



# National Health Council

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September 11, 2018

The Honorable Scott Gottlieb, MD  
Commissioner, Food and Drug Administration  
Dockets Management Staff (HFA-305)  
5630 Fishers Lane, Rm. 1061  
Rockville, MD 20852

Re: Patient-Focused Drug Development: Collecting Comprehensive and Representative Input; Draft Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders (Docket No. FDA-2018-D-1893)

Dear Commissioner Gottlieb:

The National Health Council (NHC) appreciates the opportunity to provide comments on the Food and Drug Administration's (FDA's) draft guidance on Patient-Focused Drug Development: Collecting Comprehensive and Representative Input.

The NHC is the only organization that brings together all segments of the health community to provide a united voice for the more than 160 million people with chronic diseases and disabilities and their family caregivers. Made up of more than 100 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, and representatives from the pharmaceutical, generic drug, health insurance, device, and biotechnology industries.

We applaud the FDA for its efforts and timely actions to encourage and guide meaningful patient engagement. The FDA's first draft guidance on Patient-Focused Drug Development (PFDD) is an important milestone in this area. The NHC appreciates that this guidance (referred to hereafter as Guidance 1) is the first of a series of guidance documents the FDA will release to address the collection and submission of patient experience data. The NHC understands these guidances must evolve to accommodate new research, evidence, and learnings in the science of patient engagement. As such, the NHC is committed to working with the FDA to ensure this and future guidances support our shared goal to strengthen patient engagement in the research, development, and regulation of medicines.

Below, we offer recommendations on how to strengthen the draft guidance, provide specific comments on the draft guidance's sections, and encourage more details on how engagement with the FDA will be operationalized.

## I. *Overarching Comments*

**Overall, we are very supportive of the general approach to Guidance 1. We believe it will lay a strong foundation for future guidances and other patient engagement activities conducted by the FDA and stakeholder community.**

Further, we appreciate the FDA's inclusion of many of the NHC's previous comments on draft documents released in 2017 to inform the discussion at the corresponding public workshop held on December 18, and development of draft Guidance 1.

Specifically, we commend the FDA's inclusion of statements in the draft guidance that: 1) emphasize the applicability and usefulness of the guidance to all stakeholders who engage patients during medical product development and review (not just for innovators of therapeutic biopharmaceuticals); 2) encourage stakeholders to leverage and engage patients as partners and advisors, not just as study subjects; and 3) acknowledge the large body of work on methods for collecting patient perspective information and other patient data that has been assembled to date, within the US and internationally, while expressing receptivity to innovative and non-traditional methods.

To further strengthen the guidance, the NHC offers the following recommendations:

- **Articulate that when patient engagement is conducted appropriately, such interaction is not regarded by the Agency to be promotion.** A clear statement from FDA would dispel the perception among some sponsors that meaningful engagement with patients during (at least some phases of) drug development and review is too risky to be pursued. The FDA has the opportunity to mitigate this concern in this first guidance.
- **Incorporate hypothetical case examples into the draft guidance that demonstrate a range of regulatory decisions that may be informed by patient experience data (PED).** As stated on FDA's website, hypothetical case examples "provide practical, supplemental information to illustrate important concepts."<sup>1</sup> In the draft guidance, the FDA directs readers to the CDER PFDD webpage to view these case examples. We encourage FDA to embed these examples directly into the guidance so that they can be more readily accessible and appropriately contextualized. The FDA could continue to add supplemental examples on its website in response to feedback, questions, and learnings from stakeholders.
- **Further articulate that the guidance is relevant for all stages of drug development and approval, not just in clinical trials.** Much of the document discusses the importance of patient engagement and collecting PED in clinical trials. While this is crucial, we are concerned the guidance may be misconstrued as being limited to only this phase, as clinical trials are not the only way to collect PED. For example, the FDA should ensure the guidance addresses decisions and the full breadth of opportunities in which to engage patients in the preclinical stages. The guidance should include information on when important patient experience and natural history data should be gathered, e.g., early in the process to inform clinical trial design, regulatory decision making across the life cycle of product development, determining whether clinical outcomes assessments (COAs) or other endpoints are patient-centered and meaningful to the target patient population, and when ensuring materials are accessible and understandable by patients. It would be helpful to include clear statements that patient engagement goes far beyond just clinical trials.

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<sup>1</sup>FDA. Patient-Focused Drug Development Guidance Series for Enhancing the Incorporation of the Patient's Voice in Medical Product Development and Regulatory Decision Making. <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm610279.htm#collapseOne> (accessed August 28, 2018).

## *II. Section-Specific Comments*

### ***General Considerations for Collecting Patient Experience Data***

We support the FDA's focus in Guidance 1 on ensuring "representativeness," including outlining a definition of what the term means in the context of collecting PED. The language in this guidance can help stakeholders form an initial understanding of what constitutes a representative sample, but we encourage the FDA to continue to expand the discussion of the methodology and best practices to achieving representativeness in studies.<sup>2</sup> The NHC previously convened a multi-stakeholder roundtable to produce a white paper on the topic entitled "*Tackling Representativeness: A Roadmap and Rubric*." The paper provides a set of consensus-based recommendations and key considerations regarding characteristics of "good" patient representativeness and offers a tool for those engaging patients to help them think about how to (as best as possible) achieve representativeness for their research objective. The language in Guidance 1 is consistent with our white paper, and we encourage the FDA to continue to consult it as you conduct further work in this area.

### ***Methods for Collecting and Analyzing Patient Experience Data***

The NHC appreciates the detailed exploration of methods to collect and analyze patient experience data. This section provides stakeholders with an initial, baseline understanding of the FDA's perspective on certain methods. We note, however, that language within this section of the guidance focuses heavily on sample size calculation and mentions saturation for qualitative research. We believe other research methods to gather or analyze individual patient experiences, such as ethnography<sup>3</sup> or interpretative phenomenological analysis (IPA)<sup>4</sup>, may also be useful for informing study protocols, informed consent documents, and conceptual models.

As discussions around methods in future guidances become more technical, the NHC urges the FDA to provide stakeholders with clarity on the right level of rigor needed to collect PED based on its intended use, general guardrails for what is acceptable, and what good methods for collecting PED can look like, while providing flexibility for the appropriate use of novel methods. While there are common elements for all studies such as a protocol, structured data collection, and analytical approaches, the guidance could be strengthened with the addition of commentary that addresses some of the differences that might be observed in studies required to inform specific types of regulatory decisions, acknowledging the level of evidence required for each type of decision as well as the level of certainty that might be required. Because the science of patient input is an evolving field, use of innovative methods can help efficiently strengthen methodological rigor when thinking about meaningful patient engagement.

### ***Operationalizing and Standardizing Data Collection and Data Management***

We encourage FDA to further clarify this section. Specifically, under *Standard Approaches to Consider for Collecting and Managing Data*, we call to the FDA's attention the following:

- With regard to Locating Patients/Sites (line 878), we recommend the FDA suggest patient groups may be able to help with enrolling patients. Identifying patients and optimizing patient selection can help ensure representativeness.

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<sup>2</sup> The National Health Council, *Tackling Representativeness: A Roadmap and Rubric*, available at: <https://www.nationalhealthcouncil.org/sites/default/files/Representativeness%20in%20Patient%20Engagement.pdf> (accessed August 28, 2018).

<sup>3</sup> Ethnography is the study of social interactions, behaviors, and perceptions that occur within groups, teams, organizations, and communities.

<sup>4</sup> Interpretative phenomenological analysis (IPA) is an approach to psychological [qualitative research](#) and aims to offer insights into how a given person, in a given context, makes sense of a given [phenomenon](#). In IPA, the researcher aims to learn about an individual's personal experiences, where participants are viewed as storytellers.

- Under Collecting Data, we note that “Social Media and Identifiable Patient Communities” is listed in Table 6, but not the preceding bulleted list also in Table 6 (lines 915-919). We recommend that it be added to the list, as this represents a distinct method.
- Under “What are some key considerations when using questionnaires to collect patient experience data?” (line 992), we recommend the FDA include language in the final guidance noting that patient input can help ensure questionnaires and other materials intended to be read/used by patients are easy to understand, provide the right level of information, and reflect patient vernacular. This step underscores the importance of ensuring patients are meaningfully engaged and their expertise leveraged throughout the entirety of the drug development process, including in the design of questionnaires.
- Additionally, the Draft Guidance does not address a repository for the storage of disease-focused patient experience data that is collected. The repository should include not only the data collected but also details about the study design, analysis and data quality. The repository would allow patient groups and industry to collaborate in a non-competitive space.

### *Glossary*

We commend the FDA for creating a glossary of important and commonly used terms that will enable stakeholders to use standardized terms and definitions. Inconsistent use of terms leads to confusion, miscommunication, and misunderstandings. Going forward, it will be critical for the FDA to consistently use and emphasize these terms and reference the glossary itself whenever appropriate. The FDA should plan to update the glossary as refinement or further clarification of terms is needed, and when new terms need to be added.

We appreciate the FDA’s addition of the term “caregiver” to this glossary. Informal caregivers (often described as “family” or “unpaid” caregivers) play a wide range of roles in the care of patients, including assisting with activities of daily living and medical or nursing tasks. It is important to distinguish caregivers as separate stakeholders and clarify how their perspectives may/may not be considered, depending on a given situation or set of circumstances. Factors such as relationship to the patient, co-residence, main problem or illness requiring care, and overall strain can impact how a caregiver delivers care and how they observe the progression of disease in the patient. While caregivers have a role in PFDD, they should not always be presumed to be a proxy for the patient. Patient autonomy is a key goal of PFDD, especially in conditions such as dementia or mental illness, where the caregiver’s input should be additive to that of the patient. As the FDA has done in clinical outcome assessment (COA), we recommend that the FDA distinguish the role of the caregiver from the patient, including examining when it is appropriate for caregivers to serve as proxy or observer. We encourage FDA to consider how the relationship between caregiver and patient, and caregiving burden, may impact reporting of data and care delivery. Clarifying the role of the caregiver in future references and when the caregiver might serve in these roles would be helpful.

Further, we appreciate the distinction made between the definitions of “patient” and “patient advocate.” These appropriately capture the breadth of patient community and its representation.

Finally, we encourage the FDA to acknowledge that COAs, such as patient-reported outcomes (PROs), in drug research and development should be patient focused. While we appreciate FDA’s baseline definitions of COAs and PROs in the glossary of the draft guidance, we caution that COAs and PROs, as defined, are not always inherently patient centered.<sup>5</sup> For example, an older legacy PRO measure,

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<sup>5</sup> Oehrlein EM, Perfetto EM, Love TR, Chung Y, Ghafoori P. Patient-Reported Outcome Measures in the Food and Drug Administration Pilot Compendium: Meeting Today's Standards for Patient Engagement in Development? Value Health. 2018 Aug;21(8):967-972. doi: 10.1016/j.jval.2018.01.004.

developed based on information that clinicians reported as important may not have been informed by patients. Thus, the outcomes prioritized may not correspond with patient-prioritized outcomes. We understand that future guidances will address COAs and endpoint selection in more detail. However, early recognition of the distinction between a measure that is simply a patient report versus patients reporting on something that is very important to their disease experience.

### *III. Operationalizing Engagement with the FDA*

The FDA should continue to establish and articulate pathways for stakeholders, including sponsors and patient groups, to engage with and submit patient-experience data to the Agency. We agree with the FDA that early and frequent engagement throughout drug development on the inclusion of patient experience data in submissions is important. However, there is little information and instruction in the draft guidance on how this will be operationalized. The current drug review and approval process does not include a step 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.

We recognize that some of the upcoming infrastructure changes, including the recently announced intention to “modernize the organization and functions of CDER’s Office of New Drugs”<sup>6</sup> could be aimed at helping to address some of these gaps. Commissioner Gottlieb has previously indicated that some of the restructuring within this office is aimed specifically at better incorporating patient engagement throughout the Agency, in its culture, and its outputs. However, the specifics of the reorganization and eventual guidance to stakeholders in this area are still unclear. To successfully implement a process for engagement, the FDA will need to outline the appropriate steps to take as well as the appropriate contacts.

In addition, the FDA should be able to describe what the entire process will look like 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. The NHC encourages as much detail in the guidance as possible on how these interactions will be operationalized and looks forward to helping disseminate this message once the Agency has something more extensive to share.

We thank the FDA for the opportunity to provide comments on draft Guidance 1. As previously stated, it is a very strong draft that will significantly further our shared goal of integrating the patient perspective into the research, development, and regulation of medicines. We 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, including at the upcoming public workshop on October 15-16, 2018.

Please do not hesitate to contact Eric Gascho, our Vice President of Policy and Government Affairs, if you or your staff would like to discuss these issues in greater detail. He is reachable by phone at 202-973-0545 or via e-mail at [egascho@nhcouncil.org](mailto:egascho@nhcouncil.org).

Sincerely,



Marc Boutin, JD  
Chief Executive Officer

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<sup>6</sup> FDA. Statement from FDA Commissioner Scott Gottlieb, M.D., on proposed modernization of FDA’s drug review office. Available at <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm609647.htm> (Accessed August 28, 2018).