

Early Feasibility Medical Device Clinical Studies

US FDA recently issued important draft guidance that describes new approval policies for early feasibility medical device clinical studies of significant risk devices. This article discusses the draft guidance and pilot programme that US FDA has initiated for testing the new policies.

US FDA recently issued several important draft guidance documents regarding the conduct of medical device clinical studies in the United States. On 15 August 2011, the agency issued a draft guidance document on design considerations for pivotal clinical studies for medical devices,¹ which describes various study design principles relevant to the development of medical device clinical studies that can be used to fulfil premarket clinical data requirements. On 10 November 2011, US FDA issued draft guidance that describes proposed methods for allowing a clinical study to begin under certain circumstances, even when there are outstanding issues regarding study approval application.² On the same date, US FDA also issued draft guidance on the development and review of Investigational Device Exemption (IDE) applications for early feasibility studies of significant risk devices.³ US FDA approval of an IDE application is required before a sponsor is allowed to conduct a clinical study with a significant risk device. The regulations governing this process are contained in 21 CFR Part 812, Investigational Device Exemptions.

This article discusses draft guidance on early feasibility studies. The guidance should be of interest to companies developing innovative medical devices that are considered a significant risk by US FDA, where device development would benefit from early clinical studies in the United States that would provide proof of principle and initial clinical safety data. Thus, companies developing such devices should carefully review the draft guidance document to determine whether the proposed policies will meet their needs or whether they can suggest modifications for improvement. Comments should be submitted to US FDA by 8 February 2012 to be considered during development of the final



version of the guidance document. The process of submitting comments is described on the US FDA website (www.fda.gov) and also in the *Federal Register* notice announcing the availability of the guidance document.⁴ The early feasibility study pilot programme is discussed later.

Early feasibility study draft guidance

Early feasibility study draft guidance is a 28-page document intended to facilitate the early clinical evaluation of medical devices in the United States under the IDE regulations, using risk mitigation strategies that appropriately protect human subjects in early feasibility studies. It contains detailed advice regarding the manner in which companies should seek approval of an IDE for an early feasibility study. The guidance has the following major sections:

1. Introduction
2. Overview
3. Regulatory Background
4. Targeting Approval for an Early Feasibility Study IDE Application
5. Report of Prior Investigations
6. Investigational Plan
7. Iterations During Early Feasibility Studies
8. Next Steps in Clinical Evaluation
9. Conclusion



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Appendix 1: Device Evaluation Strategy Example

Appendix 2: Device Iteration Example

Sections 1 and 2 (Introduction and Overview) define and discuss the scope of the guidance and what US FDA considers to be early feasibility clinical studies. Section 3 (Regulatory Background) discusses the relevant sections of the US Food, Drug and Cosmetic Act and IDE regulations. Section 4 (Targeting Approval for an Early Feasibility Study IDE Application) describes the overall process of ensuring that the information in the IDE application is appropriate for early feasibility studies. It also describes the proposed new policy of basing approval of an IDE application for an early feasibility study on less nonclinical data than would be expected for a traditional feasibility study. Section 5 (Report of Prior Investigations) provides very detailed guidance on the type of information that should be provided in an IDE application for early feasibility clinical studies. Section 6 (Investigational Plan) emphasises the need for a thorough risk analysis and risk mitigation strategies. Section 7 (Iterations during Early Feasibility Studies) describes the new policies intended to directly facilitate the timely implementation of changes to the investigational device or clinical protocol. Section 8 (Next Steps in Clinical Evaluation) describes actions that sponsors can take after obtaining clinical information from early feasibility studies depending upon the sta-

bility of the device design, availability of adequate data to justify the next study, and purpose of that clinical study. Section 9 (Conclusion) emphasises the importance of a high degree of interaction between US FDA and the sponsor and use of the pre-IDE process in ensuring successful implementation of the guidance.

Appendix 1 provides an example of a device evaluation strategy, discussed in subsection 5.2.2, which could be submitted as a pre-IDE to obtain US FDA feedback on the overall device development plan by identifying the types of information or levels of testing that may be needed to move beyond the early feasibility study. Appendix 2 includes examples of the types of changes that may be appropriate for five-day notification during an early feasibility study as discussed in subsection 7.1, Changes requiring FDA notification (five-day notice), and contingent approval as described in subsection 7.2, Changes requiring FDA approval.

Draft guidance definition of early feasibility studies

The new policies described in the draft guidance apply to early feasibility studies only. Companies evaluating the potential usefulness of the policies for their own device studies should ensure that US FDA agrees that the studies are early feasibility studies.

The Introduction to the draft guidance document defines various types of clinical studies based on US FDA's current thinking.



- **Early feasibility study:** Limited clinical investigation of a device early in development, typically before the device design has been finalised, for a specific indication (an innovative device for a new or established intended use or a marketed device for a novel clinical application, for example). It may be used to evaluate the device design concept with respect to basic safety and device functionality in a small number of subjects (generally fewer than 10 initial subjects), when this information cannot be readily provided through additional nonclinical assessments or appropriate nonclinical tests are unavailable. Information obtained from an early feasibility study may guide device modifications. An early feasibility study does not necessarily involve the first clinical use of a device.
- **First in human (FIH) study:** Type of study in which a device for a specific indication is evaluated for the first time in human subjects. This document only discusses FIH studies that meet the definition of an early feasibility study.
- **Traditional feasibility study:** Clinical investigation that is commonly used to capture preliminary safety and effectiveness information on a near-final or final device design to adequately plan an appropriate pivotal study. As compared to an early feasibility study, more nonclinical (or prior clinical) data are necessary for approval to initiate a traditional feasibility study;

however, a traditional feasibility study does not necessarily need to be preceded by an early feasibility study.

- **Pivotal study:** Clinical investigation designed to collect definitive evidence of the safety and effectiveness of a device for a specified intended use, typically in a statistically justified number of subjects. It may or may not be preceded by an early and/or traditional feasibility study.

The draft guidance points out that these studies are **not intended to generate definitive data** to independently support a marketing application in place of a pivotal clinical study.

The Introduction also provides additional useful information concerning not only what early feasibility studies are, but also what they are not. For example, the draft guidance points out that these studies are not intended to generate definitive data to independently support a marketing application in place of a pivotal clinical study.

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This is an important point because some companies believe the marketing clearance or approval can be obtained from data generated from early feasibility studies.

This section of the draft guidance also states that early feasibility studies have a broader purpose than traditional feasibility studies, which are intended to provide initial safety and effectiveness information for a near final or final device design or generate data to guide the development of a pivotal clinical study. By contrast, the draft guidance states that the clinical experience obtained from an early feasibility study increases the efficiency of the device development process, as this experience may be used to:

- identify appropriate modifications to the procedure or device
- optimise operator technique
- refine the intended-use population
- refine nonclinical test plans or methodologies and
- develop subsequent clinical study protocols.

Additional guidance is also provided on how to determine whether a clinical study falls into the early feasibility, traditional feasibility or pivotal category. To avoid preventable delays, the guidance also advises contacting US FDA before an IDE submission to determine whether the proposed investigation can be classified as an early feasibility study.

Early feasibility study IDE pilot programme

In a 10 November 2011 *Federal Register* (FR) Notice,⁵ US FDA announced that it was requesting nominations of sponsors of innovative device technologies to participate in a pilot programme for early feasibility study IDE applications conforming to the policies outlined in the newly issued draft guidance on early feasibility study IDEs. The FR notice states that US FDA began accepting nominations for participation in the pilot programme on 12 December 2011.

The agency believes that the benefits of participating in the pilot programme include facilitating development of innovative prod-

ucts in the United States and evaluating the new approaches for modifications made during early feasibility studies, as specified in the early feasibility study draft guidance. Information gained during the pilot programme will be considered during development of the final guidance document.

Because of US FDA resource constraints, the programme will be limited to nine sponsors. Companies interested in participating in the programme should inquire without delay following the procedures specified in the FR notice.

References

1. Draft Guidance for Industry, Clinical Investigators, and Food and Drug Administration Staff - Design Considerations for Pivotal Clinical Investigations for Medical Devices (15 August 2011); www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm265553.htm.
2. Draft Guidance for Industry, Clinical Investigators, Institutional Review Boards, and Food and Drug Administration Staff - FDA Decisions for Investigational Device Exemption (IDE) Clinical Investigations (10 November 2011); www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm277669.htm.
3. Draft Guidance for Industry and Food and Drug Administration Staff - Investigational Device Exemptions (IDE) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies (10 November 2011); www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm277670.htm.
4. US *Federal Register* Notice: Draft Guidance for Industry and Food and Drug Administration Staff; Investigational Device Exemptions for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human Studies; Availability (10 November 2011); FR Doc. 2011-29117; Vol. 76, No. 218, pages 70150-70151; www.gpo.gov/fdsys/pkg/FR-2011-11-10/pdf/2011-29117.pdf.
5. US *Federal Register* Notice: Pilot Program for Early Feasibility Study Investigational Device Exemption Applications (10 November 2011); www.gpo.gov/fdsys/pkg/FR-2011-11-10/pdf/2011-29116.pdf.

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1-20W	GTMD1000	100-240VAC 50/60Hz	5VDC	1	1
1-50W	GTMD1000	100-240VAC 50/60Hz	5VDC	1	1
50-60W	GTMD00143 (3016)	100-240VAC 50/60Hz	12-30VDC	1	1
0-65W	GTMD1000	100-240VAC 50/60Hz	5VDC	1	1
100W	GTMD1000	100-240VAC 50/60Hz	5VDC	1	1
180W	GT-1800P12Y (W222E)	100-240VAC 50/60Hz	12VDC	1	1
300W	GTP-300-XA	100-240VAC 50/60Hz	12-48VDC	1	1
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