - Time-consuming, non-informative testing delays access to the device for patients who may have limited treatment alternatives
- Includes acknowledgement that it may be acceptable to defer some testing until the device design has been finalized for use in a pivotal study

Other Reasons Why JIT is Legit

- An early feasibility study incorporates enhanced risk mitigation strategies and patient protection measures as compared to a pivotal study
- Highly selected patients will be enrolled and will receive individualized care and monitoring
- The guidance *does not* recommend that sponsors prematurely initiate clinical testing when further useful and appropriate nonclinical testing can be performed to advance the device's development

An EFS must be supported by an appropriate benefit/risk analysis, including justification for the types and amount of data needed to support study initiation.

JIT in Practice: *Device Evaluation Strategy (DES)*

A “Device Evaluation Strategy” within the Report of Prior Investigations is needed to describe and justify the appropriate testing to support initiation of the clinical study

- Provide the “thinking” behind the device development program
- Justify what is sufficient, rather than testing for the sake of testing

Device Evaluation Strategy Focus

- Support basic device functionality
 - An expectation of acceptable clinical use and that the device will function as intended
- Address significant safety concerns
 - Address basic device safety, including, but not limited to, sterility, biocompatibility, electromagnetic compatibility, chemical compatibility (e.g., with concomitant drugs, chemicals, cleaners)
 - Characterize catastrophic failure modes and identify associated risk mitigation approaches

Device Evaluation Strategy Methodology

The design concept, including the clinical context for the device design, provides the foundation for the device evaluation strategy which involves identifying:

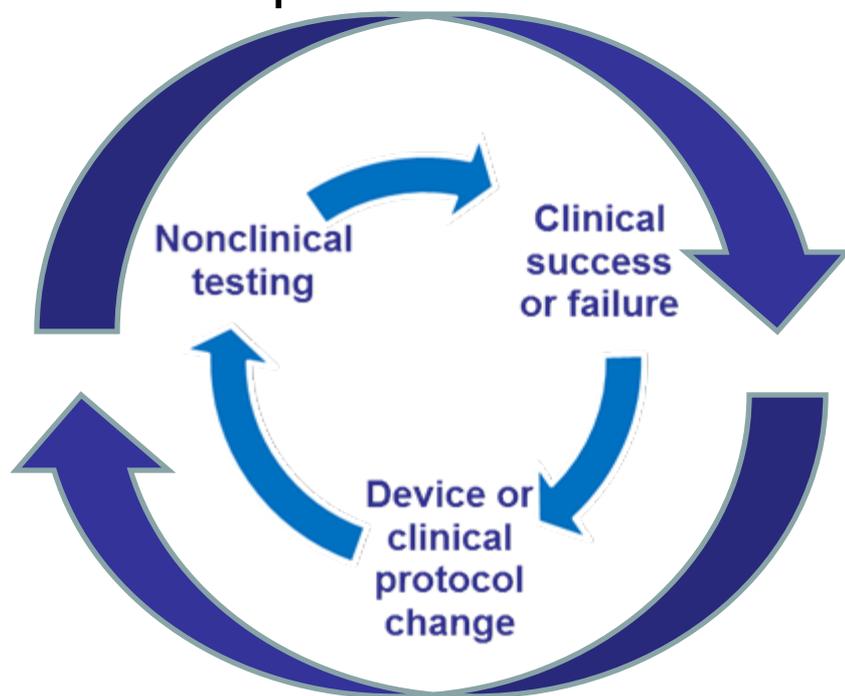
- Device and procedure-related attributes necessary to obtain the desired performance,
- Failure modes that might occur if each attribute is not achieved,
- How the failures could affect the device or patient, and
- What information is needed or available to evaluate the attribute or failure mode.



After Study Initiation:

Iterative Device Development Process

- Experience and knowledge gained from initial study subjects can guide device or protocol changes
- Rounds of regulatory submissions and review can delay the implementation of changes and impede study progress



- The EFS Guidance includes new approaches to facilitate timely device and clinical protocol modifications during an early feasibility study

New Approaches

1. More changes can be made through 5-day notification rather than requiring FDA approval

- Many changes will not affect the interpretation of the results as results do not depend on statistical analyses or pooling data among study subjects

2. Contingent approval

- Approval of anticipated or proposed device changes can be obtained contingent on the completion of an agreed-upon test plan and reporting of test data
- After successful completion of testing, the sponsor can begin to study the modified device without additional FDA action

3. Interactive review

- Encourages communication between FDA and the sponsor within the 30-day review cycle to address deficiencies

Next Steps

Subsequent clinical evaluation depends on the stability of the device design, the availability of data to justify the next study, and the purpose of the clinical study

- Expansion of the early feasibility study
 - e.g., further device iterations are expected
- Either a traditional feasibility or a pivotal study
 - Device design is near-final or final,
 - Early feasibility study results support the initial safety of the device and proof of principle, and
 - Adequate non-clinical data are available

Update: EFS Guidance Revisions

Based on Pilot Experience and Comments

- Emphasized **benefit/risk** concepts throughout the document
- Improved the **Report of Prior Investigations** section to clarify the information that will be useful to justify study initiation
- Added a **Design Controls** section
- Included more guidance on drafting the **informed consent form** for an EFS
- Suggested **pre-submission topics** for discussion between the sponsor and FDA

Current Efforts and Remaining Uncertainties

- Intra- and extramural training programs are being developed
- Many sponsors have committed to ‘test the waters,’ conducting EFS studies in the US
- Outstanding questions:
 - Will other sponsors take the plunge?
 - Is there sufficient value-added in doing US EFS?
 - Are the non-regulatory, clinical trial challenges surmountable?

Additional Information

- Early Feasibility Study Guidance available at:
<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM279103.pdf2>
- EFS questions?
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