Huntington's Disease Society of America

June 5, 2026

Re: Request for Information and comments
Docket No. FDA-2026-N-3947

Kyle Diamantas
Acting Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, Maryland 20993

Dear Mr. Diamantas,

The Huntington's Disease Society of America (HDSA) appreciates the opportunity to provide comments regarding the impact of Patient-Focused Drug Development (PFDD) meetings and related patient engagement activities.

HDSA is a leading national organization dedicated to the care and cure of Huntington's disease (HD), a rare and fatal hereditary disorder that manifests as a neurological disease with both physical and psychiatric components. If one parent has HD, their children have a 50 percent chance of inheriting HD. Our focus is to promote and support research to find a cure for HD; help people and families affected by the disease; and educate the public and healthcare professionals about HD.

Currently, there is no clinically available pharmacological, biological, or surgical agent or method which slows or stops the progression of HD. HDSA supports continued research to better understand HD, as well as improve access to quality treatment by financially supporting 60 HDSA Centers of Excellence and 9 Clinical Partner Sites covering 37 states plus the District of Columbia. HDSA has a long history of supporting people living with HD and family members through a network of 47 Chapters and Affiliates that provide access to locally-based social workers and support group meetings.

While current research tools measure clinical decline in cognitive and motor function using the HD Integrated Staging System (HD-ISS), they often miss many of the impacts that patients and families say shape their everyday lives and treatment decisions. To fill this gap, HDSA commenced an initiative in 2024 to develop the first Patient-Centered Core Impact Set (PC-CIS) for Huntington's disease.

A PC-CIS is a standardized, patient-prioritized list of the everyday impacts a disease and its treatments have on a patient's, caregiver's, and family's life. It is broader than traditional

clinical outcomes. HDSA is using the National Health Council framework for creating an HD PC-CIS. The first step in that framework is to gather patient and care giver input. The 2024 HDSA Externally-led Patient Focused Drug Development Meeting for People Living with Pre-symptomatic and Early-stage and Mid-stage Huntington's Disease (HDSA EL-PFDD) has been an important step in this process. Our responses to the questions focus on how the HDSA EL-PFDD meeting supports this initiative.

1. **How have PFDD meetings informed patient communities and stakeholder engagement activities?**

The HDSA EL-PFDD meeting transformed how the Huntington's disease community engages with researchers, regulators, industry sponsors, and healthcare providers by creating a formal structure for incorporating lived experience into decision-making. Through these efforts, patients and families have become active contributors rather than passive participants in drug development discussions.

Further, the HDSA EL-PFDD meeting serves as one of the primary sources for the development of a Huntington's Disease Patient Centered Core Impact Set (HD PC-CIS). This initiative is directly informed by the Voice of the Patient Report—output from that meeting capturing the perspective from people with the lived experience of HD on the impact of living with HD.

This initiative engages individuals living with HD, caregivers, clinicians, researchers, and advocacy organizations to identify the symptoms and disease impacts that matter most to patients across all stages of disease progression. The HDSA EL-PFDD meeting discussions have strengthened trust between stakeholders and encouraged broader participation from traditionally underrepresented voices within the HD community.

The HDSA EL-PFDD activities also increased awareness among stakeholders that Huntington's disease affects far more than motor symptoms alone. During the meeting patients and family members consistently identified cognitive, psychiatric, functional, and social impacts as critical contributors to disease burden, helping shape a more holistic understanding of the condition.

2. **What scientific questions, research initiatives, or identified gaps in the understanding of a disease or condition have resulted from PFDD meetings?**

The HDSA EL-PFDD meeting and related engagement activities highlighted significant gaps between traditional clinical outcome measures and the real-world experiences of people living with Huntington's disease. One of the most important scientific questions raised through HDSA's PC-CIS initiative is whether current endpoints adequately capture the symptoms and functional impacts that patients consider most meaningful.

The initiative has identified that a gap exists, and there is a need for improved measurement tools related to cognitive decline, psychiatric symptoms, communication challenges, loss of independence, and caregiver burden. These insights encourage research efforts focused on developing patient-centered outcome assessments and validating endpoints that better reflect quality of life and day-to-day functioning.

Additionally, the HDSA EL-PFDD-meeting discussions have reinforced the need for longitudinal research that reflects disease variability across stages of HD and among diverse patient populations. This is particularly relevant to people living with pre-symptomatic Huntington's disease who emphasized they are seeking meaningful benefit before substantial neurodegeneration and clinical symptoms occur.

There remains a need for validated endpoints and outcome measures capable of detecting meaningful treatment effects in pre-symptomatic populations, reinforcing the importance of developing and qualifying sensitive biomarkers, functional assessments, and patient-centered endpoints that can support clinical trials aimed at delaying disease onset or slowing progression before symptoms become clinically apparent.

These efforts are helping to advance a more comprehensive scientific understanding of disease progression and treatment benefit.

3. In what ways has patient input from PFDD meetings informed medical product development programs or strategies?

Patient input has played an increasingly important role in shaping medical product development strategies for Huntington's disease. Patient testimony during the HDSA EL-PFDD meeting provided valuable insight into the level of risk many individuals and families affected by Huntington's disease are willing to accept in exchange for the possibility of slowing, delaying, or preventing disease progression. Given the fatal and progressive nature of HD and the absence of disease-modifying therapies, participants consistently expressed a willingness to consider treatment-related risks that may differ from those associated with less severe conditions. This patient perspective can help inform FDA benefit-risk assessments and assist biopharmaceutical sponsors in designing development programs, clinical trials, and regulatory strategies that better reflect patient preferences and priorities.

Through HDSA's HD PC-CIS initiative, patients and caregivers have identified priority symptoms and functional outcomes that may not be fully represented in traditional trial designs. These insights have been shared with the medical product development industry and inform

conversations around endpoint development, selection of meaningful clinical outcomes, and trial participation considerations. Sponsors and researchers are increasingly recognizing that successful therapies should demonstrate improvements in aspects of disease that patients identify as most burdensome and meaningful.

Patient input has also informed operational aspects of clinical trials, including reducing participant burden, improving accessibility, incorporating caregiver perspectives, and considering the practical realities of living with a progressive neurodegenerative disease. As this initiative develops it will further encourage collaboration among advocacy organizations, academic researchers, and industry partners to align development programs with patient priorities from the earliest stages of research.

4. How has patient input gathered during PFDD meetings been integrated into or otherwise affected clinical practice?

The HDSA EL-PFDD meeting has helped clinicians better understand the broad and multidimensional impact of Huntington's disease on patients and families. Insights generated through the development of the HDSA HD PC-CIS initiative provide opportunity for comparative effectiveness research that can be adopted by clinicians with an emphasis on the importance of addressing cognitive, emotional, behavioral, and functional symptoms alongside motor manifestations.

As a result, healthcare providers will increasingly recognize the value of multidisciplinary and patient-centered care approaches that reflect patient-identified priorities. The initiative will also encourage clinicians to incorporate more meaningful patient and caregiver discussions into routine care, including conversations about quality of life, independence, mental health, and caregiving challenges.

5. Please describe any other outcomes or effects resulting from PFDD meetings.

The HDSA EL-PFDD meeting contributed to an ongoing cultural shift in how the Huntington disease community participates in medical product development and healthcare decision-making. Specifically, the meeting empowered patients and caregivers to share their experiences with confidence and to advocate for research and policy priorities that reflect real-world needs. Most importantly, the HDSA EL-PFDD meeting has reinforced the understanding that people living with Huntington's disease and their caregivers are essential partners in the development of therapies, care models, and policies that meaningfully improve their lives.

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HDSA appreciates the FDA's continued commitment to Patient-Focused Drug Development and the meaningful incorporation of patient experience data into regulatory decision-making. The Huntington's disease community has demonstrated that patients and families possess unique expertise about the realities of living with this devastating condition and the outcomes that matter most in their daily lives. Through initiatives such as HDSA's EL-PFDD meeting and the development of the Huntington's Disease Patient-Centered Core Impact Set, we are working to ensure that these perspectives are systematically captured and translated into research, clinical care, and medical product development. We encourage the FDA to continue supporting frameworks and opportunities that elevate the patient voice and advance the development of therapies that address the full impact of disease on individuals and families. Thank you for the opportunity to provide these comments and for your ongoing partnership with the rare disease community.

Sincerely,

Amy Gray
President and Chief Executive Officer
Huntington's Disease Society of America