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Current, Former US FDA Advisory Committee Members' Reform Idea: Allow Conflicted Experts

by Sue Sutter

Conflicted experts should be allowed to participate as nonvoting members and panels should take a benefit-risk vote on product-specific applications, the majority of respondents said in a survey conducted by 3D Communications.

The US Food and Drug Administration should leverage subject matter experts with conflicts of interest as nonvoting participants in advisory committee meetings, a survey of past and current panel members found.

Among more than 400 respondents, 67% said conflicted experts should be able to participate in advisory committees as nonvoting members, while 23% said they should be allowed to attend as voting members and 10% said they should not be able to participate.

In addition, 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. Furthermore, 86% said the FDA should present the proposed verbatim indication for drugs and biologics and ask the external experts to vote on the appropriateness of the language based on the available evidence.

Key Takeaways

- In a survey of current and former advisory committee members, two-thirds of respondents said conflicted subject matter experts should be allowed to participate as nonvoting panel members.

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The survey was conducted by 3D Communications, a consulting firm that prepares sponsors for advisory committees. 3D submitted the results, including comments entered into the free text fields, to the FDA's public docket on advisory committee optimization. The comment period closed on 13 August.

The survey was intended to provide more insight into the perspectives of advisory committee members beyond those that the FDA heard at a 13 June listening session on advisory committee reforms, said Jim DiBiasi, 3D Communications' cofounder.

- Respondents overwhelmingly favored voting on product benefit-risk and said the FDA should adopt procedures to explain why it ultimately takes a discordant decision.
- Most respondents want to give sponsors adequate time to answer clarifying questions, but some worry about prolonging the meeting too much.

The FDA had invited comment on three broad areas: advisory committee composition, service on a commitee as a special government employee, and public perception and understanding of advisory committees. (Also see "*US FDA Adcomm Reform: Does Listening Session Suggest No Major Near-Term Changes?*" - Pink Sheet, 29 Apr, 2024.)

> ***"We thought wouldn't it be great if FDA actually got the opinions of the former advisory committee members." – 3D Communications' Jim DiBiasi***

Several current and former consumer and patient representatives addressed the first and third topics. However, only four individuals with advisory committee experience signed up to speak about SGE service, and only three actually testified.

DiBiasi told the *Pink Sheet* he was surprised that so few panel members spoke at the listening session.

"We thought wouldn't it be great if FDA actually got the opinions of the former advisory committee members," he said.

More Than 1,600 Surveyed

3D Communications summarized the topics discussed by meeting attendees and created 10 survey questions, which were sent to 1,654 current and former FDA advisory committee members. This list encompassed voting members, temporary voting members and nonvoting members across the three medical product centers who participated in a meeting in the past 10 years.

3D received 414 responses, a 25% response rate. More than two-thirds of respondents participated in meetings for the Center for Drug Evaluation and Research or Center for Biologics Evaluation and Research, and more than half of respondents participated in one to three advisory committees in the past five years.

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Conflicted SMEs

Responses to several of the questions provided a clear direction for the FDA, DiBiasi said.

For example, respondents overwhelmingly said that subject matter experts should be allowed to participate, but not vote, in adcomms even if they have conflicts of interest.

Financial conflicts make it difficult to find panelists for many meetings. However, “I don’t understand why they don’t use subject matter experts more often as nonvoting members ... especially in the area of rare diseases and orphan diseases,” DiBiasi said.

“I think at least having them involved in the conversation would be valuable," one respondent said in the free text section of the survey. "COIs, as long as disclosed, should not be an absolute contraindication to participation.”

“I think [it] would entirely depend upon the nature of the COI, e.g. past, current, financial, etc., in some cases, would not recommend inviting them to participate,” another respondent said.

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Benefit-Risk Vote On The Proposed Indication

On voting, “clearly there’s a mandate they should continue to vote on benefit-risk, at least,” DiBiasi said. In the survey results, 54% of respondents said they strongly agreed and 41% agreed that there should be a voting question on benefit-risk for product-specific applications.

More than 80% of survey respondents also favored voting on the proposed indication verbatim based on the available evidence.

Commissioner Robert Califf has expressed disdain for what he calls the "gladiator vote" on product-specific applications, preferring instead to convene advisory committees for general drug development issues that span multiple products. (Also see "*US FDA Advisory Committees' Future: Drug-Agnostic Panels, More Debate Time*" - Pink Sheet, 22 Feb, 2023.)

However, external and internal figures, including Oncology Center of Excellence Director Richard Pazdur, have pushed back against Califf's preference for eliminating voting. (Also see "*Eye On ODAC: Former Members, FDA's Pazdur Talk Pre-Meeting Mindsets, Impact Of Sponsor's Experts*" - Pink Sheet, 20 Mar, 2024.)

At the listening session, industry, public interest group and academic representatives also urged the agency not to abandon voting because it is an important accountability measure. (Also see "*Advisory Committees: US FDA Should Explain Divergent Decisions But Keep The Vote*" - Pink Sheet, 19 Jun, 2024.)

The benefit-risk vote "is an absolutely crucial part of the meeting," one respondent said. "People who have been quiet are forced to take a position and explain why. This is the most public part of the whole approval process, and needs to be maintained."

However, several respondents said the questions must be worded so the voting results are not biased.

"The questions should be fair and balanced without steering the vote to the answer they want or avoid questions whose answers they may not want to hear," one respondent said.

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The Open Public Hearing

More than half of the advisory committee members who answered the survey believe the FDA should take more proactive steps to inform patients and consumers of advisory committee meetings and encourage participation during the open public comment period. However, almost one-third of respondents had no opinion on the subject, suggesting the issue is not a high priority for many current and former panel members.

Some FDA officials and advisory committee members have raised concerns that generally only

patients who benefit from an investigational drug, or their caretakers or principal investigators, are likely to testify during the open public hearing, providing a slanted view of the drug's benefit-risk profile.

At the listening session, consumer groups and academics said OPH testimony is not sufficiently diverse and does not reflect the negative experiences with investigational drugs. In contrast, patient groups said the OPH should pay more attention to the lived experience of patients. (Also see "*US FDA Advisory Committee Open Public Hearing Changes Urged*" - Pink Sheet, 5 Jul, 2024.)

Three-quarters of survey respondents said the agency should continue allowing remote participation for OPH speakers, a practice that began during the COVID-19 pandemic. As the FDA returns to in-person advisory committees in the fall, the OPH session likely will embrace a hybrid format. (Also see "*The Wait Is Over: US FDA Advisory Committees Returning To In-Person Meetings Come Fall*" - Pink Sheet, 26 Feb, 2024.)

The agency recently announced the first fully in-person meeting for a drug application, a 9 September review by the Antimicrobial Drugs Advisory Committee of *Iterum Therapeutics plc*'s oral sulopenem product. (Also see "*Back To White Oak: US FDA Adcomms Go Fully In-Person, Starting With Antimicrobials Panel*" - Pink Sheet, 7 Aug, 2024.)

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Time For Clarifying Questions

On the operational aspects of meetings, 72% of respondents agreed or strongly agreed that advisory committees should allow adequate time for sponsors to comprehensively address all questions and concerns raised by committee members.

However, free text responses reflected concerns that providing more time for sponsors and the FDA to respond to clarifying questions could cause meetings to drag on too long or even span multiple days.

"Within certain limits, and also with guardrails on the amount of time sponsors have to answer individual questions so that they remain focused," one respondent said.

"Sponsors often pivot to answer a question different from the one asked. There must be a time limit for practical purposes," another respondent said.

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Publicly Explaining Discordant Decisions

In line with feedback at the listening session, the majority of respondents said the FDA should make meeting materials available earlier than the current standard of two business days prior to a meeting.

> ***"Advisory committees are advisory, not governing, but we put immense effort in getting to a consensus opinion. It should not be lightly ignored." – Survey respondent***

Establishing clear procedures for the FDA to publicly explain why a regulatory action differed from an advisory committee recommendation also gained overwhelming support among the current and former adcomm members surveyed.

"I don't know how the FDA should address this discordance. This being said, the fiasco concerning Aduhelm cannot be repeated," one respondent said, referencing the FDA's surprise decision to grant accelerated approval for *Biogen, Inc.*'s Alzheimer's drug despite an overwhelmingly negative advisory committee recommendation.

"Advisory committees are advisory, not governing, but we put immense effort in getting to a consensus opinion. It should not be lightly ignored," another respondent said.

This article was reported and previously published by Citeline's Pink Sheet newsletter.

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