NATIONAL HEALTH COUNCIL
Celebrating 100 Years

Board of Directors

Chairperson
Ann Palmer
Arthritis Foundation

Chairperson-Elect
Gary M. Reedy
American Cancer Society

Vice Chairperson
Diana Gray, MA
Hydrocephalus Association

Secretary
Matt Eyles
America's Health Insurance Plans

Treasurer
Lisa Simpson, MB, BCh, MPH, FAAP
AcademyHealth

Immediate Past Chairperson
Steve Taylor
Sjögren's Foundation

Nancy Brown
American Heart Association

Tracey D. Brown, MBA, BChE
American Diabetes Association

LaVarne A. Burton
American Kidney Fund

Tanisha Carino, PhD
Alexion

Chester "Chip" Davis Jr., JD
Association for Accessible Medicines

Patricia Furlong
Parent Project Muscular Dystrophy

Stevan W. Gibson
Lupus Foundation of America

Paul Gionfriddo
Mental Health America

Dory Kranz
National Alopecia Areata Foundation

Rod Mackenzie, PhD
Pfizer

Cassandra McCullough
Association of Black Cardiologists

Steve Miller, MD
Cigna

Gary Puckrein
National Minority Quality Forum

Susan Sherman, MHA
The LAM Foundation

Stephen J. Ubl
Pharmaceutical Research
and Manufacturers of America

Ex Officio Member
Marc Boutin, JD
Chief Executive Officer
National Health Council

February 3, 2020

The Honorable Stephen Hahn, MD
Commissioner, Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: Patient-Focused Drug Development Guidance: Incorporating Clinical Outcome Assessments into Endpoints for Regulatory Decision-Making; Public Workshop; Request for Comments; Docket No. FDA-2019-N-4900

Dear Commissioner Hahn,

The National Health Council (NHC) is pleased to provide comments on the Food and Drug Administration's (FDA) discussion documents related to Guidance 4: "Incorporating Clinical Outcome Assessments into Endpoints for Regulatory Decision-Making." The NHC appreciates the work and thought that the FDA is putting into the development of this draft guidance document.

Founded in 1920, the NHC brings diverse organizations together to forge consensus and drive patient-centered health policy. The NHC provides a united voice for the more than 160 million people with chronic diseases and disabilities and their family caregivers. Made up of more than 140 national health-related organizations and businesses, the NHC's core membership includes the nation's leading patient advocacy organizations, which control its governance and policy-making process. Other members include health-related associations and nonprofit organizations including the provider, research, and family caregiver communities; and businesses representing biopharmaceutical, device, diagnostic, generic, and payer organizations.

Comments specific to this discussion document

We appreciate the FDA's commitment to evolving the science of patient engagement through your series of guidances. While the discussion document covers complex material, we appreciate the FDA including "Key messages in this section" tables throughout. This helps make the material more accessible to a broader range of stakeholders, including members of the patient community. Additionally, since drug development is a global endeavor, we also appreciate the FDA's collaboration with the international regulatory community. Citations of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) reports throughout the draft discussion document are helpful in promoting efficiencies and consistency across regulatory requirements.

Patient engagement is useful when determining the timing of assessments.

We agree with the FDA that the Clinical Outcome Assessment (COA) data collection schedule should correspond directly with the natural course of the disease or condition (i.e., acute, chronic, or episodic), research questions to be addressed, trial duration, disease stage of the target patient population, and current treatment of patients, and be administered within the expected time frame for observing changes in the concept(s) of interest."

Additionally, COA data collection should correspond with patients' day-to-day life flow to the greatest extent possible. For example, if the target population is working-age adults, attempting to collect data in the middle of the day may be desired based on a research objective (e.g., timing since last dose), but is unlikely to fit into the schedule of a working adult. We recommend engaging members of the patient community when determining timing of assessments, in particular when assessing administration burden and schedule. Improving convenience for patients is also likely to reduce missing data.

Participant burden must be considered and reduced.

We agree with the FDA that neglecting to adequately account for participant burden may lead to missing or inaccurate data. In addition to the FDA's recommendation that respondent fatigue should be considered when evaluating validity, we feel strongly that such burden should also be avoided as much as possible. Patient engagement, for example through mock trial participation, may be useful in identifying the right balance between data collection needs and minimizing participant burden. Some recommendations from the FDA's guidance on *Enhancing the Diversity of Clinical Trial Populations*[1] may be applicable to this section.

[1] Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs Guidance for Industry. Food and Drug Administration, White Oak, MD. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enhancing-diversity-clinical-trial-populations-eligibility-criteria-enrollment-practices-and-trial

Overarching comments related to PFDD guidance development process

Case examples should demonstrate how PFDD Guidances 1-4 build upon one another.

We appreciate the FDA including illustrative case examples of the estimand framework. The case examples are particularly useful for understanding how intercurrent events can be addressed. To better tie together the guidances, it would be helpful for the case examples to not only describe the estimand framework, but also what preceded it. For example, a paragraph or table describing the following information:

- How comprehensive and representative input was collected
- What methods were used to identify what is important to patients
- Process and considerations when selecting, developing or modifying fit-for-purpose COAs

We understand that the data may need to be developed in some way. However, it is critical that all stakeholders understand how data from work done under a previous guidance is needed to inform the work in a subsequent guidance.

Glossary modifications

We appreciate the FDA including a glossary of standardized terms and definitions. To avoid confusion, miscommunication, and misunderstanding, we recommend the following modifications to the glossary:

Patient engagement:

Concern #1: The current definition provided of "patient engagement" is unnecessarily and inaccurately restrictive to only patient engagement with the FDA and its staff.

Recommendation #1: For this reason, we believe the term defined here should be changed to refer specifically to "patient engagement with the FDA."

Concern #2: Given that the FDA encourages patient engagement throughout drug development and not solely to develop data to submit to the Agency, and that other organizations (not just the FDA) conduct patient engagement in research, we believe that a broader definition of is needed. We suggest the FDA adopt the following definition of "patient engagement in research" provided by ISPOR:

Recommendation #2: "Patient engagement in research: Refers to 'the active, meaningful, authentic, and collaborative interaction between patients and researchers across all stages of the research process, where

research decision-making is guided by patients' contributions as partners, recognizing their unique experiences, values, and expertise.'"[2]

Patient-centered outcome:

Concern: phrasing of the definition, "an outcome that is important to patients' survival, functioning, or feelings as identified or affirmed by patients themselves, or judged to be in patients' best interest by providers and/or caregivers when patients cannot report for themselves" to be unclear and cumbersome.

Recommendation: We suggest revising it to read "An outcome identified or affirmed by patients as important to patients, particularly in terms of survival, functioning, feelings."

Patient-focused/patient-centered:

Concern: The NHC finds the definition of the terms "patient-focused"/ "patient-centered" problematic because it omits the act of actively engaging with patients.

Recommendation: We recommend replacing the current definition with the following definition: "Patient centered: any process, program, or decision focused on patients in which patients play an active role as meaningfully engaged participants and the central focus is on optimizing use of patient-provided information."

Observational research:

Concern: We believe that this definition does not refer to "observational research," but rather to "observation," a specific method under the observational research umbrella. The term "observational research" is reviewed in-depth within the "Framework for FDA's Real-World Evidence Program." In that document an "Observational Study" is defined as "a non-interventional clinical study design that is not considered a clinical trial." Additional definitions for prospective and retrospective observational studies are provided separately. It is important to note that "observational research" can rely on either quantitative or qualitative methods and naturalistic observation is an example of just one, qualitative observational research method.

Recommendation: We recommend adopting the definition of "observational research" included in the Real-World Evidence framework and replacing the definition currently associated with observational research with "observation [method]" in the glossary.

[2] Defining Patient Centeredness and Engagement in HEOR: Proposed Definition and Stakeholder Response. Forum Presentation presented at the: ISPOR 2018 Annual Meeting; May 21, 2018; Baltimore, MD. https://www.ispor.org/docs/default-source/presentations/1388.pdf?sfvrsn=ccb5658d_1.

"Patient partner" and "science of patient input":

Concern: We recommend broadening the definition of "patient partner" and "science of patient input" to acknowledge that use of these terms is not limited to medical-product development. Rather, these terms are common and used elsewhere, and this draft guidance applies these terms to in context of medical-product development.

Recommendation: We suggest the following definitions:

- Patient Partner: "An individual patient, caregiver, or patient advocacy group that engages other stakeholders to ensure patients' wants, needs, and preferences are represented in activities related to medical-product development and evaluation [insert process, program, or decision focused on patients]. Here, the insertion would be medical-product development."
- Science of Patient Input: "Methods and approaches of systematically obtaining, analyzing, and using information that captures patients' experiences, perspectives, needs, and priorities in support of. [insert process, program, or decision focused on patients]. Here, the insertion is medical-product development."

In addition to the recommendations above, we observed that a number of methods-related terms cited in the discussion document are not cited or defined in the glossary (e.g., ecological momentary assessment within the discussion of recall periods). It would be useful to cite an external reference or provide a definition for these terms.

Conclusion

We thank the FDA for the opportunity to provide comments on the discussion document. We wholeheartedly support the FDA's work to advance meaningful patient engagement and look forward continuing to engage with the Agency to develop these important ideas further.

If you have any questions or would like to discuss these issues further, please contact Eric Gascho, our Vice President of Policy and Government Affairs, at (202) 973–0545 or egascho@nhcouncil.org. Thank you again for the opportunity to provide feedback.

Sincerely,

Marc Boutin, J.D.

Chief Executive Officer