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September 8, 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: Office of Women's Health Strategic Priorities; Establishment of a Public Docket; Request for Comments

Dear Commissioner Hahn:

The National Health Council (NHC) appreciates the opportunity to provide comments as the Food and Drug Administration's (FDA's) establishes its Office of Women's Health (OWH) Strategic Priorities public docket. The OWH mission is critical to reducing health disparities that disproportionately affect women. We agree that the FDA has unique role in protecting and promoting women's health.

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 drug, and payer organizations.

Overarching Comments

FDA should work across the agency to address disparities affecting women.

While we wholeheartedly support the OWH's focus on addressing gender disparities, we believe that the FDA should also work throughout the agency to identify the unique needs of and address disparities faced by women. While the OWH can serve an important role, it is important that its focus be incorporated throughout the culture and operations of the agency. An emphasis on bringing issues affecting women to the forefront of the FDA and ensuring that there is sufficient expertise on the topic, should exist in all aspects of the FDA, ranging from the Commissioner's office to each review division. This could be a comparable process to the FDA's current approach to rare disease, where Rare Disease Program staff are embedded in each review division.

The NHC particularly asks the FDA to include women with complex chronic diseases and disabilities in its emphasis on improving women's health. As FDA noted in its draft guidance on Enhancing the Diversity of Clinical Trial Populations, "failure to include complex participants in a development program may lead to a failure to discover important safety information about use of the investigational drug in patients who will take the drug after approval." For many individuals, the ability to take part in the drug-development process is an empowering step that aligns with their health care goals and could allow earlier access to treatments to significantly improve health outcomes. A focus on this population, not only in clinical trials, can help ensure that the FDA considers how medical products work in a real-world setting.

Many of the comments we are providing, particularly relating to representativeness, are similar to those we submitted to the Office of Minority Health and Health Equity (OMHHE) and other previous communications with the agency. We encourage the OWH and the OMHHE to work together closely to address issues of representativeness and other intersectional issues identified in these comments.

Product Development Efforts

FDA should encourage industry engagement with women throughout the product lifecycle.

The NHC has previously commented on the FDA's patient-focused drug development (PFDD) discussion documents related to Guidance 2: "Methods to Identify What is Important to Patients" and Guidance 3: "Selecting, Developing or Modifying Fit-for-Purpose Clinical Outcomes Assessments (COAs)." As we noted in those comments, patient engagement in product development occurs at two levels:

- Patients engaged as partners informing the drug-development process; and
- Patients participating to provide data on the patient experience to inform development and studies.

We have previously expressed the concern that historically the primary role of patients has been limited to their role as a study subject and have supported FDA's recent efforts to enhance patient engagement throughout the product development process. We urge FDA to connect overall patient engagement efforts with those efforts specifically designed to engage patients from underserved populations. This includes women, and especially women of color, and continued engagement and bi-directional communications between FDA and patients, including those with disabilities and complex health care needs, to understand real-world treatment experiences of underserved populations.

The NHC believes strongly that the scope and breadth of patient involvement in developing and communicating experiences with treatments are fundamental to any efforts to increasing diversity in medical product development. In practical terms, this means that those engaged - patients, caregivers, advocates, and advocacy organizations - should be *representative* of the target patient population. Patient engagement strategies that fail to focus on securing perspectives of populations representative of a specific disease state, will likely fall short of delivering the diversity essential to OWH's efforts.

In 2017, the NHC convened a half-day Roundtable with key stakeholders, including representatives from patient groups, life science companies, value-assessment framework developers, payers, research organizations, and the FDA. We focused first on building a consensus understanding of what "representativeness" means when applied within the context of product development, regulatory decision-making, and value assessments¹. Stakeholders agreed that representativeness means that a sufficient number and types of people are included in the engagement activity to ensure that those engaged can speak on behalf of the target population. It refers to "who" and "how many" individuals to include in an interaction (e.g., discussions intended to inform strategies on securing a diverse set of clinical-trial participants) in order to, as closely as possible, engage with individuals that represent the broader, target patient population.

The NHC urges OWH to work across the FDA toward actionable guidance provisions that reduce the burden of clinical-trial participation as a step toward more diverse enrollment.

Clinical-trial populations that reflect the diversity of the patient population for a specific disease is an ideal that is rarely attained due to challenges associated with study participation. FDA has previously recognized that the burden associated with study participation can severely hamper diversity in clinical trials. These burdens include:

¹ National Health Council. Tackling Representativeness: A Roadmap and Rubric, (<https://www.nationalhealthcouncil.org/wp-content/uploads/2019/12/Representativen...>)

- Requiring participants to make frequent visits to clinical-trial sites may overly burden elderly, children, disabled, and cognitively impaired individuals requiring transportation or caregiver assistance, as well as participants in rural areas located far from research facilities;
- Financial costs of travel and lost work income;
- Time commitments interfering with work and family responsibilities; and
- A general mistrust and/or misunderstanding of clinical research among some populations and subpopulations.

These burdens can be significantly higher for women because women are still taking on a higher burden of unpaid work despite increasing participation in the workforce. According to data² from the Organization for Economic Cooperation and Development, in the U.S., women spend about four hours a day on household obligations, compared with about 2.5 hours for men. Women are twice as likely to be employed hourly at the minimum wage³, and therefore more likely to face economic and time barriers to participation.

The NHC urges OWH to work across agency functions to address impediments that deter diverse clinical-trial populations and encourage sponsors to address these issues with patient engagement as early in clinical development planning as possible. A meaningful dialogue with the patient community can inform sponsors of the best ways to facilitate enrollment without impeding study validity (e.g., reduced frequency of study visits and use of technology to collect data on safety and efficacy). Perceptions of burden may vary significantly across disease states (e.g., added burden associated with mobility challenges is different from burden related to lost income), and patient engagement is crucial to determining strategies that are most effective and valuable to underserved patients.

The OWH could further enhance its value to the stakeholder community by working to operationalize elements of FDA's general guidance on reducing clinical-trial participant burden, including:

- Encouraging clinical-trial sites in geographic locations with a higher concentration of racial and ethnically diverse patients;
- Working with sponsors to incorporate diversity considerations when selecting health care providers to assist with clinical-trial recruitment; and
- Facilitating bi-directional public outreach and education.

We further urge the FDA to recognize that efforts to promote diverse clinical-trial enrollment should begin early in development planning. OWH could fill vital information gaps on the prevalence of disease among women to help inform target trial participants. As part of this activity, it would also be helpful to provide guidance to industry on how to

² <https://stats.oecd.org/index.aspx?queryid=54757>

³ <https://nwlc.org/issue/minimum-wage/>

navigate the complexity of enrolling appropriately diverse trials for U.S. approval while considering global prevalence factors that may vary in other countries in which the sponsor is seeking regulatory approval.

This proactive approach to patient engagement, with an eye toward ensuring that activities include a patient population representative of the disease state, would enable greater understanding on study participation barriers. Similarly, any granularity with respect to gender is dependent on ensuring that engagement captures a representative population. For example, there are racial health disparities linked to maternal mortality. Any study in this area needs to include a diverse population of women. Ideally, engagement efforts throughout a product lifecycle should be sufficiently flexible to accommodate divergent needs associated with geographic factors and differences in age, race, cognitive function, socioeconomic status, and language proficiency. Finally, continuing this engagement beyond the FDA-approval process to maintain a bi-directional mechanism for communicating patient experience would facilitate more efficient identification of any disparities in patient response to treatment.

Education and Outreach

OWH initiatives should improve information available to clinicians and patients on diverse experiences.

The NHC encourages OWH to devise outreach and engagement initiatives that will likely translate into improved patient outcomes. For individuals with chronic diseases and disabilities, information on the benefits and risks of incorporating a new treatment into disease management is rarely available when a product is introduced to market. For the most part, negative effects from medications are monitored on a case-by-case basis with clinicians adjusting dosage and treatment type according to how an individual reacts to prescribed treatments. OWH can play a role in identifying how the benefit-risk profile may vary by genders and ensuring that the clinician community is aware of these gender-specific factors, how they might influence outcomes, and what actions the patient and clinician should take.

FDA should reach out to patient organizations and provide guidance to industry to bridge the knowledge gap about medical products' performance in women.

The NHC has actively engaged with the FDA and other stakeholders over the past several years to ensure the patient voice is meaningfully represented in product development. The NHC has worked to build consensus across a range of issues to advance the dialogue on patient engagement, from identifying key priority areas and topics for guidance development to providing feedback and suggestions on a common glossary of terms.

We remain committed to ensuring that a range of patient voices is represented through early, meaningful, proactive patient engagement. FDA outreach to industry and the

scientific community should stress the benefits of engaging patient organizations – and organizations that specialize in reaching patients in underserved populations specifically - early so that underserved population considerations can be incorporated into all aspects of product development. Clear guidance to clinical trial sponsors and manufacturers that enables development of evidence on divergent responses to new treatments, including differences in clinical benefit and adverse events, without inhibiting efficient study design or jeopardizing product approval is an important step toward achieving OWH's objectives.

Conclusion

We appreciate the opportunity to provide input into the areas and types of engagement the FDA's OWH should prioritize in the coming year(s), and potential mechanisms that can be used to implement them. We continue to support the FDA's work to identify, address, and reduce disparities in health care experienced by underserved, and underrepresented populations through meaningful patient engagement. We look forward to continuing to engage with the agency, including the OWH, as it further defines and executes its strategic priorities.

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,

A handwritten signature in black ink, appearing to read "MBoutin", with a long horizontal flourish extending to the right.

Marc Boutin, JD
Chief Executive Officer National Health Council