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To Join Or Not To Join: The Challenges Of A Joint FDA-Sponsor Adcomm Briefing Document

by

3D Communications' Nathan Gede says challenges related to submission timing, length and review format explain why sponsors may be reluctant to agree to a "point-counterpoint" style advisory committee briefing document, despite the Oncology Center of Excellence's move in that direction.

Since 2018, several divisions within the US Food and Drug Administration's Center for Drug Evaluation and Research and Center for Biologics Evaluation and Research have encouraged industry sponsors to submit a joint briefing document with the FDA in advance of advisory committee meetings.

While the current process for joint briefing documents is voluntary, the FDA has recently made public *statements* that any sponsor that does not select a joint briefing document should be prepared to defend their choice at an adcomm.

Briefing documents are a critical element of adcomm meetings. These documents are the first and most comprehensive expressions of the sponsor's and FDA's positions for the meeting.

At face value, the idea of a "joint" briefing document implies collaboration,

Note From The Editor

The article was written by Nathan Gede of 3D Communications in response to recent *Pink Sheet* *coverage* about the FDA Oncology Center of Excellence's push for use of a joint sponsor-FDA briefing document for advisory committees rather than separate documents. The article describes 3D's experience with the factors that have fueled sponsor hesitation to opt into a joint briefing document.

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transparency and openness. If done right, it could provide advisory committee members, patients and the public with a streamlined approach for reviewing and understanding the data.

So why might sponsors choose to stick with a separate briefing document? Is it a simple aversion to change?

OCE declined the *Pink Sheet*'s invitation to write its own commentary in response to 3D's opinion piece. OCE said: "The center's response is that sponsors are encouraged to discuss any concerns about the point-counterpoint document with the relevant oncology division that they have been communicating with throughout the product review process."

Having worked with dozens of sponsor teams considering this choice, 3D Communications has identified practical challenges for sponsors regarding submission timing, length and review format for the joint briefing document. These challenges stem from an underlying concern of sponsors around their uncertainty of the FDA issues to be discussed at the adcomm.

BELOW IS A SNAPSHOT OF HOW THE JOINT BRIEFING DOCUMENT PROCESS UNFOLDS COMPARED TO SEPARATE SPONSOR AND FDA BRIEFING DOCUMENTS.

Consideration	Joint Briefing Document	Separate Briefing Documents
Due Dates for Briefing Document Submissions	Sponsor: At least 2 months prior to adcomm FDA: 20 calendar days prior to adcomm	Sponsor: 22 business days prior to adcomm FDA: 20 calendar days prior to adcomm
Length of Sponsor Briefing Document	Body: 30 pages Appendices: 10 pages	No set limits
Review Structure Prior to Adcomm	Following sponsor submission of completed briefing document sections, the FDA provides counterpoint positions within a highlighted section to draw attention without the ability of sponsor to address added concerns.	The FDA receives the sponsor briefing document 22 business days prior to the adcomm. The FDA submits its own briefing document 20 calendar days prior to the adcomm.

Uncertainty Around Concerns, Discussion Topics

Uncertainty of FDA concerns and discussion topics creates major inefficiencies in adcomm preparation and typically leads sponsors to choose separate briefing documents.

To effectively prepare for an adcomm, companies need to understand what topics will be discussed along with the underlying concerns, limitations and issues that have prompted the question(s) to the advisory committee. For a drug or biologic product, those issues typically do not become known until the FDA briefing document is received by the sponsor 20 calendar days before the adcomm.

This uncertainty introduces three significant barriers to the use of a joint briefing document.

- Requiring the sponsor to submit their joint briefing document one month earlier than a separate briefing document dramatically affects their ability to tackle the FDA's concerns. The briefing document content is intended to anticipate FDA issues and potential discussion points the agency will raise at the advisory committee meeting. An earlier due date means the sponsor will have less time to investigate and address issues that may be discussed during a late-cycle review meeting.

- Limiting the number of pages a sponsor can submit reduces the ability of sponsors to comprehensively present the data and provide context around gaps and limitations. The traditional format for adcomm briefing documents allows the FDA and sponsor to provide any material necessary for the panelists to be informed on the meeting's topics. This is especially important for sponsors since the FDA's specific issues may be unknown at the time of briefing document submission, and it is therefore incumbent upon the sponsor to ensure their coverage of the data is more comprehensive than a joint briefing document would typically allow. Note that while there are no limitations on length for a traditional briefing document, all data included must have been previously submitted to the FDA. While briefing documents should be concise, it is essential that the adcomm members have sufficient material to engage in a balanced and informed discussion on the meeting issues.

- The current point-counterpoint review structure creates a potential imbalance of perspective in favor of the FDA over the sponsor. The reality is that in most adcomms, the sponsor and FDA have substantive differences in how they interpret the issues and how the data support their respective positions. Sponsors submit their sections of a joint briefing document based on speculation of the actual issues and are not afforded an equitable opportunity to review and comment on the FDA's counterpoints prior to release of the briefing document to the committee members. This imbalance allows the FDA to focus on the issues they dispute whereas the sponsor creates their briefing document effectively in the dark, without an opportunity to respond to FDA counterpoints.

This uncertainty also explains why sponsor briefing documents are often longer than their FDA counterparts. Sponsors are effectively trying to make educated guesses on the issues and questions the FDA will raise to the committee.

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The mid-cycle review meetings are intended to communicate ongoing review issues but frequently do not resolve uncertainty. The meeting is held while the review is ongoing and topics for a future adcomm are still evolving. This typically results in vague communication of the issues and significant uncertainty regarding how those review issues might be shared with an advisory committee.

Generating a briefing document without knowledge of regulator discussion topics – as done today – means that sponsors must have the flexibility to determine content that is relevant for understanding benefit-risk. That is why it may be counterproductive to ask a sponsor to submit a joint briefing document with more limitations on length, content and deadlines, without any additional guidance on the issues or the ability to react to FDA concerns.

Source: 3D Communications

What's The Solution?

The FDA's goal of streamlining the preparation process for adcomm members by submitting a joint briefing document has merit, and all parties have a vested interest in an efficient review process, including adcomms. However, the solution should be a process that provides more bilateral consideration and open/iterative discussions between the FDA and sponsors.

The concept of a collaborative briefing document is not new for the FDA. In fact, the Center for Devices and Radiological Health has had a more collaborative process in place for years with some key differences. The first is that the CDRH process is more iterative. CDRH and medical device makers exchange draft executive summaries (i.e., briefing documents), review the other party's materials, and provide comments on them before they are sent to the adcomm members. This process could be adapted to CDER/CBER. Following a process that has been time-tested at the FDA may be a more prudent option for both sponsors and the FDA.

The FDA may be surprised to find that sponsors would be amenable to earlier briefing document timelines, as well as page and content limitations, if the FDA made a concerted effort to be more transparent around the discussion topics and key issues for an adcomm.

Under the current structure, the joint briefing document option will, and should, remain available to sponsors. It is important, however, that both the FDA and sponsors consider the factors outlined above for separate briefing documents to ensure advisory committee members can conduct a more comprehensive and objective evaluation. Given these factors, it seems

unwarranted to call out or otherwise stigmatize a sponsor that elects to submit a separate briefing document from the FDA for such a critical meeting.

We at 3D Communications hope that all parties continue to take a circumspect view of all potential factors and perspectives that may give rise to such a decision. We encourage industry and the FDA to continue working together to refine the process to make joint briefing documents a more attractive option for all parties.

Nathan Gede is 3D Communications' chief operating officer and leads the regulatory communications division. Over the last 20 years, 3D has partnered with more than 300 health care companies, preparing them for more than 450 advisory committee meetings.