National Health Council

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December 18, 2019

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

Re: Patient-Focused Drug Development: Methods to Identify What Is Important to Patients; Draft Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders (Docket No. FDA-2019-D-4247)

Dear Commissioner Hahn:

The National Health Council (NHC) is pleased to provide comments on the Food and Drug Administration's solicitation for comments Patient-Focused Drug Development: Methods to Identify What Is Important to Patients; Draft Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders (Draft Guidance 2).

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 professional and membership associations; nonprofit organizations with an interest in health; representatives from the pharmaceutical, generic drug, health insurance, device, and biotechnology industries; and research, provider, and family caregiving organizations.

We appreciate FDA's commitment to evolving the science of patient engagement through your series of guidances. We commend FDA for seeking to reach a broad swath of the healthcare stakeholder community – including the patient community, when developing this series. We understand the challenge that this presents in terms of the level of detail to provide. Below, we offer recommendations on how to strengthen Draft Guidance 2 and provide specific comments on the draft guidance's sections.

Overarching Comments

Case examples

The NHC has previously recommended FDA develop a set of hypothetical case examples for stakeholders to have a better understanding of the types of studies and methods FDA views as good practice for patient engagement. This guidance includes a number of such examples, which we believe will be very helpful for sponsors looking to incorporate the patient perspective into their studies.

Misalignment between overall objective of the draft guidance and direction of the draft content

There appears to be misalignment between the overall, stated objective of the Guidance and the direction of the content of the draft Guidance. Guidance 2 is intended to describe "Approaches to identify what is ***most*** important to patients with respect to their experience as it relates to burden of disease and burden of treatment." The draft guidance describes methods to collect patient experience data, which includes information on concepts important to patients. However, the methods are not directed at getting to what is *most* important. In fact, patient preference study designs, which assess the relative desirability of alternatives (i.e., identify what is ***most*** important to patients) are not described at all.[1] Indeed, the draft guidance expressly states that patient preference information/patient preference study designs are not addressed and refers to the Center for Devices and Radiological Health (CDRH) 2016 Guidance.

We recommend that the final guidance direct stakeholders to review the Medical Device Innovation Consortium (MDIC) Patient Centered Benefit-Risk (PCBR) Project, both the Framework Report and Catalogue of Methods, alongside the CDRH guidance.[2]

Since patient preference studies are useful for identifying tradeoffs that inform what is most important, this is an important shortcoming of the current draft guidance. While CDRH's guidance includes very useful, introductory information on patient preferences, the information provided on methods is very limited. It does not include insights and drug-development-specific nuances gleaned through recent initiatives, such as the Innovative Medicine Initiative's Patient Preferences in Benefit-Risk Assessments during the Drug Life Cycle (IMI PREFER) project.[3,4]

Additionally, the draft guidance does not address whether there are important nuances that researchers should consider when identifying what is ***most*** important with respect to burden of disease versus burden of treatment. For example, special considerations related to inclusion/exclusion criteria (e.g., burden of disease among those who are treated versus not treated) could be relevant.

Therefore, we recommend reorganizing the draft guidance to initially describe methods for gathering what is important in general and then homing in on what is ***most*** important to patients, which would include considering patient preferences for outcomes and treatments.

In addition, this document appears to be specific to identifying patient-centered outcomes that will become endpoints in clinical trials, which is a very narrow view of patient-focused drug development. The methods described are useful for a variety of patient-focused product development applications and should be applied to patient-focused drug development in general, across all aspects of the medical-product life cycle. As we have stated in previous draft guidance comment letters[5,6], we believe these guidance documents should be applicable to patient engagement in medical-product development beyond just clinical trial applications.

We recommend that FDA state the guidance is more broadly relevant to all phases of the drug-development lifecycle, not only to inform endpoint development for trials. For example, what matters most to patients may be applied to identifying a patient-centered mode of administration rather than only to design a patient-centered trial endpoint.

Draft guidance content on methods

The main body of the draft guidance focuses on methods that are already well understood by the qualitative research community, but possibly not to all researchers or other stakeholders, while appendices appear to focus on more novel methodologies. The rationale for describing certain methods in the body of the draft guidance and others as appendices is unclear. FDA has been a leader in encouraging innovation and advancement in the field of patient-engagement research methods. If FDA prefers to keep novel methods as appendices, it would be helpful to state in the body of the text that methods described in appendices are not less important or potentially less appropriate than the traditional methods described in the body of the text. In parallel, it would be helpful for FDA to provide additional guidance on which novel methods (e.g., social media listening) are appropriate in which contexts.

Level of detail provided differs substantially between methods

The draft guidance provides substantial detail for certain methods, while only briefly referencing others. To reduce this imbalance, we recommend making reference to detailed texts and existing resources that are widely available for these methodologies rather than describing the methods and their strengths and limitations in detail. Hence, more methods and methods issues could be captured and referred to rather than described. For example, page 7 describes “some important considerations for focus groups.” It is our view that these considerations, along with those listed on page 19, are broadly applicable across methods and could be expanded upon and reorganized into general considerations guidance. We recommend that the guidance provide a common set of considerations that should apply to all methods and then add specific considerations on a method-by-method basis.

Specific Comments

Section II, Methods to Identify and Understand What is Important to Patients

This section begins with a discussion of Background Research. Literature reviews are inarguably an important step in documenting the importance of a research question, avoiding duplication, and generally conducting sound research. However, the published literature, in particular the published literature on patient-reported outcome measure development, rarely describes how patients were engaged.[7,8] As a result, the peer-reviewed literature does not always reflect patient priorities. Past literature may focus only on endpoints of importance to clinicians which might misdirect questions when gathering the patient perspective. At the same time, the literature might be useful in divulging findings from past qualitative research

conducted with patients and families that could be useful and promote efficiency. While literature reviews could be conducted simultaneously with initial qualitative research (e.g., listening sessions), to avoid bias, they should not necessarily precede initial qualitative research intended to identify broadly what is important to patients.

Thus, we recommend the Guidance caution against relying too heavily upon the current peer-reviewed, clinical literature when developing qualitative interview guides for interviews with patients unless the research is to identify past qualitative studies.

Additional guidance related to facilitated discussions at patient meetings

We would appreciate the FDA providing additional information regarding "facilitated discussions at patient meetings." FDA- and externally-led patient-focused drug development (PFDD) meetings are described briefly as a useful source of public input and patient perspectives. Additional detail on FDA's current thinking regarding the application of patient-provided input stemming from PFDD meetings would be useful. Additionally, patient groups often host annual patient meetings or regional meetings to hear from diverse groups of patients and to also provide education. The frequency and geographic diversity of these meetings present an opportunity to gather insights from diverse groups of patients. The NHC believes that learnings gleaned from these meetings are valuable when they are part of a structured research continuum that includes additional, more rigorous approaches to data collection. To ensure best use of limited resources, we encourage FDA to describe how an externally-led PFDD meeting or other facilitated discussion can contribute to a holistic, structured research plan. It would also be useful to describe additional, lower-resource intensive alternatives.

We also believe it is important to encourage a variety of engagement methods to collect patient-provided information. We suggest that the FDA encourage use of the broad range of methods and to communicate that voice-of-the-patient meeting are just one mechanism. We fear that some stakeholders believe they must hold these meetings as their only recourse. Instead, we believe that existing voice of the patient reports – when available – are an important component of the literature review or early phase research.

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 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 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 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."*[9]

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 definition below:

> *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.*[10,11]

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.[12] The term "observational research" is reviewed in-depth within the "Framework for FDA's Real-World Evidence Program."[13] 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.[13] 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.

"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 the 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 activity is related to 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 ~~the development and evaluation of medical products~~. [insert process, program, or decision focused on patients]. Here, the activity is related to medical product development.*

Patient preference:

Recommendation: Including the following language (also from CDRH)[1]:

> ***Patient preference****: [insert: Qualitative or quantitative assessments] ~~A statement~~ of the relative desirability or acceptability to patients of specified alternatives or choices among outcomes or other attributes that differ among alternative health interventions.*

Representativeness:

Recommendation: Replace "intended" patient population with "target" patient population.

"Online patient communities":

Recommendation: Include a formal definition of "online patient communities."

> *Online patient communities: Internet-based platforms that unite patients who have been diagnosed with a disease. They offer support, networking and/or information sharing.[14,15] Platforms may also help patients record health information and/or become involved in research. For researchers, online patient communities can be a useful resource for identifying patients to recruit as advisers or to participate in a study (e.g., qualitative study on patient experience, clinical trial participant, or surveys of opinions/experiences). Online communities are operated by patient organizations, provider groups, and others including for-profit organizations.[16]*

Operationalizing Engagement with the FDA

In addition to the recommendations above, we reiterate our recommendation encouraging FDA to provide more details on how stakeholders can engage FDA on topics related to PFDD. The current drug review and approval process does not include an opportunity for sponsors or other stakeholders to meet with the FDA to address PFDD-related questions, nor are there designated points of contact for regular engagement within the FDA. FDA should describe what the process entails and provide guidance on how to prepare for interactions with the Agency (e.g., who from the FDA would be there, which groups within the FDA will be represented, what certain meetings will entail, and what information, if any, sponsors or patient groups are expected to prepare in advance of the meeting) so all parties can make effective use of these engagements.

Conclusion

We thank the FDA for the opportunity to provide comments on draft Guidance 2. 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

References

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