4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2011-D-0790]

Food and Drug Administration Decisions for Investigational Device Exemption Clinical Investigations: Guidance for Sponsors, Clinical Investigators, Institutional Review Boards, and Food and Drug Administration Staff; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of the guidance entitled "FDA Decisions for Investigational Device Exemption (IDE) Clinical Investigations." This guidance document was developed to promote the initiation of clinical investigations to evaluate medical devices under FDA's IDE regulations. The guidance is intended to provide clarification regarding the regulatory implications of the decisions that FDA may render based on review of an IDE and to provide a general explanation of the reasons for those decisions.

DATES: Submit either electronic or written comments on this guidance at any time. General comments on Agency guidance documents are welcome at any time.

ADDRESSES: An electronic copy of the guidance document is available for download from the Internet. See the SUPPLEMENTARY INFORMATION section for information on electronic access to the guidance. Submit written requests for a single hard copy of the guidance document entitled "FDA Decisions for Investigational Device Exemption Clinical Investigations" to the Office of the Center Director, Guidance and Policy

Development, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, rm. 5431, Silver Spring, MD 20993-0002; or the Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, rm. 3128, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your request.

Submit electronic comments on the guidance to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Identify comments with the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Owen Faris, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, rm. 1522, Silver Spring, MD 20993-0002, 301-796-6210; or Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, rm. 7301, Silver Spring, MD 20993, 240-402-7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA seeks to encourage medical device research and innovation to address important clinical needs and improve patient care. In many cases, device development and evaluation include clinical investigation. This guidance document has been developed to facilitate the initiation of clinical investigations to evaluate medical devices under FDA's IDE regulations, part 812 (21 CFR part 812).

FDA approval of an IDE submission allows the initiation of subject enrollment in a significant risk clinical investigation of a medical device. This guidance is intended to provide clarification regarding the regulatory implications of the decisions that FDA may render based on review of an IDE and to provide a general explanation of the reasons for those decisions.

In an effort to promote timely initiation of subject enrollment in clinical investigations in a manner that protects study subjects, FDA has developed methods to allow a clinical investigation of a device to begin under certain circumstances, even when outstanding issues regarding the IDE submission remain. These mechanisms, including Approval with Conditions, Staged Approval, and communication of outstanding issues related to the IDE through Study Design Considerations and Future Considerations, are described in this guidance.

FDA's decision-making process for IDEs was modified with passage of the Food and Drug Administration Safety and Innovation Act (FDASIA) (Public Law No. 112-144). Section 601 of FDASIA amended section 520(g) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 360j(g)) to specify certain situations in which FDA cannot disapprove an IDE. Section 520(g)(4)(C) of the FD&C Act states that, consistent with section 520(g)(1), FDA shall not disapprove an IDE because: (1) The investigation may not support a substantial equivalence or de novo classification determination or approval of the device; (2) the investigation may not meet a requirement, including a data requirement, relating to the approval or clearance of a device; or (3) an additional or different investigation may be necessary to support clearance or approval of the device. However, the Agency recognizes that some IDE

sponsors may wish to ensure that a pivotal study's design may support a marketing application if it is successfully executed, meets its stated endpoints, and does not raise unforeseen safety concerns. FDA is interested in working interactively with sponsors to assist in addressing important limitations with such a study that might impair its ability to support a future marketing application.

In the draft guidance, issued on June 14, 2013 (78 FR 35937), FDA specifically sought public comment on three questions. Based on its consideration of that feedback, the Agency has revised the guidance as discussed further in this document.

A. Inclusion of Study Design Considerations in FDA's Decision Letters

If FDA believes that modifications to the study design unrelated to the safety, rights, or welfare of study subject are needed to enable a sponsor to rely on the study as primary clinical support for a future marketing approval or clearance, those modifications will be noted as "study design considerations" (SDCs). Sponsors are not required to modify the investigational plan to address SDCs. However, if these considerations are not addressed, the study design may not support the study goals (e.g., a future marketing application). The draft guidance proposed that SDCs be included in a section of the IDE decision letter.

FDA received comments from several stakeholders proposing that FDA provide SDCs and its assessment of the study design in a communication separate from the decision letter. Other stakeholders expressed support for inclusion of SDCs in the letter. Still others focused on ensuring that the decision letter clearly conveys whether FDA believes the study design is adequate to support its goals, even if the actual SDCs are conveyed separately from the letter.

Based on the comments received, FDA believes that sponsors and other stakeholders may misinterpret SDCs included in the body of a decision letter as issues that are required to be addressed. Therefore, FDA intends to convey SDCs in a separate attachment included with the decision letter, rather than in the body of the letter. The decision letter itself will state whether FDA believes that the study design is adequate to support the study goals or whether FDA recommends study design considerations to enable it to do so. If FDA recommends SDCs, FDA's letter will note the following: "These recommendations do not relate to the safety, rights or welfare of study subjects, and they do not need to be addressed in order for you to conduct your study." FDA will continue to engage with stakeholders on this issue and may make modifications to this approach in the future.

B. Inclusion of Future Considerations in FDA's Decision Letters

Future considerations are issues and recommendations that FDA believes the sponsor should consider in preparing for a marketing application or a future clinical investigation. Future considerations are intended to provide helpful, non-binding advice to sponsors regarding important elements of the future application that the IDE may not specifically address. FDA sought comment on whether future considerations should be communicated in its IDE decision letters or whether they should be sent to the sponsor in a separate communication. FDA received comments proposing that the Agency provide future considerations as a separate communication and not in the decision letter. Based on the comments received, FDA intends to convey future considerations in a separate attachment included with the decision letter rather than in the body of the letter.

C. Utility of the Proposed Pre-Decisional IDE Process

The draft guidance proposed a new mechanism for review and interaction for pivotal IDEs called the Pre-Decisional IDE. The process included a comprehensive FDA review of a draft IDE prior to formal IDE submission, followed by written feedback from FDA and an interactive discussion between FDA and the sponsor. The goal of the Pre-Decisional IDE was to facilitate the development of an improved IDE submission more likely to be approved as well as a study design adequate to support a future marketing application.

FDA specifically sought comment on the expected utility of the Pre-Decisional IDE process. Some commenters expressed support for the proposal and felt that it might shorten the time to full approval of pivotal IDE studies. Other commenters expressed concern that the Pre-Decisional IDE process itself might be too time-consuming or require extensive FDA resources that could be better allocated elsewhere. Based on the comments received and FDA's consideration of the points raised, FDA will not pursue the Pre-Decisional IDE at the present time.

II. Significance of Guidance

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the Agency's current thinking on decisions for IDE clinical investigations. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute and regulations.

III. Electronic Access

Persons interested in obtaining a copy of the guidance may do so by downloading an electronic copy from the Internet. A search capability for all Center for Devices and Radiological Health guidance documents is available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm. Guidance documents are also available at http://www.regulations.gov. or http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm. Persons unable to download an electronic copy of "Decisions for Investigational Device Exemption Clinical Investigations," may send an email request to CDRH-Guidance@fda.hhs.gov to receive an electronic copy of the document. Please use the document number 1783 to identify the guidance you are requesting.

IV. Paperwork Reduction Act of 1995

This guidance refers to previously approved collections of information found in FDA regulations. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in part 812 have been approved under OMB control number 0910-0078.

V. Comments

Interested persons may submit either electronic comments regarding this document to http://www.regulations.gov or written comments to the Division of Dockets Management (see ADDRESSES). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management

between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at http://www.regulations.gov.

Dated: August 13, 2014.

Leslie Kux,

Assistant Commissioner for Policy.

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