DMC vs IRB: What's the Difference?

By James Riddle, Vice President of Research Services & Strategic Consulting
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Clinical trials can be complex. Multiple treatment arms, various dosing schedules and regimens, placebo controls, multifaceted endpoints, blinded study staff, pragmatic design elements, and multinational sites all fuel the complexity. Not surprisingly, clinical trials receive a lot of oversight from regulatory agencies as well as independent committees, who oversee different aspects of the trial. Institutional review boards (IRB), also known outside the US as research ethics boards (REB), ethics committees (EC), or independent ethics committees (IEC), are likely the most well-known of the independent oversight committee functions. (For the sake of simplicity, in this article we'll refer to this committee as an IRB.)

However, depending on the nature of the trial, other independent committees may be involved in oversight, including institutional biosafety committees (IBC), scientific review committees (SRC), endpoint adjudication

committees (EAC), and data monitoring committees (DMC), just to name a few. All play an important role in providing trial oversight, keeping participants and research staff safe, and helping the IRB make its determination that a trial has an adequate safety monitoring plan as required by FDA regulation 21 CFR 56.111(a)(6).

In this blog we will take a look at the specific role DMCs play in overseeing research, and how IRBs rely on the independent DMC's oversight of interim trial data to ensure an adequate safety monitoring plan is in place.

What Is an Independent Data Monitoring Committee (DMC)?

A DMC is an independent group of experts that conduct a periodic review of accumulated interim data during a clinical trial. DMCs are strenuously recommended for certain clinical trials by both US FDA and EU EMA guidelines.

Particularly in trials with a blind or placebo control, the purpose of the DMC is to review unblinded trial data as it is collected to detect and report safety concerns, early evidence of benefit or harm, and futility of the treatment, using criteria outlined in the clinical trial protocol. DMCs are typically comprised of 5-6 members, including biostatisticians and clinicians, who all must be independent of the trial sponsor.

Sponsors are responsible for creating the DMC for the trial or engaging an independent firm to create and administer the DMC on the sponsor's behalf. Many sponsors use independent administrators to support separation and independence of the DMC as an independent oversight committee.

The DMC will typically operate under a detailed charter outlining what data the committee will review, how members are selected and vetted for conflicts, and other operational considerations governing how the committee will be run, including the format for reporting and providing recommendations back to the sponsor.

Understanding When Data Monitoring Committees Are Needed

FDA guidance outlines when the agency expects a DMC to be created. However, sponsors may engage independent DMCs for other types of studies, and on occasion, the IRB may determine there is a need for a DMC as part of the clinical protocol's overall data safety monitoring plan.

In brief, the FDA recommends that sponsors consider using a DMC when:

- The trial is blinded or has endpoints, such that an independent group must evaluate unblinded data to determine if the study has met pre-determined endpoints, futility, or other stopping rules and should be terminated early
- There are other reasons for a safety concern, e.g., a particularly invasive procedure
- There is prior information suggesting the possibility of serious toxicity where interim analysis of adverse event data is necessary to determine if toxicity endpoints are met
- The trial is large, or of long duration, and multicenter, where a single group in needed to evaluate and analyze the consolidated interim study data

Most commonly DMCs are created for later phase, randomized, drug and device studies where there is a need for an independent committee to evaluate interim study data for emerging participant safety issues and to determine

if stopping rules have been met.

The DMC is advisory to the sponsor and provides an opinion, based on interim analysis, as to whether the trial should continue as it has been, receive changes to the trial design, or be stopped early. Most DMC charters give the committee the power to make recommendations only. Unlike the IRB, which under the FDA regulations has authority to disapprove or terminate approval for research (21 CFR 56.113) the DMC only plays an advisory role to the sponsor.

What's the Difference Between a Data Monitoring Committee (DMC) and a Data Safety Monitoring Board (DSMB)?

FDA guidelines use the terminology of "independent clinical trial data monitoring committees" – quite a mouthful. For short, both FDA and EMA simplify to "data monitoring committee" as the term describing the group, independent of the sponsor, who is charged with looking at the data to determine when trial endpoints, and other milestones, are met.

In North America, these groups are also referred to as data safety monitoring boards (DSMBs). In other parts of the world, they are also known as data and safety monitoring committees (DSMCs), independent data monitoring committees (IDMCs), and other similar titles. Regardless of the name, the concept and purpose of these committees are the same – providing independent oversight of certain aspects of the study, and in blinded research evaluating unblinded study results to determine if endpoints and other milestones have been met.

Where Do DMCs Fit With IRB Review?

US FDA regulations stipulate IRBs must determine that "where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects." (21 CFR 56.111(a)(6))

The IRB must determine if an adequate "**plan**" is in place to adequately monitor data to "**ensure**" the safety of the participants (emphasis added). This is typically referred to in the clinical protocol document as the "data safety monitoring plan" (DSMP).

One of the primary ways a sponsor satisfies this regulatory requirement is to utilize an independent DMC as part of the plan. The IRB will typically view a monitoring plan which incorporates an independent DMC as "adequate provision" to ensure data is being monitored for safety.

During the trial, as part of the required continuing review process, IRBs typically request copies of the DMC's recommendations to the sponsor. In this way, the IRB can leverage the work of an independent DMC and its recommendations to determine if there is any new information which may impact the IRB's decision to approve the research to continue, require alterations to the research, inform participants of potential new risk information, or not approve the research to continue (21 CFR 56.109(f)).

Conclusion

IRBs do not see unblinded study data and are not in a position to know unilaterally if trials have met stopping

rules. They must rely on review by the independent DMC, and other oversight committees, to work collaboratively to protect clinical trial participants.

At Advarra, our IRB diligently reviews each trial's data safety monitoring plan to ensure it is adequate to satisfy the FDA regulatory criteria. Many times, the safety monitoring "plan" will include an independent DMC, and in these circumstances, the IRB routinely verifies if the DMC recommends stopping the trial early or making any changes to reduce participant risk. The DMC and IRB are two committees, with different roles and focuses, both working together to independently oversee a clinical trial and the safety of the participants

More insights on Advarra's requirements for DMC can be found in our IRB Handbook for Investigators, Institutions, Sponsor, and Sponsor Representatives in CIRBI (login required).

Have questions about how IRBs review plans for data monitoring? Get free answers to your most pressing research questions in 1 business day when you Ask the Experts-Ask Advarra.– ASK THE EXPERTS!

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