4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2012-D-0530]

Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff; Guidance for Industry 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 "Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with FDA Staff." The purpose of this guidance is to provide an overview of the mechanisms available to application sponsors through which to obtain FDA feedback regarding potential or planned medical device submissions reviewed in the Center for Devices and Radiological Health (CDRH) and the Center for Biologics Evaluation and Research (CBER), including the Pre-Submission program (formerly the pre-Investigational Device Exemption (pre-IDE) program). In addition, the guidance provides recommendations regarding information that should be included in a Pre-Submission Package. This guidance also describes the procedures that CDRH and CBER intend to follow when manufacturers, their representatives, or application sponsors request a meeting with review staff.

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: Submit written requests for single copies of the guidance document entitled "Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with FDA Staff" to the Division of Small Manufacturers, International and Consumer Assistance, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, rm. 4613, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your request, or fax your request to 301-847-8149. See the SUPPLEMENTARY INFORMATION section for information on electronic access to the guidance.

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: Program Operations Staff (IDE), Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993-0002, 301-796-5640; or Elizabeth Hillebrenner, Office of In Vitro Diagnostics and Radiological Health, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, rm. 5616, Silver Spring, MD 20993-0002, 301-796-6346; or Stephen Ripley, Center for Biologics Evaluation and Research (HFM-17), Food and Drug Administration, 1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448, 301-827-6210.

SUPPLEMENTARY INFORMATION:

I. Background

Since its establishment in 1995, the pre-IDE program has been a successful resource for both medical device applicants and the FDA. Originally, this program was designed to provide applicants a mechanism to obtain FDA feedback on future IDE applications prior to their submission. Over time, the pre-IDE program evolved to include feedback on other device submission program areas, such as Premarket Approval (PMA) applications, Humanitarian Device Exemption applications, Evaluation of Automatic Class III Designations (de novo petitions), Premarket Notification (510(k)) Submissions, and Clinical Laboratory Improvement Amendments Waiver by Application, as well as to address questions related to whether a clinical study requires submission of an IDE.

The purpose of this guidance is to update the pre-IDE program to reflect this broader scope and make important modifications to reflect changes in the premarket program areas as a result of the Food and Drug Administration Amendments Act of 2007 (Pub. L. 110-85). This guidance also further expands the scope of the program to include those devices regulated by CBER, including those that are regulated as biologics under the Public Health Service Act and require submission of an Investigational New Drug Application (IND) and/or a Biologics License Application. Accordingly, FDA is changing the name for this program from the pre-IDE program to the Pre-Submission (Pre-Sub) program.

Though successful, the Pre-Sub program has faced challenges, and the guidance is intended to address them and improve the Pre-Sub program by: (1) Describing the types of information that FDA would recommend submitting in order to get the best possible feedback from FDA; (2) outlining the process by which FDA meetings should be scheduled; and

(3) explaining the Agency's expectations regarding advice given during the Pre-Sub process. This guidance outlines clear recommendations for sponsors and FDA staff.

In addition to the Pre-Sub program, the guidance addresses other types of FDA feedback already available to applicants through other mechanisms. The Food and Drug Administration Modernization Act of 1997 (FDAMA) (Pub. L. 105-115) established two types of formal early collaboration meetings ("determination meetings" as described in section 513(a)(3)(D) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and "agreement meetings" as described in section 520(g)(7) of the FD&C Act) to provide clear direction for testing and development of devices requiring clinical investigations to support marketing. FDAMA also requires that FDA, upon written request, must meet with a PMA applicant no later than 100 days after the receipt of a PMA application that has been filed to discuss the review status of the application (referred to as a "day-100 meeting" and described in section 515(d)(3) of the FD&C Act). For other premarket submissions under review, FDA will also grant meetings on an informal basis to discuss our requests for additional information to better ensure that the formal response to FDA's request will fully address the outstanding questions (these meetings are referred to as "submission issue meetings"). FDA will respond to requests for a determination (called "study risk determinations") whether a proposed device study is exempt from or subject to the IDE regulation (21 CFR part 812). For device studies that are subject to the IDE regulations, FDA will also provide its determination whether the study is a significant risk or nonsignificant risk study in response to a voluntary request for this information. In some cases, sponsors may wish to inform or educate FDA about ongoing device development or planned submissions without a specific request for feedback. FDA will, as resources allow, grant requests for such "informational meetings."

As part of the Medical Device User Fee Amendments of 2012 (MDUFA III), FDA committed to instituting a structured process for managing Pre-Subs. This final guidance establishes such a structured process for submission and management of Pre-Subs as well as other types of requests for feedback. In addition, the guidance describes how FDA will internally track these requests as "Q-Submissions," or "Q-Subs," including what types of submissions will be handled as supplements and amendments to an initial Q-Sub. FDA has also revised the optional CDRH Cover Sheet (Form FDA 3514) to include submission types that more closely track with the types of feedback requests discussed in the guidance.

FDA intends to provide the best possible advice in accordance with the information provided by the sponsor, to ensure it is captured accurately in the meeting minutes drafted by the sponsor, and commit to that advice unless the circumstances sufficiently change such that our advice is no longer applicable, such as when a sponsor changes the intended use of their device after we provide feedback. It is also our intention to hold timely meetings with appropriate staff and managers present, as resources permit. However, both our ability to provide advice and to hold timely meetings are dependent on our receiving the necessary information from the sponsor in advance of the meeting.

Finally, the guidance describes the procedures that CDRH and CBER intend to follow when manufacturers, their representatives, or application sponsors request a meeting with review staff as the preferred method of feedback in response to a Pre-Sub, as an early collaboration meeting, or to discuss an existing regulatory submission. This guidance also recommends how to prepare for meetings with FDA staff.

In the Federal Register of July 13, 2012 (77 FR 41413), FDA announced the availability of the draft guidance document. Interested persons were invited to comment by October 11,

2012. Seventeen sets of comments were received with multiple recommendations pertaining to the administrative processes and policies regarding the Pre-Sub program and meetings with FDA staff. The guidance was revised to provide a broader overview of available mechanisms for FDA feedback prior to a planned submission, with references to other existing guidance documents for those mechanisms where available. The guidance was also reorganized to discuss the various feedback mechanisms first, with a second section including specifics about meeting procedures that apply to all types of FDA feedback mechanisms where a meeting or teleconference is requested. Finally, an acceptance checklist for these submissions has been added as an appendix to clearly outline how FDA intends to determine if a Q-Sub meets the definition of the identified Q-Sub type, and to determine if a qualifying request is administratively complete. It is not necessary for each element in the checklist to be present for the submission to be accepted. Instead, the acceptance checklist is intended to ensure only that the submission includes sufficient information for FDA to provide the requested feedback and/or identify the appropriate FDA attendees so that the meeting or teleconference can be scheduled.

FDA received comments regarding the proposed timeframes for feedback to be provided to the applicant. Specifically, the guidance outlines a proposed target of 75 days, but generally no longer than 90 days, for feedback in response to a Pre-Sub. Comments requested that FDA modify the guidance to include a timeframe of 60 days for response to a Pre-Sub. As part of the MDUFA III Commitment Letter (Ref. 1), FDA agreed to improve the Pre-Sub process "as resources permit," but, because there were no additional resources provided for this program as part of the overall MDUFA III program, the recommended timeframe for FDA feedback in a Pre-Sub represents the time in which FDA believes that feedback generally can be provided without the application of additional resources to this specific program.

Some comments expressed concern regarding FDA's recommendation that if more than 1 year has passed since our last feedback on key clinical trial design elements without a submission to the Agency, the sponsor should contact the review branch to confirm that the previous advice is still valid. The guidance has clarified that the reason for this recommendation is because clinical practice (including available alternative therapies or diagnostics) is rapidly evolving. The guidance has been further modified to clarify that a new Pre-Sub to the Agency is no longer recommended. Instead, confirmation that prior feedback is still valid can be accomplished through a phone call to the lead reviewer or branch chief.

In response to other minor substantive and editorial comments, FDA revised the guidance document to clarify the processes and policies as appropriate.

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 requests for FDA feedback, including the Pre-Sub program, and meetings with FDA staff. 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 using the Internet. A search capability for all CDRH guidance documents is available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm. Guidance documents are also available at http://www.regulations.gov. To receive "Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and

Meetings with FDA Staff," you may either send an email request to dsmica@fda.hhs.gov to receive an electronic copy of the document or send a fax request to 301-847-8149 to receive a hard copy. Please use the document number 1677 to identify the guidance you are requesting.

IV. Paperwork Reduction Act of 1995

This guidance also refers to previously approved information collections 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 21 CFR part 803 are approved under OMB control number 0910-0437; the collections of information in 21 CFR part 807, subpart E are approved under OMB control number 0910-0120; the collections of information in 21 CFR part 812 are approved under OMB control number 0910-0078; the collections of information in 21 CFR part 814 are approved under OMB control number 0910-0231; and the collections of information for Request for Feedback on Medical Device Submissions are approved under OMB control number 0910-0756.

V. Comments

Interested persons may submit either electronic comments to http://www.regulations.gov or written comments regarding this document 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.

VI. Reference

The following reference is available electronically at http://www.regulations.gov. (FDA has verified the Web site address in this reference section, but we are not responsible for any subsequent changes to the Web site after this document publishes in the Federal Register.)

1. MDUFA III Commitment Letter, April 18, 2012, available at http://www.fda.gov/downloads/MedicalDevices/NewsEvents/WorkshopsConferences/UCM295454.pdf.

Dated: February 12, 2014.

Leslie Kux,

Assistant Commissioner for Policy.

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