December 5, 2024

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852-1740

c/o David Gebben
Center for Devices and Radiological Health
Food and Drug Administration
10903 New Hampshire Ave., Bldg. 66, Rm. 1316
Silver Spring, MD 20993-0002

RE: Docket FDA-2015-D-1580: Draft Guidance - Incorporating Voluntary Patient Preference Information over the Total Product Life Cycle

Dear Dr. Gebben:

On behalf of the undersigned organizations, we appreciate the opportunity to provide comments on the Food and Drug Administration's (FDA) draft guidance "Incorporating Voluntary Patient Preference Information over the Total Product Life Cycle." We commend FDA's continued leadership in advancing patient-centered medical product development and regulatory decision-making. This updated guidance represents an important step forward in recognizing that patient preference information (PPI) can and should inform the entire product lifecycle, not just benefit-risk assessments at the time of approval.

We particularly applaud FDA's:

- Expansion of the guidance scope to encompass the total product lifecycle
- Recognition that PPI can inform multiple stages of product development and review
- Acknowledgment that care partners' perspectives may be relevant in appropriate situations
- Detailed recommendations for study design and conduct
- Inclusion of practical examples demonstrating PPI application

While the draft guidance provides a strong foundation, we believe there are opportunities to further strengthen its impact across several key themes:

1. Strengthening the Role of Patient Preference Information

We recommend removing the word "voluntary" from both the title and throughout the document. As demonstrated on page 2, line 56, FDA already communicates quite clearly that guidance documents "describe the Agency's current thinking on a topic and should be viewed only as recommendations." This standard disclaimer language effectively conveys the non-binding nature of guidance documents, making the additional qualifier "voluntary" unnecessary. Moreover, the use of "voluntary" may inadvertently diminish the perceived value and importance of patient preference information in regulatory decision-making. The guidance appears to expand the scope and application of FDA's consideration of PPI beyond just the approval/benefit-risk decision to include the total product lifecycle, making the continued

emphasis on its voluntary nature particularly misaligned with the document's broader goals. By removing this qualifier, FDA can better emphasize the integral role of patient preference information while still maintaining its standard approach to guidance documents as recommendations rather than requirements.

2. Expanding Stakeholder Engagement

While the draft guidance provides valuable direction for industry sponsors, its current framing may unnecessarily limit its impact and application. Throughout the document, references to stakeholders primarily focus on industry, with occasional mentions of FDA staff. However, the development and use of patient preference information involves a much broader ecosystem of stakeholders. Patient groups, care partners, healthcare practitioners, and advocacy organizations all play crucial roles in identifying research priorities, designing studies, recruiting participants, and implementing findings. By expanding the guidance's scope to explicitly recognize and provide recommendations for these stakeholders, FDA can foster a more collaborative and effective approach to patient-centered product development.

3. Clarifying PPI Applications Beyond the Benefit-Risk Approval Decision

The guidance's historical roots in benefit-risk assessment are evident in its current structure and emphasis. We applaud FDA for expanding this guidance beyond that phase of product development. Our experience suggests that PPI can provide crucial insights throughout the product lifecycle - from early needs assessment through clinical trial design and post-market evaluation. However, the guidance would be strengthened by more fully exploring expanded applications and providing clear direction on how different types of preference evidence can inform different decisions. Additionally, the relationship between PPI and other forms of patient input, such as patient experience data and patient-reported outcomes, needs clearer articulation to help stakeholders understand when and how to use different approaches.

4. Strengthening Methodological Guidance

While the draft guidance provides helpful overview of methodological considerations, stakeholders would benefit from more specific direction regarding evidence standards for different applications. For example, when is qualitative preference information sufficient versus when are quantitative studies required? When must preference heterogeneity be assessed and quantified? What level of scientific rigor is needed for different types of regulatory decisions? By providing clearer direction on these questions and including more diverse examples of PPI applications, FDA can help ensure that preference studies are appropriately designed for their intended use.

To address these themes, FDA may wish to consider the following specific modifications:

Strengthening the Role of PPI

- Title Page: Remove "Voluntary" from guidance title "Incorporating Voluntary Patient Preference Information over the Total Product Life Cycle" to reflect PPI's integral role in product development and evaluation
- Page 4, Line 123-126: Expand "FDA may consider certain submitted PPI" to instead emphasize how PPI contributes to the totality of evidence, reflecting its role as an expected component of product development rather than an optional addition

- Page 7, Lines 250-252: Replace "PPI might be useful for the following device characteristics" with "More rigorous and scientifically valid PPI generation is particularly useful where medical products have the following characteristics" to shift from permissive to directive language while maintaining FDA's standard guidance approach
- Page 10, Line 348: Add language clarifying that while submission of PPI remains at the discretion of sponsors (as with all guidance recommendations), its development and consideration should be viewed as an integral part of product development rather than an optional add-on

Stakeholder Engagement

- Page 1, Line 28: Replace "FDA encourages industry to consider patient experience data" with "FDA encourages the use of patient experience data in medical product development and evaluation" to reflect broader stakeholder engagement
- Page 3, Line 90: Expand "This guidance…is intended to provide updated recommendations to industry and FDA staff" to explicitly include patients, care partners, healthcare practitioners and patient advocacy organizations

Scope of Application

- Page 1, Line 33: Revise "Patient perspective on benefit and tolerance for risk may be considered in FDA's assessment" to "Patient perspectives on the relative benefits and risks of treatment options may be considered at any stage of FDA's regulatory decision-making process" to better reflect the expanded scope and application of PPI
- Page 7, Line 250: Add introductory paragraph: "PPI may be helpful to any stakeholder engaged in any stage of the medical product lifecycle where knowing the patient community's preferences for any outcome or health state may impact decisions related to that product…"
- Page 8, Line 275: Expand case examples to include:
  - PPI study to identify novel endpoints and sub-populations (Hauber B, Mange B, Zhou M, Chaudhuri S, Benz HL, Caldwell B, et al. Parkinson's Patients' Tolerance for Risk and Willingness to Wait for Potential Benefits of Novel Neurostimulation Devices: A Patient-Centered Threshold Technique Study. MDM Policy Pract. 2021;6(1):2381468320978407.)
  - PPI study to establish clinical trial statistical design (Medical Device Innovation Consortium (MDIC). Using Patient Preference Information in the Design of Clinical Trials Framework. Arlington, VA: MDIC; 2022 Apr.)
- Page 10, Line 348: Add references to use of PPI in breakthrough pathway designations and different phases of drug/biologic development
- Page 10, Lines 360-362: Add language regarding "patient tolerance for uncertainty of benefits or risk (which can impact significance thresholds)" and "preference-weighted composite endpoints"

Methodological Guidance

- Page 14, Line 508: Clarify when identification and quantification of preference heterogeneity is more valuable to FDA decision-making

- Page 15, Lines 521-523: Strengthen language to indicate that patient input in attribute selection is a requirement, not optional, and that qualitative research of patient perspectives on attributes is a requirement of good preference study design
- Page 17, Line 590: Add reference to "Best Practices for Communicating Benefit, Risk, and Uncertainty for Medical Devices" (Liliana Rincon-Gonzalez. Best Practices for Communicating Benefit, Risk, and Uncertainty for Medical Devices [Internet]. MDIC; 2021 Sep [cited 2024 Oct 25].
- Page 30, Line 1030: Incorporate key findings from IMI-PREFER publications regarding methods assessment, specifically:
  - On measuring patient benefit-risk preferences (Bekker-Grob E de, Soekhai V, Levitan B, Veldwijk J, Juhaeri J. Report on methods for measuring patient benefit-risk preferences in medical treatment. IMI-PREFER Deliverable. 2021 Nov 25.)
  - On suitability of preference methods across product lifecycle (Veldwijk J, De Bekker-Grob E, Juhaeri J, Van Overbeeke E, Tcherny-Lessenot S, Pinto CA, et al. Suitability of Preference Methods Across the Medical Product Lifecycle: A Multicriteria Decision Analysis. Value Health. 2023 Apr;26(4):579-88.)

We recognize that our recommendations could expand the scope of the guidance. However, we believe these additions would better fulfill the promise of patient-focused medical product development, and better serve all stakeholders in the process.

Thank you for your consideration of these comments. We look forward to continuing to work with FDA to advance the science of patient input and its application throughout the medical product lifecycle.

Sincerely,

Alliance for Aging Research
Alliance for Women's Health and Prevention
ALS Association
Bone Health and Osteoporosis Foundation
Caregiver Action Network
Cure HHT
HealthyWomen
Huntington's Disease Society of America
Obesity Action Coalition
Prevent Blindness
Society for Women's Health Research
StopAfib.org
The American Society of Consultant Pharmacists (ASCP)
The Headache and Migraine Policy Forum
The Marfan Foundation
The Mended Hearts, Inc.