2018

Patient Engagement in Medical Device Clinical Trials

DISCUSSION DOCUMENT

PATIENT ENGAGEMENT ADVISORY COMMITTEE

PATIENT ENGAGEMENT IN MEDICAL DEVICE CLINICAL TRIALS

Patient Engagement Advisory Committee (PEAC)

PEAC DISCUSSION DOCUMENT

Disclaimer: This discussion document is for discussion purposes only and does not represent draft or final guidance. It is not intended to propose or implement policy changes regarding patient engagement or the applicable statutory and regulatory requirements.

Introduction

The Patient Engagement Advisory Committee (PEAC) provides advice to the Commissioner or designee, on complex issues relating to medical devices, the regulation of devices, and their use by patients. The Committee may consider topics such as: Agency guidance and policies, clinical trial or registry design, patient preference study design, benefit-risk determinations, device labeling, unmet clinical needs, available alternatives, patient reported outcomes and device-related quality of life or health status issues, and other patient-related topics. The Committee in intended to provide relevant skills and perspectives, in order to improve communication of benefits, risks, clinical outcomes, and increase integration of patient perspectives into the regulatory process for medical devices.[1]

The Food and Drug Administration (FDA) is holding its next PEAC meeting on November 15, 2018 and has developed this discussion document with the following objectives:

- Define "patient engagement" in medical device clinical trials.
- Explain the value and positive impact of engaging patients in the design, conduct, and communication of clinical trials.
- Describe barriers and challenges in engaging patients for clinical trials.
- Outline how and when sponsors[2] can engage patients in the design and conduct of clinical trials.

FDA seeks further input from patient and patient advocacy stakeholders, the medical device industry, clinical researchers, and others on this topic. FDA intends to use this feedback to inform future draft

[1] More information about PEAC can be found at: https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/PatientEngagementAdvisoryCommittee/default.htm

[2] 21 CFR 812.3(n): Sponsor means a person who initiates, but who does not actually conduct, the investigation, that is, the investigational device is administered, dispensed, or used under the immediate direction of another individual. A person other than an individual that uses one or more of its own employees to conduct an investigation that it has initiated is a sponsor, not a sponsor-investigator, and the employees are investigators.

guidance[3] in this area. In particular, FDA seeks further comment from the public on the following questions:

A. Is the proposed definition of "patient engagement" clear? If not, what changes provide further clarity to define and distinguish patient engagement activities from other patient-related activities? Is the proposed term "patient advisor" clear? If not, is there another term that better reflects a patient's role in the context described in this document?
B. Are the value and beneficial impact of engaging with patients during the clinical trial process clearly identified and compelling? If not, how could this be strengthened?
C. Does this discussion document identify major barriers and challenges currently impeding sponsors from engaging with patients throughout the clinical trial process? If not, what additional barriers and challenges limit patient engagement opportunities? What additional steps/processes can be considered to address such barriers and challenges to further promote patient engagement?
D. Do the opportunities and timeframes outlined in this document for engaging patients include the major categories of interest to patient, sponsor, provider, and clinical researcher stakeholders? If not, what additional measures are relevant for consideration?
E. Are there other opportunities not addressed in this document that FDA could consider to better facilitate patient engagement in clinical trials?

Background[4]

Timely U.S. patient access to innovative beneficial medical technology increasingly depends on compelling evidence of not just improvements in objective clinical outcomes, but also positive patient experience and demonstrated value to the healthcare system. U.S. device trials often face significant challenges enrolling patients. Nearly half do not meet specified enrollment goals, and many clinical research sites do not meet enrollment targets, including 15% of sites that fail to enroll a single patient.[5] Retaining patients for the duration of the trial is also a significant challenge, particularly for trials with longer follow-up periods. Over recent decades, clinical trial protocols have grown increasingly complex, with a greater number of endpoints, more eligibility criteria, more procedures, more clinic visits required of the patients, more data points, and a greater collection of data that is not considered core to the study's

[3] This draft guidance is on CDRH's Fiscal Year 2019 (FY 2019) Program Guidance Development "A-list."
[4] The information from this section can also be found in the 2017 Meeting Materials of the Patient Engagement Advisory Committee. Available at: https://www.fda.gov/advisorycommittees/committeesmeetingmaterials/patientengagementadvisorycommittee/ucm578522.htm
[5] Getz K. Improving Protocol Design Feasibility to Drive Drug Development Economics and Performance. *International Journal of Environmental Research and Public Health*. 2014;11(5):5069-5080

primary objectives. Furthermore, conducting studies often takes longer, involves more sites and countries, and involves more protocol amendments. All of these factors can contribute to increased time and cost to study sponsors, increased unnecessary burden and risk exposure to patient participants and the healthcare system, and delays in U.S. patient access to beneficial medical technology innovations.

Historically, medical device developers have worked with leading healthcare providers, clinical researchers, and FDA to design and conduct clinical trials. This process often does not incorporate input from the patients in the design and conduct of the trial, capture outcomes important to patients, or adequately communicate trial results to the trial participants. By engaging patients throughout the process, clinical trials may become more patient-centric and reflect patient values, leading to improved clinical trial quality and greater uptake of results by patients and providers when making treatment decisions, ultimately leading to earlier U.S. patient access to beneficial medical devices.

FDA believes medical device clinical trials designed with patient input may be more likely to enroll and retain patients, collect information meaningful to patients and other key stakeholders, and be successfully completed. FDA has processes for sponsors to receive feedback on their approach to engaging patients in their clinical study design (Pre-Submission Program).

On October 11-12, 2017, the Patient Engagement Advisory Committee (PEAC met to discuss and make recommendations on the topic of patient input into medical device clinical trials. The 2017 meeting's discussion topics included patient involvement in the design of clinical trials; patient recruitment, enrollment and retention; and communication of study results to trial participants. The PEAC discussed the opportunities and barriers that patients experience when attempting to collaborate with industry on the design of clinical trials. Although it was acknowledged that multiple organizations are working to help reduce or remove barriers and improve accessibility for patients in the clinical trial arena, the PEAC agreed regulators could help clarify opportunities for patient engagement in the clinical trial development process. In a consensus recommendation, the PEAC suggested that FDA and industry develop a framework to de-mystify patient engagement in the clinical trial process. Based on this recommendation, FDA is pursuing various efforts in patient engagement in clinical trials, including additional workshops and the development of guidance.

Discussion Questions

1. **Proposed Definition.** *What is patient engagement in the context of medical device clinical trials?*

In a clinical research context, the Patient Centered Outcomes Research Institute (PCORI) defines patient engagement as "meaningful involvement of patients through the research cycle from the design to the implementation and dissemination of research results."[6]

Within medical device development, FDA's Center for Devices and Radiological Health (CDRH) proposes the following draft definition for discussion:

> "Patient engagement" refers to activities that involve patient stakeholders sharing their experiences, perspectives, needs, and priorities to help inform the design, the implementation, and dissemination for medical product development and assessment.

Importantly, CDRH views this differently from interactions that sponsors or clinical researchers (also called "investigators") may have with patients as research participants during the specific clinical trial investigation. For the purposes of this discussion document, we identify two distinct roles for patients[7] who interact with researchers, sponsors, or FDA on clinical trials: ***patient advisors*** and ***patient research participants***. In this document, the term "patient advisors" refers to stakeholders who can provide perspectives of patients participating in a trial, but are not the actual research participants.

CDRH acknowledges that patient research participants are referred to as "human subjects"[8] in statute and regulations, but patients have voiced concerns with this terminology; therefore, in this document, the term "patient research participants" is used in lieu of "human subjects."

Use of the term "patient" in this document means all patients and includes patient advisors and patient research participants.

2. **Value and Impact.** *What is the value and beneficial impact of engaging patients in the design, implementation, and dissemination of clinical trials?*

   Similar to key clinical opinion leaders and site investigators, patients may provide recommendations that positively impact how a study is designed and conducted, improve the patient experience during

[6] What We Mean by Engagement [Internet]. Dissemination and Implementation Framework and Toolkit. 2018 [cited 2018 Sep 14]; Available from: https://www.pcori.org/engagement/what-we-mean-engagement
[7] The term "patient" refers inclusively to people who receive health care services, including family members, friends, and other care partners, and any consumers of health care. (http://aircpce.org/sites/default/files/PCM%20Principles_April182017_FINAL.pdf)
[8] 21 CFR § 50.1 (2017). Protection of human subjects.

the trial, and improve the relevance, quality and impacts of study results. Patient engagement may help to address common device trial challenges, resulting in:

- Faster patient recruitment;
- Better patient retention;
- Fewer protocol revisions;
- Fewer protocol deviations/violations;
- Better quality data; and
- More relevant data on outcomes that matter to patients and demonstrate value to payers and healthcare systems.

3. **Challenges.** *What are current barriers and challenges to patient engagement in medical device clinical trials?*

The traditional process of designing and conducting a clinical trial does not typically include the opportunity for patient engagement. During and following the 2017 PEAC meeting, CDRH heard from sponsors and patient groups interested in engagement but concerned about specific barriers and challenges that prevent them from pursuing patient engagement activities in clinical trial design. Some of these real and perceived barriers included the following:

- Site investigators' reluctance to allow their patients to engage with sponsors, except as patient research participants;
- Patients being uninformed about clinical trial methodology;
- Sponsors having limited resources and time to participate in some engagement activities; and
- Perception that FDA does not allow patient engagement since such could be perceived as illegal marketing of devices.

4. **Approaches.** *How might sponsors engage patients in medical device clinical trials?*

Sponsors are encouraged to be clear in their clinical trial development plan about which patient-involved activities are part of the research plan (for patient research participants) and which are patient engagement efforts (for patient advisors). Sponsors are encouraged to identify patient advisors and clearly define the patient advisors' role early in the development process. To ensure the patient advisors feel empowered to voice their perspective, it is suggested that sponsors educate them about clinical trials, the approaches to managing the condition of interest, and how the device may work.

An empowered patient perspective may be integrated into the overall processes of designing and conducting clinical studies.

Some examples of patient engagement activities to potentially improve clinical studies include, but are not limited to:

- Gathering patient perspective on the enrollment criteria (both inclusion and exclusion);
- Designing a flexible follow-up schedule with patients and clinicians that may accommodate patients traveling farther distances, such as remote data collection;
- Working with patients to design and improve the informed consent document to ensure patients understand the information presented for the clinical studies;
- Organizing a focus group with underrepresented patients at a site to better understand their values and how best to communicate and recruit these patients for the trial;
- Discussing with patients what endpoints are clinically-meaningful in the treatment of their disease/condition;
- Including patient-reported outcomes (PROs)[9] as study endpoints to better reflect outcomes that are important to patients;
- Considering the use of mobile technologies for virtual or remote follow-up evaluations and data collection;
- Conducting a patient preference[10] study to help understand the benefit-risk tradeoffs among patients for the proposed treatment or multiple treatment options used for the condition; and
- Collaborating with a patient advocacy group to understand the optimal way to communicate the research results from the trial with the patient research participants and the patient community.

A variety of other groups have considered ways to engage patients and patient partners. Some of these groups have summarized the results of their efforts and have published approaches including the Clinical Trials Transformation Initiative (CTTI Recommendations on Effective Engagement with Patient Groups Around Clinical Trials), Faster Cures (Faster Cures Resource Library for Patient

[9] See FDA's *Guidance for Industry; Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims*, issued December 2009 (http://www.fda.gov/downloads/Drugs/Guidances/UCM193282.pdf).

[10] See FDA's *Guidance for Industry, FDA Staff and Other Stakeholders: 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*, issued August 2016. (http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm446680.pdf).

Engagement, and Faster Cures "The Research Acceleration and Innovation Network" for Patient Engagement), and PCORI (Patient-Centered Outcomes Research Institute – Engagement in Research).

5. **Timeframe.** *When can input be gathered from patient advisors and incorporated into the clinical trial?*

   Sponsors may consider involving patient advisors during the early planning phases of the clinical trial so that identifying and engaging with the patient advisors does not lead to study delays. The design of clinical trials is often a process that incorporates the perspectives of healthcare providers, clinical site coordinators, the sponsor's trialist, and chief medical officer. Patient advisors have insight into challenges that may be encountered with certain study designs, reveal outcomes that may not have been considered by the sponsors, and relay obstacles to patient retention that could potentially be mitigated by modifying the structure of clinical visits.

   In innovative areas or new target patient segments, we encourage sponsors to confer with patient advisors early during trial development, when the research question and the approach to answering it are being developed. In more established areas, patient input on draft protocols may translate into time and cost-saving improvements which make the design more patient-centric and may be incorporated before review of the protocol and informed consent documents by the FDA or institutional review boards (IRB).[11]

   For ongoing studies that face significant challenges with patient recruitment and/or retention, sponsors may want to consider involving patient advisors along with clinical site personnel to troubleshoot and propose potential solutions.

   Both patients and sponsors who attended the 2017 PEAC meeting expressed interest in communicating study results to patient research participants. Patient advisors could play a role in developing and disseminating study findings.

Conclusions

[11] See FDA's *Institutional Review Board (IRB) Written Procedures: Guidance for Institutions and IRBs*, issued May 2018 (https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM512761.pdf).

FDA encourages patient engagement in medical device clinical trials in appropriate circumstances. This discussion document provides an overview of the potential value, as well as a summary of the challenges, of involving patient advisors in the design, implementation and conduct, and dissemination of clinical trials. This discussion document also identifies a variety of ways sponsors might engage patients to design more patient-centric trials, which may be more likely to enroll and retain patients, collect information meaningful to patients and other key stakeholders, and facilitate trial completion. FDA believes appropriate patient engagement may lead to improved clinical trial efficiency, quality, and greater uptake of results by patients and providers when making treatment decisions, ultimately leading to earlier U.S. patient access to beneficial medical devices. The discussion and the feedback FDA receives on this topic is intended to inform the framework for draft guidance on the topic. The proposed examples presented serve only as a basis for dialogue in the evolving and growing area of the science of patient input.

Please submit your comments regarding this discussion paper to https://www.regulations.gov, Docket No. FDA-2018-N-4171 by January 14, 2019. Additional information can be found on FDA's webpage, https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHPatientEngagement/default.htm