NATIONAL HEALTH COUNCIL
Celebrating 100 Years

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August 23, 2020

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

RE: FDA-2010-N-0128 for Reauthorization of the Prescription Drug User Fee Act; Public Meeting; Request for Comments.

Dear Commissioner Hahn:

The National Health Council (NHC) appreciates the opportunity to provide a reponse to the Food and Drug Administration's (FDA's) request for comments on the next cycle of the Prescription Drug User Fee Act (PDUFA). In recent reauthorizations of PDUFA, the NHC has supported a number of provisions to bring the patient perspective into drug development and modernize the development and regulation of treatments for people with chronic diseases and disabilities. We look forward to working with the FDA to make further advances in PDUFA VII.

Created by and for patient organizations 100 years ago, the NHC brings diverse organizations together to forge consensus and drive patient-centered health policy. We promote increased access to affordable, high-value, sustainable health care. Made up of more than 140 national health- related organizations and businesses, the NHC's core membership includes the nation's leading patient organizations. 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.

As we shared at the July 23, 2020 stakeholder meeting convened by the FDA, the NHC recommends the next PDUFA should address:

- Expansion and Enhancement of Core Outcome Set Program to Increase Patient-Centricity and Impact;
- Continued Examination of the Potential Regulatory Uses for Real-World Evidence (RWE);
- Decreasing Burden through Digital Clinical Trials;
- Embedding Patient-Experience Data Throughout the Knowledge Management System; and
- Evolving the Science of Patient Engagement through Increased FDA Staff Capacity.

Expansion and Enhancement of Core Outcome Set Program to Increase Patient-Centricity and Impact

In 2018, FDA announced a small pilot program to fund external organizations to develop publicly available core sets of clinical outcome assessments (COAs) and related endpoints. In PDUFA VII, this work should be expanded through greater funding with a goal of creating a systematic approach beyond the pilot phase, with a focus on a greater level of patient involvement and an expansion beyond COAs only to include all concepts important to patients (e.g., biomarkers, survival, etc.) .

Core outcome sets are agreed upon, standardized sets of outcomes (often with related measures, and/or endpoints identified) that should be gathered and reported at a minimum in research of specific areas of health or health care. These sets are commonly developed by groups like the Center for Medical Technology Policy (CMTP), the International Consortium for Health Outcomes Measurement (ICHOM), and Core Outcome Measures in Effectiveness Trials (COMET).

We would like to offer a few areas where the existing work of FDA projects can be improved to better involve patients, be useful for a greater number of decision makers in the health ecosystem, and ensure that they are truly patient-centered. Currently, the emphasis of the FDA-funded work appears to be on deriving a core set of clinical outcome assessment measures based on environmental scans of literature, past clinical trials, and other study data to find existing measures with minimal upfront patient engagement. This is problematic for the following reasons:

- Past research has demonstrated limited or no patient engagement in development of many legacy measures documented in the literature or used in previous clinical trials.[1]
- Patients may prioritize concepts that cannot be captured by COA measures.

To ensure greater patient centricity and expanded utility, we propose the concept of Patient-Centered Core Outcome Sets. This process would involve patients and other stakeholders in the health ecosystem pre-competitively joining together to identify a broad set of concepts that matter most to patients in specific disease states. Concepts would then be prioritized through a structured, multi-stakeholder consensus process (e.g., delphi panel). From the emerging core set of concepts, core sets of measures and endpoints would evolve. Importantly, because the consensus process would include all stakeholders and look at all outcomes that matter to patients, they would include, but go beyond, clinical outcome assessment measures.

This will make the core outcome set suitable for a greater number of uses, including quality measurement, value assessment, coverage decisions, and value-based agreements. The end result will be a more efficient process that relieves the burden on patient organizations, who are often asked to identify patient needs throughout every step of product lifecycle. Similarly, it will create efficiency for product sponsors, who have multiple teams within the company collecting information in disparate ways, potentially delaying broad access to new treatments.

By continuing and modifying the existing Clinical Outcomes Assessment Core Outcome Set project, the FDA can help the patient community by helping to standardize terms, methods, and approaches, similar to the role they are playing in patient-focused drug development (PFDD). The FDA also can encourage and facilitate multi-stakeholder collaboration. The Agency has a long track record of setting standards while allowing flexibility to encourage advancement in the field, which can serve an important role here. Finally, the FDA can serve a convening role to help the community determine what infrastructure needs exist to make Patient-Centered Core Outcome Sets real and far reaching.

Continued Examination of the Potential Regulatory Uses for Real-World Evidence (RWE)

In addition to the RWE Framework developed as part of PDUFA VI implementation, FDA has funded pilot programs on usage of RWE and real-world data (RWD) to support clinical development. As the science continues to evolve, the learnings from the pilots can inform additional work and potentially include more formalized pilots under PDUFA

[1] 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;21(8):967-972. doi:10.1016/j.jval.2018.01.004

VII. Any such expansion of the pilot program should require or strongly encourage patient engagement and include more transparent reporting requirements to ensure that lessons learned can be utilized by not just future sponsors but all stakeholders. Engaging patients can yield new research questions that can be studied using RWD sources. For example, a recent study examined atrial fibrillation (AFib) "triggers." That is, what triggered an individual AFib episode. While patients have long discussed possible triggers (e.g., caffeine, stress) on online forums, very little formal research has examined these possible triggers.[15] As a direct result of patient engagement, researchers fielded a survey asking paroxysmal AFib patients to document their personal triggers for an AFib episode and identified potential disease mechanisms that could fuel further novel clinical research.[16] Importantly, the triggers most commonly identified are modifiable (i.e., alcohol, caffeine, exercise, lack of sleep).

Decreasing Burden through Digital Clinical Trials

The FDA, industry, and the NHC have long shared the goal of reducing the burden of participating in clinical trials. We were pleased to comment on FDA's 2019 draft guidance on increasing clinical trial diversity, which included an important section that focused on decreasing the burden of participation. One element of that section was the recommendation of greater use of mobile technology to track safety and efficacy. This year, the COVID-19 pandemic made the use of these tools even more important, as clinical-trial sponsors used them more frequently to continue ongoing trials even when their trial sites were closed down. Additionally, as the FDA guidance highlights, using digital tools to decrease the frequency of site visits by participants can be an important tool to ensuring clinical-trial populations are representative of the relevant patient population.

While the NHC supports greater deployment of these tools, our outreach to member companies has shown that the results of their use are mixed, largely because some companies engaged patients to learn how include the technology in the participants' daily life-flow, but others have not.

PDUFA VII should include funding for pilot programs to better understand how patient engagement can improve the use of mobile technology to create clinical-trial efficiency, reduce participant burden, and improve patient centricity.

Embedding Patient-Experience Data Throughout the Knowledge Management System

The FDA is in the process of developing a knowledge management system and portal to provide FDA staff access to and analysis of prior regulatory decisions. Concurrently, the FDA has developed a template for reviewers to denote what patient experience data was submitted by sponsors and how those data were used in the review process. Through greater resources, the NHC would like to see these two efforts be incorporated together by implementing the knowledge management system in a way that ensures

patient-experience data and other emerging data such as RWD is systematically captured for use in future decisions.

Evolving the Science of Patient Engagement through Increased FDA Staff Capacity

Much of PDUFA's success relates to additional funding to hire needed staff. PDUFA VI also included provisions to allow faster hiring processes and more flexibility to offer competitive salaries. These provisions should be continued and improved.

Of particular importance, the NHC would like to see greater investment in staff in numbers and skills to evaluate sponsors' patient-engagement plans and hold earlier and more frequent meetings to discuss the plans with industry. Under the current PDUFA authorization, the agency's resource constraints have limited its ability to hold additional meetings to discuss patient-engagement plans, resulting in this important discussion being a relatively small part of the sponsors' formal meetings. With greater resources, the FDA can hire more staff with the right skills to hold more frequent meetings, or meetings focused solely on patient-engagement plans, to ensure sponsors collect the right patient-experience data to meet the FDA's expecations.

Conclusion

We appreciate the opportunity to provide input into the next round of PDUFA. Please do not hesitate to contact Eric Gascho, 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.

Sincerely,

Marc Boutin, JD
Chief Executive Officer
National Health Council