Academic chartered data safety committees versus industry sponsored data safety committees: The need for different recommendations

Dear Editor,

We read with great interest the recently published paper by Calis et al.[1] We applaud the authors and the working group for developing this important set of recommendations for data monitoring committees (DMC). Recommendations for organizing a DMC are long overdue. Our academic institution has had a formal DMC for many years which administratively reports to an academic official who directs the research efforts. It has a formal charter and broad membership that includes clinicians, clinical trial specialists, and a biostatistician. It accepts for review studies that require a DMC (usually phase II or III trials) and are not sponsored by industry, which usually set up their own DMC. Most studies are supported by the institution, US Government research funding sources (e.g. National Institutes of Health (NIH), Centers for Disease Control and Prevention), or research foundations.

The recommendations by Calis et al. appear to be focused on a DMC organized by industry (e.g. drug company or device manufacturer). However, a standing DMC organized by an academic institution often operates using a different set of rules with regard to the following: (1) reporting structure, (2) independence, and (3) conflicts of interest. In addition, and in contrast to an industry-sponsored DMC, an academic DMC often determines whether such oversight is necessary and is in the best interest of subject safety. All clinical trials need a plan to assure subject safety, but safety and trial integrity in low risk or small trials may be better served by an independent safety monitor with direct reporting to an Institutional Review Board (IRB). Finally, there is an intermediate type of academic DMC; a study-specific DMC constituted for a multicenter study run through academic institutions and funded by the NIH or a research foundation.

First, Calis et al. recommended that DMC reports be "provided to a steering committee or sponsor leadership group authorized to act on these recommendations, and not to those directly involved with implementation of the trial." At our academic institution, our DMC reports are sent to the principal investigator (PI) and then forwarded by the PI to our IRB. The IRB has the authority to require modifications in the study, suspend enrollment in the study, or terminate the study. The PI may also forward the DMC report to the funding source for the study.

Second, Calis et al. recommended that "independence from the trial sponsor is critical for the DMC to fulfill its central role of protecting vulnerable study participants from unpredictable harm that may arise during the course of a trial." Typically, industry-sponsored DMCs are composed of members who receive no funds (e.g. employment, research funds) or benefits (e.g. stock) from the company. However, academic DMCs are typically composed of faculty and employees of the academic institution. Independence is assured, in part, by policies similar to those that govern the academic IRB that prohibit interference in the functioning of the DMC. We are unaware of any academic DMC that includes only members who receive no funds or benefits from the academic institution. For the intermediate type of DMC, members are generally not from the centers conducting the study but will usually have their own funding from the NIH and are thus not strictly independent from the trial sponsor.

Finally, Calis et al. recommended that

> Conflict of interest must be regularly disclosed, assessed, and managed for all DMC members….Activities or relationships deemed to have the potential to undermine independence of DMC members may result in disqualification from DMC service; therefore, both actual and perceived conflicts should be disclosed. Even the perception of a conflict of interest can damage the credibility of the DMC and raise questions about its conduct and recommendations.

At academic DMCs, all members routinely disclose potential conflicts. Members with a close relationship to the research or investigators (e.g. co-investigator, mentor, etc.) abstain from participating in the review.

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However, members in the same department or school are usually permitted to participate in the review.

Again, we thank Calis and his collaborators for this important paper. However, we think the recommendations should be revised to take into account the unique features of an academic DMC.

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Reference

1. Calis KA, Archdeacon P, Bain R, et al. Recommendations for data monitoring committees from the Clinical Trials Transformation Initiative. *Clin Trials* 2017; 14: 342–348.

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