PFDDworks

From voices to value

VIA ELECTRONIC DELIVERY

August 13, 2024

Robert M. Califf, MD
Commissioner
U.S. Food and Drug Administration
5630 Fishers Lane
Rockville, MD 20852

RE: Docket No. FDA-2024-N-1809 for "Listening Session: Optimizing FDA's Use of and Processes for Advisory Committees"

Dear Dr. Califf:

On behalf of the undersigned participants in *PFDDworks*, a collaborative of patient advocacy leaders engaged in patient-focused drug development activities, we appreciate this opportunity to provide comments to the Food and Drug Administration (FDA) in support of its ongoing efforts to modernize the Advisory Committee function. If any of the signatories or their respective organizations have provided independent comments, those should be considered the highest priorities of those parties.

Structure and Process

- We recognize that Advisory Committees were launched following the Kefauver-Harris Amendment of 1962, when a charge was added to the FDA's remit to assess the effectiveness of candidate therapies, in addition to their safety, to ensure the agency has access to relevant expertise to inform that evaluation. Over the past 60 years, the enterprise to develop an increasingly wide array of novel medical products and to meet regulatory requirements to demonstrate safety and effectiveness has become increasingly complex. In the last decade, the agency has invested in its commitment to patient-focused drug development, adding new elements to the evidence base that must be elicited and considered as part of the review for marketing approval. These advances make the role of advisory committees even more crucial, to supplement the Agency's internal expertise with individuals who hold specialized types of knowledge that can help to illuminate and make meaning of the assembled evidence and assessment of potential benefits, harms, and risks.

  However, today it seems that Advisory Committee meetings related to specific candidate therapy reviews often take on more of a "litigation" posture where the sponsor and agency each present their positions on the data in a quasi-adversarial manner with the Advisory Committee acting as the "jury" in voting on specific questions including, often, whether the data supports approval to market. Since the FDA cannot

delegate its regulatory decision-making to the Advisory Committee, a meeting format that instead focuses on generating insights on key issues such as the nature of the condition to be treated, challenges in trial design and resulting data, the meaningfulness of the increment and measure of change, the acceptability of risks and harms, and other essential insights should be employed. Moreover, the topics and questions to be addressed in an Advisory Committee meeting should be made public at least two weeks in advance to enable more effective participation by all stakeholders.

- The FDA's publication of the patient-focused drug development guidance series, along with related statutory and administrative authorities, ensures that rigorous qualitative and quantitative patient experience data (PED) can be incorporated into clinical development and regulatory decision-making. FDA has regularly communicated the value of patient experience data (PED) for its understanding of burdens of the condition, outcomes of priority interest to patients and caregivers, nature and degree of meaningful change, and burdens and unmet needs relative to existing therapies, yet this information has not been consistently brought forward in Advisory Committee meetings. When there is relevant PED available on matters under discussion by an Advisory Committee, including Voice of the Patient reports or Patient Listening Session summaries for the disease area at issue, FDA should include this information both in the background materials for Advisory Committee members and in the agency's presentation during the meeting.

- The members of an Advisory Committee are selected based on pertinent expertise. To ensure these insights are obtained in an appropriate, balanced manner, the Advisory Committee chair should not facilitate the meeting. FDA should either develop independent staff (i.e., FDA employees who do not report to the center/division leaders managing the reviews) or engage external professional meeting facilitators who are skilled at delivering an inclusive and objective discussion.

<u>Composition and Participation</u>

- Given the extent to which the FDA has committed to including rigorous patient perspectives in its decision-making, it stands to reason that each Advisory Committee meeting should include a temporary member with lived experience expertise in the condition for which a candidate therapy would be indicated if approved (unless a standing patient member of the committee meets that requirement).

- The FDA's conflict-of-interest policies for Advisory Committee members are an important tool for ensuring that expert views are as objective and transparent as possible. At the same time, it can be very challenging to identify qualified individuals who have no relationship whatsoever to the sponsor of a candidate therapy, particularly when it involves a rare condition. FDA policies provide flexibility in these situations provided there are appropriate disclosures and other steps are taken to mitigate bias. We urge FDA to enable patient representatives with lived experience in the specific

condition to participate on an Advisory Committee, either as standing or temporary members, including if they have an association with one or more advocacy organizations that may have received funding from the sponsor involved in a specific meeting. Disclosure of any relationship will mitigate potential conflicts.

- We encourage a review of how the roles of Consumer representatives and Patient representatives are described, viewed, and managed by the agency. According to information posted on the agency's website, Consumer representatives on FDA advisory committees are expected to "analyze scientific data, understand research design, discuss benefits and risks, and evaluate the safety and efficacy of products under review." FDA specifically looks for individuals who have "an affiliation with and/or active participation in consumer or community-based organizations."

  According to FDA's website, Patient representative candidates are "carefully recruited and trained to prepare them to serve. It's through this engagement that we learn of patient needs, priorities, and preferences and gather meaningful data that informs medical product development and decision making." This unique role is certainly important to the Committee's composition, although it's unclear why a Patient representative wouldn't also have the same responsibilities as those ascribed to Consumer representatives, especially since Patient representatives are provided special training to serve on Advisory Committees.

  In addition to role clarity, we urge FDA to consider how Patient representatives are recruited. Individuals interested in serving as Consumer representatives apply for membership. By contrast, Patient representatives are identified through the FDA's Patient Representative Program. FDA recruits Advisory Committee participants with experience in disease areas on an as-needed basis by posting to the FDA Patient Representative web page. This passive manner of recruiting interested individuals may be quite limiting in reaching interested individuals who meet participation requirements, especially in light of the expanded interactions the agency now has with many patient communities through the PFDD initiative, Patient Engagement Collaborative, Patient Engagement Advisory Committee, and Patient & Caregiver Connection programs.

  A further curious distinction drawn by the agency between these roles is that Patient representatives who serve on CDER/CBER-related advisory committees have voting privileges; those who serve on CDRH-related advisory committees do not have voting privileges. There is no limitation on voting privileges for Consumer representatives. While Consumer representatives are expected to have an affiliation with and/or active participation in a consumer or community-based organization, there may be the appearance of greater scrutiny of prospective Patient representatives' affiliations within the disease community(ies) they seek to represent.

- The advent of online participation in Advisory Committee meetings, particularly making statements during the Open Public Hearing portion, has been an important development to encourage participation by those who cannot easily travel to an in-person meeting at the FDA facilities. We encourage the agency to continue to employ this technology for public access as the meetings return to an in-person or hybrid format. We also encourage the opportunity for members of the public, including members of the patient community for the condition at issue for a given Advisory Committee meeting, be permitted to attend in person if personal circumstances enable them to do so.

  When interest among the public in speaking during the Open Public Hearing exceeds the time allotted, using a lottery to select speakers may not serve the objectives of the meeting. The resulting randomness of perspectives shared during this important forum has the unfortunate consequence of being the time that advisory committee members themselves are seen to leave the room, multi-task, or otherwise shift their attention. A more constructive process for eliciting essential perspectives relevant to the Advisory Committee's deliberations would enhance both the Committee's understanding of the issues they are asked to consider, weigh, and advise on and the public's understanding of the process.

We are grateful for the opportunity to share our perspectives, observations, and recommendations with you on this vital topic to advance patient-focused drug development and public health.

Sincerely,

Eda Baykal-Caglar, Director, Patient Engagement, The Michael J. Fox Foundation for Parkinson's Research

Kuldip Dave, Senior Vice President, Research, The ALS Association

Ryan Fischer, Chief Operating Officer, Foundation for Angelman Syndrome Therapeutics

Pat Furlong, Founding President and CEO, Parent Project Muscular Dystrophy

Russ Paulsen, Chief Operating Officer, UsAgainstAlzheimer's

Patrick Wildman, Senior Vice President, Advocacy & Government Relations, Lupus Foundation of America