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Embrace the opportunities in a changing FDA advisory committee landscape

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Over the past 4 years, we've seen seismic shifts in the conduct of FDA Advisory Committee meetings (AdComs). Changes already in place and those on the horizon are creating new challenges for Sponsors. The biggest challenge has been adapting to the virtual format, which then morphed into a hybrid format, and is now transitioning back to in-person meetings.

In addition, Sponsors have had to deal with tighter timelines for point-counterpoint briefing documents and shared Q&A with the FDA. We've also seen a shift toward meetings laser-focused on the FDA's issues, more discussion and fewer voting questions, more dangling accelerated approval meetings, and more multi-sponsor meetings to review the benefit/risk of an entire drug class. These challenges also create opportunities for a productive and transparent dialog with clinicians and regulators.

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Virtual vs In-Person AdComs

For over 50 years, the FDA has sought external expert advice to guide their regulatory decision making, and the present-day AdCom format was established in the 1990s. That format remained largely unchanged until the COVID-19 pandemic ushered in the first virtual AdComs and marked the beginning of unprecedented changes in how the FDA conducts these meetings.

Virtual AdComs created challenges for Sponsors, making it more difficult for sponsors to make a critical connection with their audience and for committee members to engage in a more organic and collaborative discussion.

Consequently, many say a continuation of virtual or hybrid meetings would be detrimental to all parties involved. But for others, the flexibility offered by virtual meetings is valuable. Virtual meetings do not require travel, which can translate into greater availability of expert panelists and more informed decisions.

Virtual meetings also offer easier access for Open Public Hearing participants, for whom in-person participation might be a barrier. This increased flexibility and accessibility is expected to continue, at least in part. Use of AI could focus on improving efficiencies in publications development rather than jumping too quickly into its content-generation capabilities, where plagiarism and invented references are major shortcomings.

The transition back to face-to-face meetings is beginning. The FDA Oncology Division held its first in-person post-pandemic Oncologic Drugs Advisory Committee (ODAC) April 12, and other divisions have followed. That being said, Deputy Commissioner Namandjé Bumpus, MD, stated during an Alliance for a Stronger FDA webinar that she wants to make sure the logistics for panel members remain as simple as possible to maintain the expert panelists the FDA needs.[1] Dr. Bumpus also highlighted the importance of maintaining an online option for inclusivity; she wants to ensure "...a robust discussion, while also including opportunities for more folks to engage"." To that end, all FDA AdComs are now live streamed on YouTube.

To vote, or not to vote

A variety of other changes to the AdCom process are also on the horizon. FDA Commissioner Robert Califf has appointed Dr. Bumpus to lead a series of reforms that may alter the conduct and tenor of AdComs.[2] Dr. Califf shared that he would like to deemphasize voting questions in favor of more discussion moving forward, noting that votes are not always needed to get the necessary information from committees.[3] According to Dr. Califf, "the purpose of the advisory committee is not to produce gladiator votes, so people say the FDA does not agree with its Advisory Committees. The purpose is to get advice, and the best advice is not whether this drug should be approved. That decision should be made by full-time civil servants."[4] Others at the FDA, including Dr. Richard Pazdur, Director of the Oncology Center of Excellence (OCE), disagree and instead stress the need for voting questions to help the review team "make a binary decision [on] whether to or not to approve a drug."[5]

Dr. Bumpus prefers flexibility, indicating that the most important reason for an AdCom is gathering information that informs decision-making. At a recent webinar, she stated that voting should be on an as-needed basis and that she would like to leverage AdComs to solicit advice earlier in the clinical development process.[1] This sentiment was echoed by recently retired FDA Commissioner Janet Woodcock, who like Dr. Califf, doesn't like "the courtroom-style drama," and she suggested that AdComs should be used earlier in the drug approval process, such as during clinical trial design, rather than to critique the data only at the end of the process.[6]

Indeed, AdComs in 2023 already began to deemphasize voting questions in favor of discussion questions. Even so, there were still 23 meetings last year that had voting questions, leaving only 2 meetings that focused solely on discussion.[7] To get the feedback they need, the FDA typically asks the committee 2 or 3 discussion questions, which may be followed by at least 1 voting question, and committee chairs urge committee members to elaborate on the rationale for their vote.

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The oncology division driving innovation

The OCE, led by Dr. Pazdur, has always been a driving force for innovation at the FDA. The Oncology Division conducts more AdComs than any other and has led efforts to return to in-person meetings. Unlike other divisions, ODAC meetings are typically a half day, and the agenda has recently changed such that the committee can ask questions of either the Sponsor or the FDA during one shared 30-minute Q&A session. That format has led to more back and forth rebuttal and often feels more like a speed debate than a focused discussion of the issues. It puts tremendous pressure on the Sponsor to defend their data and their position.

In 2019, the OCE piloted the point-counterpoint briefing document (BD), similar to an Assessment Aid, that combines the Sponsor's and the FDA's position into one document and is limited to only 35 pages.[8] Sponsors must write the first draft and submit it approximately 60 days prior to the AdCom, after which the FDA adds their position to each section of the document and returns it to the Sponsor 14-21 business days prior to the AdCom. This format is preferred by many committee members, but it provides limited space for Sponsors to tell their story and put their data into context, and it comes with a much more aggressive timeline compared with the traditional BD (3-5 weeks earlier).

The role of sponsor-invited experts

At a recent FDA Workshop called ODAC Chronicles—Past, Present, & Future of Oncology Advisory Committees,[9] Dr. Pazdur had a wide-ranging discussion with a panel of former ODAC members that provides further insights. Regarding ODAC member's perceptions of key opinion leaders who present on behalf of the Sponsor, many indicated that they view them as inherently biased but less so if they can speak from experience about the drug.

Dr. Pazdur suggested that the FDA may consider routinely inviting an independent clinical expert to describe the disease background and unmet need at ODACs, as is common for indications involving rare diseases or in situations where education on the science or therapeutic landscape is needed.

More focused discussion

There has been much speculation that the FDA plans to be more targeted in their approach and convene fewer AdComs in the future. Indeed, some evidence suggests a trend toward fewer AdComs for approvals and more meetings focused on specific issues with more pointed questions to the committee to get targeted advice (similar to Scientific Advisory Group meetings in Europe). Examples of focused meetings include the dangling accelerated approval meetings to discuss confirmatory trials and multi-sponsor meetings to discuss potential withdrawal of approval for a specific drug class. Examples of pointed questions include whether the data can be interpreted or whether the FDA should wait to make a regulatory decision until more data become available. Those types of questions are a clear departure from the standard benefit/risk questions typically posed to committees.

The FDA is listening

On June 13, the FDA convened a listening session on optimizing the use and format of AdComs. More than 50 speakers registered and spoke on topics ranging from the composition of advisory committees to ways to improve the experience for committee members, and ways to ensure public awareness and understanding of the role of FDA AdComs. There were numerous creative ideas about the standard agenda, including letting Open Public Hearing speakers go first, shorter industry presentations, and more time for Q&A. Several speakers urged the FDA to communicate more about AdComs to the wider public and correct misinformation in the press and on social media. Other comments included increasing disclosure of presenters' and committee members' relationships with Sponsors and industry, the need for more subject-matter experts on the committee, and an overwhelming call to retain voting question(s).

The written docket is open until August 13, 2024, and it will be interesting to see what additional ideas and comments are brought forth.

Things to consider if you're faced with an AdCom

In this rapidly changing environment, it is more important than ever that your team is well-prepared for your AdCom. The potential for more sharply focused discussion and Q&A sessions means even greater pressure to provide a clear and compelling scientific story and concise responses to the most challenging questions.

The best advice we offer our clients, based on over 25 years of experience and more than 200 AdComs, is to prepare well in advance. Early alignment on strategy and messaging, even before NDA or BLA submission, is critical. That pre-work allows you to share your rationale for approval in your submission and gives you an immense head start should the FDA indicate an AdCom is necessary. An early start also ensures adequate time for training and practice. It is likely that most of your team members have never had to present or defend data at this type of public meeting. Proper training will calm nerves and ensure the team can present with confidence.

We also advise that you carefully consider the objective feedback provided by outside experts during your preparation process. Well-planned and facilitated mock meetings will give you an accurate assessment of how an advisory committee will view your program and your data—so take their good advice to heart. When selecting clinicians or experts to present on your behalf, it's important to make sure they will be seen by the committee as unbiased and independent and to let them present their objective perspective on the data. Ideally, they should be investigators who have clinical experience with the drug and are well respected in their field.

Finally, although AdComs are often described as debates or trials, we urge to you to view them instead as an opportunity. The AdCom allows you to educate the Committee, the Agency, and the medical community on the benefit/risk of your therapy. A clear, objective presentation and carefully considered responses to the Committee's concerns, presented by a confident, well-prepared team, go a long way to building trust and fostering a productive dialog. That allows the Committee and the Agency to make well-informed decisions, which is what the AdCom process has always been designed to accomplish. ■

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