The Data and Safety Monitoring Committee: Some final thoughts

David L. DeMets, PhD, and Salim Yusuf, MD

The randomized clinical trial (RCT) has become a principal research tool in the evaluation of new medical products, including drugs, biologics, and devices. A critical component of the RCT in studies that investigate mortality or irreversible morbidity is the Data and Safety Monitoring Committee (DSMC). The American Heart Journal has now published all seven articles in a series that presents the proceedings of a conference on DSMCs that was sponsored by the Duke Clinical Research Institute (DCRI) and the American Heart Journal. It was our privilege to serve with Dr Robert Califf and Dr Kerry Lee as cochairpersons for the conference, and it is our hope that this series on the philosophy and practice of DSMCs will be widely read.

As these articles make clear, the DSMC is a vital part of the organizational components of a clinical trial, which includes the Steering (or Executive) Committee, Data Management Center, Statistical Analysis Center (sometimes the latter two are combined into a Data Coordinating Center), and participating clinical centers. The primary charge of a DSMC is to monitor the ongoing trial for safety and for early convincing evidence of a trial benefit in the therapy under investigation, in which case it may recommend early termination of the trial for safety and for early convincing evidence of a treatment. The subcommittee functioned essentially as an early DSMC; its activities and decision making were summarized later in an article by Dr Paul Canner. Soon after, in the late 1960s and early 1970s, as other NHLBI trials were launched to study hypertension, blood diseases, and pulmonary diseases, the DSMC model was repeated and became the standard for that institute. In the early 1970s the National Eye Institute began the Diabetic Retinopathy Study and it also used a DSMC for its investigation. Over time, DSMCs became more widely used in trials sponsored by the National Institutes of Health, which now requires DSMCs for all its phase III trials. In recent years academia and industry have increasingly partnered to conduct large-scale, pivotal phase III trials for new therapies; in this environment, DSMCs have more and more frequently been integrated into the organizational structure for trials studying effects on mortality rates and irreversible morbidity outcomes.

Although some accounts of the experiences of DSMCs in specific trials have been published, the DSMC as an actual functioning entity has not, despite having a history of more than 40 years, been widely discussed in the literature. Consequently, its proliferation in contemporary studies is often accompanied by confusion about its role, scope, organization, and the rules by which it operates. The articles in this series have addressed many practical questions that any sponsor of an RCT must consider when forming such a committee. For many of...
the issues raised in these articles, there is no single point of view or consensus among the experts who assembled for the DCRI/American Heart Journal conference, all of whom have extensive experience with clinical trials and DSMCs. Yet a great deal of insight can be gained from their discussions, and many of the practical and tested recommendations in these articles speak to the very questions that the wider community often raises about trials and their DSMCs. We hope that readers of this series find it enlightening and enjoy studying the proceedings as much as we enjoyed planning and participating in the conference that inspired them.

References