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US FDA Adcomm Reform Ideas: Neutral Facilitator As Chair, Public Hearing Lottery Process Tweaks

by Sue Sutter

Proposal to have panelists rate the strength of efficacy and safety evidence on a numeric scale also draws support in written comments on ways to optimize the advisory committee process.

The US Food and Drug Administration should consider using a neutral facilitator to chair advisory committee meetings and rethink the lottery process for open public hearing speaking slots.

The agency also may want to consider asking adcomm members to rate the strength of a drug's efficacy and safety evidence on a numeric scale, either in addition to or in lieu of the formal vote on benefit-risk, stakeholders said in comments to the agency.

The comments follow the FDA's June listening session held in connection with ongoing adcomm process reform efforts. The agency sought feedback on several issues, including adcomm composition, service on the panels as a special government employee, and public perception and understanding of adcomms. (Also see "*US FDA Adcomm*

Key Takeaways

- Using a neutral facilitator to lead adcomm meetings would promote fuller, more meaningful discussion among panelists, stakeholders said.
- The OPH lottery process should be tweaked so that key stakeholder categories are each allotted a certain amount of time, comments suggested.
- Some commenters also support using a

Reform: Does Listening Session Suggest No Major Near-Term Changes?" - Pink Sheet, 29 Apr, 2024.)

Likert-type scale, in addition to or in lieu of voting, to opine on the strength of a product's efficacy and safety data.

Neutral Facilitator

The proposal for a neutral facilitator to lead meetings, if adopted, would fundamentally change the longstanding approach whereby the panel chair, who is usually a scientific or clinical expert, leads the meeting.

This approach also would go further than the position taken by FDA Oncology Center of Excellence Director Richard Pazdur, who has said the panel chair should serve as a moderator that proactively draws committee members into the discussion. (Also see "*The Wait Is Over: US FDA Advisory Committees Returning To In-Person Meetings Come Fall*" - Pink Sheet, 26 Feb, 2024.)

"Consideration should also be given to the benefits of having a neutral facilitator in charge of advisory committee meetings, a role currently filled by the chairperson, typically an expert scientist, not an expert in generating fair and meaningful conversation for informing regulatory decisions," the EveryLife Foundation for Rare Diseases said.

> ***Having a professionally trained meeting facilitator serve as a non-voting committee chair "would ensure consistency in meeting facilitation across committees and would also allow all expert voting members to focus on the meeting content and scientific discussion." – SSI Strategy's PharmApprove***

"In numerous instances, we heard from community members who have witnessed advisory committee discussions dominated by one member's perspective or be derailed by less than accurate concerns that point discussions in one direction without opportunity for others to step in and ensure a full picture of the issue is painted," the rare disease advocacy group's *comments* state.

"Expert facilitators are used in settings across public and private life to manage conversations, pull out key points and ensure objectives of the meeting are met. The FDA should consider the merits of deploying them for advisory committee discussions too."

Having a professionally trained meeting facilitator serve as a nonvoting committee chair "would ensure consistency in meeting facilitation across committees and would also allow all expert voting members to focus on the meeting content and scientific discussion," SSI Strategy's PharmApprove, a strategic communications firm, said in *comments*.

"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," PFDDworks, a collaborative of patient advocacy leaders engaged in patient-focused drug development activities, said in its *comments*.

Tweaking The OPH Lottery

The FDA heard calls at the listening session for changes to the open public hearing process. Patients urged that more attention be paid to their experience with a disease or an investigational drug, while consumer and academic groups said individuals who did not experience benefits with an investigational drug also should be heard. (Also see "*US FDA Advisory Committee Open Public Hearing Changes Urged*" - Pink Sheet, 5 Jul, 2024.)

Written comments suggested approaches to maximize the time provided for the OPH, including changes to the lottery process used when the number of people who want to speak exceeds the time allotted.

To encourage the widest participation possible, the OPH timeframes and lottery process should be consistent across advisory committees for the FDA's drug and biologic product centers, "with every effort made to extend the OPH time to provide ample speaking opportunities for registrants," the Pharmaceutical Research and Manufacturers of America's *comments* state. "More specifically, the time dedicated to OPH should reflect the duration of the entire AC meeting."

The OPH is the only time that patients who participated in a study, patients and families living with the disease, patient organizations, and others can weigh in with context that can support agency decision-making, the EveryLife Foundation said.

> ***The current OPH lottery approach "does not result in a diverse and representative array of speakers who can cover the universe of perspectives relevant to regulatory decisions." – EveryLife***

Foundation for Rare Diseases

"The limited time afforded to such comments results in the agency conducting a lottery to award speaking slots," the group said. "The lottery approach, while understandable, does not result in a diverse and representative array of speakers who can cover the universe of perspectives relevant to regulatory decisions."

"A more targeted approach would be to consider a hybrid process that identifies key stakeholder categories for each meeting and allots a reasonable time for each," EveryLife's comments state. "In cases where demand outstrips availability for those spots, then a lottery approach can be initiated. This, along with providing additional clarity to the public on the rules for the OPH, how speakers are selected and guardrails for how advisory committee members should consider such testimony, will go a long way towards public trust and understanding of the agency's decisions."

Similarly, the patient advocacy group I AM ALS *said* that while use of a lottery system for OPH speakers has served the agency well in preventing biases, "we find that this method does not guarantee diversity of perspective. Instead, we recommend a possible shift to having categories and performing a lottery within these categories. For example, individuals wishing to speak would classify themselves into a category and then be in the pool for that specific group. This ensures fairness and that diverse voices throughout the field are being represented."

Ardelyx, which went to an advisory committee in November 2022 with its phosphate absorption inhibitor Xphozah (tenapanor), suggested that sponsors should have more of a role in selecting OPH speakers. (Also see "*Dispute Resolved? Ardelyx's Tenapanor Gets US FDA Panel Nod For Dialysis Patients*" - Pink Sheet, 16 Nov, 2022.)

The current lottery system allows other groups to get in the queue before patients, "which seems unfair, and may not necessarily best serve the goal of hearing the patient voice," the company's *comments* state.

"The lottery system should be changed from a randomized system to a 'first come, first serve' basis which is one that would prioritize patients who have participated in relevant clinical trials or have real-world experience related to the impact of treatment options on their quality of life."

"We urge the agency to consider providing sponsors whose products are under review with the opportunity to offer participants with experience with the product, such as clinicians and patients, [to] speak during the open comment period (OPH)," Ardelyx said. "This should be

followed by a separate portion for other individuals, and in so doing, this allows participants to be properly present in a meaningful way versus the current OPH process which appears to be much more random."

A Likert Scale For Voting

In a recent survey by 3D Communications of current and former adcomm members, 95% of respondents either agreed or strongly agreed that there should be a voting question on benefit-risk at meetings where an application seeking approval is discussed. (Also see "*Current, Former US FDA Adcomm Members' Reform Idea: Allow Conflicted Experts To Participate*" - Pink Sheet, 13 Aug, 2024.)

Speakers at the June listening session also expressed support for retaining the voting process, saying it was important to transparency and accountability. One patient safety advocate, who also serves as an adcomm consumer rep, suggested a voting approach in which panelists indicate their level of confidence in the data on a numeric scale. (Also see "*Advisory Committees: US FDA Should Explain Divergent Decisions But Keep The Vote*" - Pink Sheet, 19 Jun, 2024.)

This suggestion found support in some written comments.

Comments from the Milken Institute's FasterCures team recommended that adcomms continue to use voting to provide recommendations to the FDA and to prompt further advisory committee discussion.

However, "a recommendation using a scaled voting mechanism like a Likert scale might allow committee members to express the ranges of certainty of their recommendations," FasterCures' *comments* state. "This method may replace dichotomous questions, which may be perceived as a determination of the committee members."

> ***"A recommendation using a scaled voting mechanism like a Likert scale might allow committee members to express the ranges of certainty of their recommendations. This method may replace dichotomous questions, which may be perceived as a determination of the committee members." – FasterCures***

Genevieve Kanter, an economist and associate professor of public policy at the University of Southern California, also suggested the agency could ask for a separate assessment of the overall

benefits and risks, each rated on a scale from one to four.

"Given that 'FDA approval of a drug means that ... the drug is determined to provide benefits that outweigh its known and potential risks,' these separate benefit and risk ratings would provide the two determinative elements of an approval stance," Kanter's *comments* state. "In this way, the agency would have useful and nuanced summary measures that provide an approval recommendation but that do not aggravate existing confusion about the role of advisory committees."

Alternatively, Kanter said the agency could request a detailed final approval recommendation document that adcomm members must submit in writing within one to two days of the meeting.

Lykos Therapeutics said a final nonbinding vote may not be the most effective way to gather expert advice for the agency's consideration. "The agency could consider alternative measurement tools, like a Likert scale, be used in place of a vote to enable committee members to effectively assess the briefing submissions," the company's *comments* state.

In June, Lykos endured a negative adcomm review of its midomafetamine for post-traumatic stress disorder. (Also see "*Therapy Component Trips Up Lykos' MDMA At US FDA AdComm For PTSD*" - Pink Sheet, 4 Jun, 2024.) The FDA subsequently issued a complete response letter, recommending the company conduct another Phase III trial of the psychedelic.

Lykos said it plans to raise concerns about the structure and conduct of the adcomm in seeking reconsideration of the CRL. The company pointed to the limited number of subject matter experts on the panel and meeting discussion that at times veered beyond the scientific content in the briefing documents. (Also see "*US FDA Advisory Committee Conduct Could Take Center Stage in Lykos Appeal of MDMA Rejection*" - Pink Sheet, 12 Aug, 2024.)