

DATA MONITORING COMMITTEES IN CLINICAL TRIALS: FDA DRAFT GUIDANCE RELEASED

Earlier this year, the U.S. Food and Drug Administration ("FDA") announced the availability of new draft guidance titled "[Use of Data Monitoring Committees in Clinical Trials](#)" ("Draft Guidance"). When finalized, the Draft Guidance will supersede the March 2006 guidance titled "[Establishment and Operation of Clinical Trial Data Monitoring Committees](#)."

A Data Monitoring Committee ("DMC") (also known as a data and safety monitoring board, a data and safety monitoring committee or an independent DMC) is a team of experts who regularly reviews data from clinical trials and recommends to the sponsor whether to continue, modify or stop a trial. Under current FDA regulations, there is no requirement for the use of DMCs except under 21 C.F.R. § 50.24(a)(7)(iv), which pertains to research studies in emergency settings, where an Institutional Review Board ("IRB") can approve a clinical trial without requiring that informed consent be obtained from all research subjects as long as certain requirements are met.

Given the growing use of DMCs, the FDA recognized in the Draft Guidance the need to provide additional guidance to help clinical trial sponsors determine when a DMC would be beneficial, while also outlining best practices for establishing and operating these committees.

Highlights from the Draft Guidance are outlined below.

DETERMINING WHETHER TO USE A DMC

According to the Draft Guidance, a key consideration in determining whether to use a DMC in a development program is "whether DMC review is practical for the particular clinical trial." The FDA acknowledges that while the practicality of having a DMC is well-established for long-term clinical trials, it is not always as clear for short-term trials. The FDA also recognizes that DMCs may not be feasible for every study, such as with trials with fast enrollment and a short follow-up period. Despite these challenges, the FDA notes that even with short-term trials specific mechanisms might still be developed to permit timely DMC evaluation (for example, via pauses in advance of dose escalation) or to conduct data and safety oversight in an expedient manner (for example, by an independent monitor).

The FDA recommends considering a DMC in situations such as: (1) when there is prior information suggesting the possibility of serious toxicity with the study treatment, or there is limited experience in the therapeutic area; (2) when the study involves vulnerable groups like neonates; or (3) in large-scale, long-term or multi-center studies. Notably, the FDA now advises that IRBs "should inquire" about the establishment of DMCs in trials that carry significant risks or involve vulnerable groups.

DMC MEMBERSHIP COMPOSITION

The FDA underscores the importance of assembling a DMC with a diverse array of expertise to oversee the integrity and safety of clinical trials. The Draft Guidance clarifies FDA expectations by strongly recommending the inclusion of at least one biostatistician with a deep understanding of statistical methods for clinical trials to align with FDA standards. The FDA also strongly encourages sponsors to proactively address the learning and training needs of DMC members before their first meeting and on the inclusion of experts in informatics and technology. The DMC should include professionals experienced in clinical trials, specialists in relevant medical fields, as well as individuals well-versed in FDA regulatory requirements and DMC operations. Finally, for trials involving significant risks or having broad public health implications, the FDA recommends adding a medical ethicist to the DMC.

CONFLICT OF INTEREST ISSUES

The FDA strongly advises careful consideration of conflicts of interest in selecting DMC members. Specifically, the Draft Guidance points out the risk of financial conflicts, where a member's financial interests could be significantly impacted by the trial's results. To that end, the Draft Guidance suggests that DMC members "should have no" financial ties to the trial's commercial sponsor or its direct competitors, refining the 2006 guidance's suggestion that members "generally have no" such relationships. This update also includes a broader scope of concern by addressing potential conflicts with the sponsor's direct competitors, an aspect that the 2006 guidance did not explicitly cover. To prevent such conflicts, DMC members, beyond receiving compensation for their committee work, are expected to maintain independence from the trial's sponsor and avoid participation in the trial outside of their DMC roles. The Draft Guidance also cautions against selecting individuals

with strong pre-existing opinions on the trial's interventions, as such intellectual biases could hinder objective data review.

PRACTICAL TAKEAWAYS

- For clinical trials with potential risks of "serious morbidity or mortality," involving vulnerable populations, or characterized by their large scale, long duration, or multi-center nature, sponsors are encouraged to establish a DMC to preserve the trial's integrity and participant safety through proper oversight. Similarly, the FDA recommends that IRBs inquire whether a DMC has been established for these types of trials, and if so, to request information about its scope and composition as part of its oversight.
- A DMC should be composed of a multidisciplinary team, including clinical trial experts, medical specialists, biostatisticians, informatics and technology experts, and, for high-risk trials, a medical ethicist.
- In selecting DMC members, sponsors should ensure both financial and intellectual conflicts of interest are identified and properly managed.

For tailored insights and guidance on how this Draft Guidance could impact your clinical trial, or if you would like assistance with comment submission, please contact:

- **Melissa Markey** at (248) 310-4876 or mmarkey@hallrender.com
- **Carolina Wirth** at (202) 780-2989 or cwirth@hallrender.com;
- **Avi Kerendian** at (214) 615-2038 or akerendian@hallrender.com;
- **Benjamin Lockwood** at (414) 721-0484 or blockwood@hallrender.com; or
- Your primary Hall Render contact.

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