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Memorandum

To: Trialists

Fr: Curtis Meinert

Re: When is a meeting a meeting?

In Matthew (Ch 18; v 20), a meeting is a gathering of two or more, but Matthew was not a trialist. Had he been he, no doubt, would have had a better definition.

You will need one if you are responsible for a trial with a data safety monitoring board (DSMB).

> *Effective July 1 (1999), all multi-site trials with data safety monitoring boards are expected to forward summary reports of adverse events to each IRB involved in the study.*
>
> *The DSMB's summary report should provide feedback at regular and defined intervals to the IRBs. The Institutes and Centers should assure that there is a mechanism in place to distribute the report to all participating investigators for submission to their local IRB. For example, after each meeting of the DSMB, the executive secretary should send a brief summary report to each investigator. The report should document that a review of data and outcomes across all centers took place on a given day. It should summarize the Board's review of the cumulative toxicities reported from all participating sites without specific disclosure by treatment arm. It should also inform investigators of the study [of] the Board's conclusion with respect to progress or need for modification of the protocol. The investigator is required to transmit the report to the local IRB.*
> (http://grants.nih.gov/grants/guide/notice-files/not99-107.html; 1999 NIH guidance for NIH-funded trials)

The guidance instructs investigators responsible for NIH-funded trials, but most IRBs are "color blind" to funding. Hence, they have the same reporting expectation regardless of how the trial is funded.

So, if you are responsible for a trial with a DSMB, how do you decide when a DSMB meeting is a meeting? Use a corollary to the "duck rule". That is, it is a meeting if it takes place after the start of enrollment and

> *It looks like a meeting, sounds like a meeting, and operates like a meeting*.

It is a meeting (hence reportable) whether it is a regularly scheduled meeting or a special meeting.

Operationally it is prudent to regard the DSMB to have met if any of the following apply:
Safety and efficacy data are reviewed
Performance data reviewed or issues of performance are considered

Votes are taken on recommendations to be passed to study leaders
Minutes are produced

It is not a meeting if quorum requirements are not met. Implicit to the quorum requirement is presence of people (usually nonvoting) to present results; typically persons from the coordinating center responsible for generating monitoring reports.

Usually, the director of the coordinating center is responsible for reporting meetings to his/her IRB and for informing heads of study clinics and other center directors of meetings so they can, in turn, inform their respective IRBs of meetings. "Standard" letters indicate the time of the meeting, method of meeting (face-to-face, conference phone), and recommendations of the committee. The typical letter does not indicate anything about results unless there is a recommendation to stop the trial for reasons of safety or efficacy.

The reporting process is not without risks, especially in relation to proprietary products tested under INDs or IDEs. Informing clinics and IRBs of meetings involves 100's if not 1,000's of people. Consider a study with 30 centers, each with a director and five staff members, and 30 IRBs, each comprised of 10 members and 5 related staff members for a total of 630 people. Double or triple that number when you consider fellow colleagues and family members.

The communications to clinics and IRBs typically does not reveal results but it does not take a genius to figure out that something is happening if meetings become more frequent. That reality, alone, can fuel rumors leading to insider trading if the trial involves proprietary products. The chance of speculation is increased if the sponsor is obliged to report meetings to regulatory authorities.