Patient Engagement in the Design and Conduct of Medical Device Clinical Investigations

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Draft Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders

DRAFT GUIDANCE

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Preface

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.

I. Introduction

The U.S. Food and Drug Administration (FDA or the Agency) values the experience and perspectives of patients and their family caregivers. FDA believes that these individuals can and should be able to provide their insights about a disease or condition, including living with that disease/condition, and the impact of medical devices in the diagnosis, treatment, and management of the disease/condition, through engagement activities. Such activities can assist the Agency in understanding the patient experience, as well as sponsors as they design and conduct medical device clinical investigations.[1]

This draft guidance is intended to:

(1) help sponsors understand how they can use patient engagement to elicit experience, perspectives, and other relevant information from patient advisors (see definition in Section IV) to improve the design and conduct of medical device clinical investigations;
(2) highlight the benefits of engaging with patient advisors early in the medical device development process;
(3) illustrate which patient engagement activities are generally not considered by FDA to constitute research or an activity subject to FDA's regulations, including regulations regarding institutional review boards (IRBs); and

[1] "Clinical investigation" is defined in 21 CFR 50.3(c) and 56.102(c).

(4) address common questions and misconceptions about collecting and submitting to FDA patient engagement information regarding the design and conduct of a medical device clinical investigation.

FDA's guidance documents, including this draft guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidance means that something is suggested or recommended, but not required.

II. Background

On October 11-12, 2017, FDA's Patient Engagement Advisory Committee (PEAC)[2] met to discuss and make recommendations to FDA regarding patient engagement in medical device clinical investigations.[3] Discussion topics included patient advisor involvement in design of clinical investigations; recruitment, enrollment, and retention of study/research participants in clinical investigations; and opportunities and barriers patient advisors face when collaborating with industry in the clinical investigation process. In a consensus recommendation, the PEAC stated that some type of framework should be developed by FDA and industry to clarify how patient advisors can engage in the clinical investigation process. Based on this recommendation, FDA is pursuing various efforts to encourage patient engagement in clinical investigations, including issuing this draft guidance document.

Before issuing this draft guidance, FDA released a discussion document to facilitate further public discussion on patient engagement in medical device clinical trials.[4] The discussion document described FDA's initial thoughts about patient engagement and its potential impact on medical device clinical investigations. The discussion document included targeted questions on which the Agency sought public feedback through an open public docket.[5] The Agency also sought public feedback on these questions during the second PEAC meeting, on November 15, 2018.[6] FDA considered comments from the discussion held during both PEAC meetings and the public docket in developing this draft guidance.

Successful adoption of legally marketed medical devices increasingly depends on patient acceptance of that technology, patients being more engaged in the healthcare process, along with

[2] See 2017 Meeting Materials of the Patient Engagement Advisory Committee, available at: https://www.fda.gov/advisory-committees/patient-engagement-advisory-committee/2017-meeting-materials-patient-engagement-advisory-committee.

[3] The 2017 PEAC meeting discussed patient engagement in clinical trials. For purposes of this guidance, we use the term "clinical investigation" as synonymous with "clinical trial."

[4] See discussion document entitled "Patient Engagement in Medical Device Clinical Trials," available at: https://www.fda.gov/media/122893/download.

[5] FDA requested comments on the discussion document through docket FDA-2018-N-4171.

[6] See 2018 Meeting Materials of the Patient Engagement Advisory Committee, available at: https://www.fda.gov/advisory-committees/advisory-committee-calendar/november-15-2018-patient-engagement-advisory-committee-meeting-announcement-11152018-11152018.

demonstrated public health benefits. FDA believes effective patient engagement can help mitigate some of the practical challenges to robust clinical investigations, including challenges concerning study/research participant enrollment and retention in the study, particularly when protocols include lengthier follow-up periods (e.g., through 2 years post-procedure) and/or frequent visits to the investigational site, which may require significant travel. Additionally, protocols for medical device investigations may be complex, with many endpoints as well as eligibility criteria that exclude some study/research participants living with the disease/condition from participating in clinical investigations. When not adequately addressed, each of these factors can contribute to increased time and cost to study sponsors, increased burden and risk exposure to study/research participants and the healthcare system, and delays in U.S. patient access to beneficial medical technologies.

FDA believes medical device clinical investigations prospectively designed with input from patient advisors may help to address common challenges faced in these clinical investigations, and could result in:

- Faster study/research participant recruitment, enrollment, and study completion;
- Greater study/research participant commitment, resulting in decreased loss to follow-up;
- Greater study/research participant compliance resulting in fewer protocol deviations/violations;
- Fewer protocol revisions;
- Streamlined data collection resulting in better quality data; and
- More relevant data on outcomes that matter to patients.

Feedback received from patients and industry at the PEAC meetings on October 11-12, 2017, and November 15, 2018, and the public docket comments related to the PEAC discussion document entitled "Patient Engagement in Medical Device Clinical Trials" indicated broad support for patient engagement in clinical investigations. Responses to questions posed by FDA at the 2017 PEAC meeting and in the docket indicated perceived barriers and challenges to such engagement including, but not limited to:

- Perception that FDA does not allow patient engagement in the design and conduct of clinical investigations;
- Patient perceptions that their input is not valued by the clinical investigation protocol development team;
- Sponsors' limited awareness, resources, and time to participate in patient engagement activities;
- Challenges finding patient advisors knowledgeable about clinical investigation methodology;
- Site investigators' reluctance to allow sponsors to engage with patients except as study/research participants;
- Logistical challenges of engaging with patient advisors in-person, which may preclude their involvement in the design of clinical investigations; and

- Challenges with determining which patient advisors or patient organizations should be engaged, and if multiple patient advisors are engaged, how to reconcile the disparate perspectives.

This draft guidance intends to address some of these perceived barriers and challenges.

III. Scope

FDA acknowledges that patient engagement may be beneficial across the total product lifecycle. This draft guidance focuses on the application of patient engagement in the design and conduct of medical device clinical investigations. This draft guidance does not address study/research participant reimbursement or compensation, promotion of investigational devices (see 21 CFR 812.7), or dissemination of clinical investigation results.

IV. Defining Patient Engagement

For purposes of this draft guidance, **patient engagement** is defined as intentional, meaningful interactions with patients that provide opportunities for mutual learning, and effective collaborations.

In the context of planning for a clinical investigation, engaging with patient advisors (see definition below) creates an opportunity to share patient experiences, perspectives, needs, and priorities during the design and conduct of a clinical investigation. Importantly, FDA views this type of patient engagement differently from interactions that sponsors or clinical researchers (also called "investigators") may have with individuals who participate in a specific clinical investigation as study/research participants.

For purposes of this draft guidance, **patients** are defined as individuals with or at risk of a specific disease or health condition, whether or not they currently receive any therapy to prevent or treat that disease/condition. Patients are the individuals who directly experience the benefits and harms associated with medical products.[7] In this draft guidance, the word "patient" also includes healthy individuals interfacing with medical devices. For the purposes of this draft guidance, we identify two distinct roles for patients who interact with researchers, sponsors, or FDA regarding clinical investigations: **study/research participants** and **patient advisors**.

In this draft guidance, the term **study/research participants** are individuals who are or become a participant in research, either as a recipient of the test article or as a control, and may include healthy individuals. FDA acknowledges that its regulations use the term "subject" or "human subject,"[8] to refer to these individuals, but patients may be familiar with a different term. Therefore, in this draft guidance, the term "study/research participant" is used instead.

[7] See FDA website entitled, "Patient-Focused Drug Development Glossary" available at: https://www.fda.gov/drugs/development-approval-process-drugs/patient-focused-drug-development-glossary.
[8] See 21 CFR 50.3(g), 56.102(e), and 812.3(p).

For purposes of this draft guidance, the term **patient advisors** refers to individuals who have experience living with a disease or condition, and can serve in an advisory or consultative capacity to improve clinical investigation design and conduct, but who are **not** study/research participants themselves. Patient advisors may include, but are not limited to, individuals who have participated in previous clinical investigations of the same disease/condition or similar device-type, individuals who were screened for but ultimately did not qualify for or did not elect to participate in a similar clinical investigation, representatives from a disease-specific or cross-cutting patient organization, healthy individuals who may be potential non-therapeutic (e.g., diagnostic) device users, or caregivers (also known as care-partners) of patients who may have experience with the disease/condition/device.

Similar to key clinical opinion leaders and site investigators, patient advisors may provide recommendations that positively impact how a study is designed and conducted, improve the patient experience during the investigation, and improve the relevance, quality, and impact of study results. However, to avoid potential real or perceived conflicts of interest, these patient advisors should not be study/research participants in the same investigation for which they are advising.

V. Questions and Answers on Patient Engagement in Medical Device Clinical Investigations

A. What approaches might sponsors use to engage patient advisors to inform the design and conduct of medical device clinical investigations?

We recommend sponsors identify patient advisors and clearly define the patient advisors' role early in the clinical investigation planning process. We encourage sponsors to be clear in their clinical investigation plan about which activities are part of the research plan (i.e., for study/research participants) versus those that are non-research patient engagement efforts (i.e., for patient advisors) that may improve the design and conduct of the clinical investigation.

Patient advisors who are educated about clinical investigations, the various approaches to managing the disease/condition of interest, and how a device may work may be better equipped and feel more empowered to voice their perspective in engagement activities. We encourage sponsors to consider using existing educational materials and/or partner with organizations that provide training for patient advisors to help them most effectively contribute.

Some patient engagement activities that may enhance the design and conduct of clinical investigations include, but are not limited to:[9]

[9] In addition to these patient engagement activities, obtaining feedback from study/research participants and from patients who did not participate in the clinical investigation (particularly those from underrepresented groups) can

- Working with patient advisors to improve the informed consent document to ensure patients understand the information presented for the clinical investigation;
- Obtaining input from patient advisors on flexible options for follow-up visits and data collection techniques to reduce unnecessary burden on study/research participants who may have challenges fulfilling the follow-up schedule. Such techniques may include allowing weekend hours, permitting the study/research participants' primary healthcare provider to perform some follow-up assessments, allowing phone or home visits by clinical researchers, or using mobile or online technologies to enable virtual or remote follow-up;
- Discussing with patient advisors their views on which potential endpoints are clinically meaningful in the treatment of the specific disease/condition;
- Working with patient advisors to inform the concepts that should be captured by patient-reported outcome (PRO)[10] measures in the clinical investigation to better reflect outcomes that are important to patients; and
- Working with patient advisors to inform the design of a patient preference[11] study to help understand the benefit-risk tradeoffs among patients for the proposed treatment or multiple treatment options used for the disease/condition.

B. When can input be gathered from patient advisors and incorporated into the clinical investigation?

Sponsors should consider involving patient advisors during the early planning phases of the clinical investigation so that their input can be incorporated while the protocol is being developed. Especially in innovative areas or new target patient segments, we encourage sponsors to confer with patient advisors when designing or planning the clinical investigation.

In more established areas, patient advisor input on draft protocols may translate into time and cost-saving improvements that also make the design more patient-centric. Such input should generally be incorporated before the final protocol and informed consent documents are submitted to the IRB[12] for review.

reveal barriers to participation, approaches to improve recruitment, challenges or other experiences during the study to help to streamline and improve future investigations.

[10] For more information on PROs see FDA's guidance "Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims," available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-reported-outcome-measures-use-medical-product-development-support-labeling-claims.

[11] For more information on patient preference information, see FDA's guidance "Patient Preference Information--Voluntary Submission, Review in Premarket Approval Applications, Humanitarian Device Exemption Applications, and De Novo Requests, and Inclusion in Decision Summaries and Device Labeling," available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-preference-information-voluntary-submission-review-premarket-approval-applications.

[12] "Institutional Review Board" is defined in 21 CFR 56.102(g). See also 21 CFR 50.3(i).

For clinical investigations that require submission of an investigational device exemption (IDE) application, this information should be included in the final protocols and informed consent documents submitted to the FDA for review as part of the IDE application.[13]

For ongoing studies that face significant challenges with study/research participant recruitment and/or retention, sponsors may want to consider involving patient advisors along with the research coordinator to troubleshoot and propose potential solutions.

C. What are the roles of IRBs and other institutional groups in patient engagement?

Under FDA's regulations, an IRB is "any board, committee, or other group formally designated by an institution to review, to approve initiation of, and to conduct periodic review of, biomedical research involving human subjects."[14] The primary purpose of IRB review is to assure the protection of the rights and welfare of humans participating as study/research participants. Access to personal information or direct engagement with study/research participants requires careful consideration of Federal, State, and local laws and institutional policies for their protection.

Because patient engagement activities with patient advisors primarily involve interaction in a consultative or advisory capacity, FDA does not generally consider these types of activities to constitute research or an activity subject to FDA's regulations on their own.[15] Therefore, FDA's research regulations, including IRB requirements, generally would not apply.

In contrast, interactions between study/research participants and investigators typically include collecting information as part of a research plan that outlines the methodological approaches to be used. Such interactions are generally in the context of a "clinical investigation" subject to FDA's regulations and must satisfy the applicable requirements, including applicable requirements at 21 CFR Part 812 (Investigational Device Exemptions), 21 CFR Part 56 (IRBs), and 21 CFR Part 50 (Protection of Human Subjects).

Because there are a variety of research contexts in which sponsors may engage with patients to obtain information on their experiences and perspectives, a full discussion of which laws may apply to such activities is beyond the scope of this draft guidance. FDA recommends that sponsors work with IRBs and Health Insurance Portability and Accountability Act (HIPAA) Privacy Boards to determine what laws may apply for a specific research activity.

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[13] For more information and resources on IDEs, please visit: https://www.fda.gov/medical-devices/device-advice-investigational-device-exemption-ide/ide-guidance.

[14] 21 CFR 56.102(g).

[15] It should be noted, however, that sponsors of clinical investigations are subject to the same applicable statutory and regulatory requirements regardless of whether patient engagement is incorporated in the design and conduct of the investigation.

D. How can a sponsor receive feedback on its patient engagement plan or patient-centered study design from FDA?

FDA encourages sponsors to integrate patient advisor input in the design and conduct of clinical investigations for medical devices in appropriate circumstances and is open to discussing patient engagement approaches through an informational meeting through the Q-Submission Program.[16] Through this process, sponsors interested in receiving feedback may pose questions to FDA, including patient engagement strategies and plans to use the patient advisor input to improve the design and conduct of a clinical investigation.

We encourage sponsors to reference any previous patient engagement activities used to inform the development of the investigational plan. Sponsors may also use and cite relevant information from their patient engagement activities in their subsequent marketing applications to FDA.

VI. Summary

FDA encourages patient engagement in medical device clinical investigations in appropriate circumstances. This document provides an overview of the potential value, as well as a summary of the challenges and potential solutions related to involving patient advisors in the design and conduct of clinical investigations. This document also identifies a variety of ways sponsors may engage patient advisors to design more patient-centric investigations that may be more likely to enroll and retain study/research participants, as well as collect information that is meaningful to patients.

If you are considering incorporating input from patient advisors in the design or conduct of your medical device clinical investigation, you are encouraged to engage in early interactions with FDA and to obtain feedback from the relevant FDA office/division on appropriate design and any applicable regulatory requirements.

FDA believes appropriate patient engagement may lead to improved efficiency and quality in the design and conduct of medical device clinical investigations and greater uptake of results by patients and providers when making treatment decisions about a legally marketed medical device, ultimately leading to earlier U.S. patient access to beneficial medical devices.

For additional resources and updates on patient engagement, please see https://www.fda.gov/about-fda/center-devices-and-radiological-health/cdrh-patient-engagement.

[16] The Q-Submission Program is used by FDA to discuss specific questions relating to a submission (current or future) with review divisions and broader device programs. For more information on the process for requesting feedback from FDA, see FDA's guidance "Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program," available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/requests-feedback-and-meetings-medical-device-submissions-q-submission-program.