PIPC Partnership to Improve Patient Care

July 5, 2023

Honorable Robert M. Califf, M.D.
Administrator
Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993-0002

Re: FDA-2023-D-0026

Dear Administrator Califf:

Thank you for this opportunity to submit comments on the Food and Drug Administration's (FDA) fourth guidance on Patient-Focused Drug Development: Incorporating Clinical Outcome Assessments (COA) Into Endpoints for Regulatory Decision-Making. Since its founding, the Partnership to Improve Patient Care (PIPC) has been at the forefront of applying principles of patient-centeredness to the nation's health care system — from the generation of comparative clinical effectiveness research at the Patient-Centered Outcomes Research Institute (PCORI), to the translation of evidence into patient care in a manner that achieves value to the patient. We applaud the FDA's attention to the concepts of patient-centeredness and patient engagement in the conduct of research and the approval process. PIPC looks forward to continuing its efforts to bring the voices of patients and people with disabilities to the discussion of how to advance patient-centered principles throughout an evolving health care system.

PIPC has long advocated for increased use of patient preference information to guide health care decisions. In the statute creating the Patient-Centered Outcomes Research Institute (PCORI), Congress defined research priorities to include patient "needs, outcomes and preferences" and charged PCORI to consider "variations in patient subpopulations," as well as to support patient and consumer representatives.[1] We believe PCORI's experience to be both relevant and insightful as the FDA works to advance COAs that are meaningful and rigorous. PIPC appreciates the FDA's commitment to patient-focused drug development (PFDD) and applauds its continued public engagement — especially with the patient community — as it refines its processes. It is fundamental that a COA process is truly centered on patients and considers the burdens they may experience in a clinical trial as well as strategies to ensure the endpoints assessed are meaningful. We agree that the solution is to engage relevant patient and caregiver stakeholders early in the process. These individuals are in the best position to advise on tactics to ensure the trial is not overly burdensome, that the trial procedures are patient-centered, and that the COAs are relevant. Therefore, we view PCORI as providing useful

[1] Compilation of Patient Protection and Affordable Care Act: Extracted sections concerning Patient-Centered Outcomes Research and the Authorization of the Patient-Centered Outcomes Research Institute (PCORI), 2010. https://www.pcori.org/sites/default/files/PCORI_Authorizing_Legislation.pdf.

insights for patient engagement in research, whereby patients and patient groups are engaged in designing the research in a manner that assures it is centered on the patient experience of care.[2] PCORI also assures that patients and patient groups are compensated for their work, a potentially useful recommendation related to designing and implementing a COA.[3] We believe that the robust patient engagement modeled by PCORI, which involves patients as research partners while being mindful of the burden and responsibilities on patients, is the gold standard and should inform the PFDD process. This model of early patient engagement could also help inform other important aspects of the clinical trial, such as its location and timing.

As you know, many patient organizations have conducted or been involved in externally- or agency-led PFDD. In those circumstances, clinical trial sponsors have an opportunity to utilize those organizations and patients with experience in gathering data on important patient outcomes and who could be very useful if engaged at the forefront of measuring the clinical outcomes of new products. As the FDA states, how patients feel, function, or survive should be reflected in the COA. Without this engagement, the value and importance of endpoints based on COAs may not otherwise be captured.

Further, the FDA's guidance identified that diseases may affect multiple aspects of feeling and functioning.[4] The fact that patients are heterogenous and may experience treatment differently should not impede sponsors from pursuing COAs. We appreciate that the FDA recognized that complete resolution of all symptoms is not essential to feel that the treatment was beneficial. The FDA's guidance also addressed the development of personalized endpoints.[5] Though we recognize the challenges, personalized endpoints are critically important tools for determining whether treatments are meeting patients' needs. We support the FDA's efforts to encourage sponsors to work closely with the patient community to develop and implement these endpoints so they may be effectively used in the clinical research process.

In discussing how to best incorporate COAs into endpoints, the FDA noted the importance of considering how closely the COA in question corresponds to patients' lived experiences. We agree with the guidance clarifying that its correspondence to changes relevant to patients is a critical component of all COAs, not just patient-reported outcomes (PROs). We also agree that for some COAs that do not directly corelate but do so indirectly, additional empirical support

[2] PCORI Engagement Rubric. PCORI (Patient-Centered Outcomes Research Institute). https://www.pcori.org/sites/default/files/Engagement-Rubric.pdf. Published February 4, 2014.
[3] PCORI, "Financial Compensation of Patients, Caregivers, And Patient/Caregiver Organizations Engaged in PCORI-Funded Research as Engaged Research Partners," Patient-Centered Outcomes Research Institute, published June 10, 2015, https://www.pcori.org/sites/default/files/PCORI-Compensation-Framework-for-Engaged-Research-Partners.pdf.
[4] Patient-Focused Drug Development: Incorporating Clinical Outcome Assessments Into Endpoints For Regulatory Decision-Making, April 2023. Pg. 9. https://www.fda.gov/media/166830/download.
[5] *Id.* at 13.

may be needed to translate scores on the measures into corresponding patient experiences.[6] It is important that sponsors work closely with the patient population in question to understand this dynamic and ensure that the impact on patient lived experience is being captured.

The FDA's guidance also acknowledged challenges related to studying rare diseases and the different parameters that may be required to develop appropriate trials, such as the potential need to use exit interviews or surveys.[7] We encourage FDA to build out this concept more throughout the guidance. There are many unique facets to both trial design for rare diseases and engaging with rare disease patients and caregivers. Weight needs to be given to these considerations that are specific to the implementation of COAs for rare diseases, giving rare communities appropriate opportunities for engagement while giving the sponsors designing trials for rare diseases a clear blueprint for their conduct.

In closing, we applaud the FDA's efforts to provide stakeholders with a standardized process for collecting and submitting patient experience data and other relevant information from patients and caregivers and to use that information in the regulatory decision-making process. We look forward to seeing Clinical Outcome Assessments as a standard practice in clinical trials.

Sincerely,

Tony Coelho, Chairman
Partnership to Improve Patient Care

[6] *Id.* at 19.
[7] *Id.* at 26.