HHS Public Access

Author manuscript

Clin Trials. Author manuscript; available in PMC 2018 April 01.

Published in final edited form as:

Clin Trials. 2017 April ; 14(2): 126–127. doi:10.1177/1740774516688917.

Rejoinder

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The roles of the DMC include safeguarding the interests of trial participants and enhancing the integrity and credibility of clinical trials. Thus, DMCs should be accountable first to trial participants, and then more broadly to care givers, institutional review boards, regulatory authorities, sponsors and the broader clinical and scientific communities. To aid DMCs to better meet these responsibilities, there is a need to identify and implement best practices to address ongoing and emerging challenges that potentially threaten DMCs' independence and effectiveness.

In his commentary, Terrin[1] advocates defining metrics for DMC performance and effectiveness to guide the development and implementation of best practices and the

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systematic collection of relevant data to evaluate them and to make well informed decisions. We agree that identification of DMC best practices should be enlightened by broad experiences. While the ideas proposed by Terrin are appealing in principle—having metrics to assess quality of performance certainly sounds useful—it is not clear how, or even whether, such metrics could be developed and implemented in a standardized way to yield useful data, given the widely disparate hypotheses tested across trials as well as the different philosophies about designs for their monitoring and early termination. There also is inherent need for judgment by DMC members in weighing the overall evidence especially when safety concerns are identified, and there is considerable diversity across trial settings in how such information would be provided and the extent to which meaningful safety issues emerge. Additionally, while DMCs often make recommendations about improving the quality of trial conduct, it is not clear how one would assess DMC performance and effectiveness in enhancing metrics regarding quality of conduct since the DMCs have at best moderate levels of indirect influence on the actual day-to-day conduct of the trial. Without knowing what sorts of metrics Dr. Terrin had in mind, and how he thought they might be developed and implemented, it is difficult to further assess the merits of his proposal. Importantly, even if the development of such metrics were feasible, considerable time and effort would be needed to develop and broadly implement a properly standardized approach that would reliably address the breadth of relevant issues.

We believe that, given the already widespread and increasing use of DMCs, there is a more urgent need to reconsider DMC best practices. A recent publication provided insights obtained through the approach of conducting a survey and a set of focus groups.[2] We pursued a complementary approach of engaging an expert panel for two days to share insights about best practices. This panel had fifty representatives from academic medical centers, academic research organizations, the pharmaceutical and biotech industry, the National Institutes of Health, and the U.S. Food and Drug Administration. The organization and agenda for the panel meeting were established by academic leaders, independently from the commercial organizations that covered meeting expenses. Our article in this issue of *Clinical Trials* summarized these discussions, providing enlightenment and recommendations for the improvement of the DMC process based on extensive insights from meeting participants rather than anecdotal evidence. These participants not only represent wide areas of expertise in the DMC process but also collectively have DMC experience in hundreds of clinical trials, with many having been involved in development and implementation of DMC guidelines for decades. We believe implementing these recommendations for consensus best practices and operating principles for effective functioning of DMCs will enhance their ability to properly meet their scientific and ethical responsibilities.

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