concepts, as far as the present clinical trial is concerned, is that the data available to date convincingly show that the drug works, that the toxicity of the drug is overwhelmingly unacceptable, and that there is little hope that the drug can ever be shown to work, respectively. To repeat, the DMC cannot mandate that the trial be stopped, or that the Clinical Study Protocol be amended. The DMC can only make recommendations to the Sponsor or investigator.

For any clinical trial, all study subjects must read, understand, and sign a consent form. But where unforeseen adverse events occur, the DMC may suggest that a new consent form be drafted, that is, a "re-consent form," and that study subjects read and sign the reconsent form. In addition, where unforeseen adverse events occur, the DMC may suggest that the Clinical Study Protocol be amended to identify the newly emerging adverse events.

Where adverse events seem to affect only one of the subgroups of the clinical study, the DMC may suggest that subjects in this particular subgroup be dropped from the study, and that potential subjects falling in this subgroup be excluded, during the on-going process of enrollment. This function of the DMC clearly shows the wisdom and advantage of defining subgroups in the Clinical Study Protocol. Hence, in configuring the subgroups in the study population, the investigator or medical writer should divide subjects into those with high, moderate, and low risk, for any foreseeable ADRs. It is much better to exclude one particular subgroup from the clinical trial than to terminate the entire clinical trial.

Along similar lines, the DMC may recommend increased surveillance of specific adverse events, where the DMC suspects that a certain type of adverse event is not being adequately detected (409).

The FDA's Establishment and Operation of Clinical Trial Data Monitoring Committees provides a brief introduction to the DMC's structure and functions (410). DeMets et al. (411) have written an indispensable account of the activities ofDSMCs.

b. The DMC Charter

The responsibilities of the DSMC are formally set forth in a DMC Charter (or DSMC Charter). The DMC Charter, which can be written by a medical writer, is tailored to the needs of the clinical trial. The Charter can provide a schedule of meetings used for interim analysis. The meetings may be scheduled according to calendar dates, or in a manner that tracks the number of patients being enrolled as the trial unfolds. If the clinical trial has stopping rules, the Charter provides the statistical bases for stopping for benefit, stopping for safety, and stopping for futility. The following is a draft of a DMC Charter, based on a composite of the author's own work, in combination with a published DMC Charter (412). The name of the company, *PharmaDrug, Inc.*, is fictional.

[409]Grant AM, Altman DG, Babiker AB, et al. Issues in data monitoring and interim analysis of trials. Health Technol. Assessment 2005;9(7) (246 pp.).

[410]U.S. Department of Health and Human Services. Food and Drug Administration. Guidance for clinical trial sponsors. Establishment and Operation of Clinical Trial Data Monitoring Committees; March 2006.

[411]DeMets DL, Furberg CD, Friedman LM. Data monitoring in clinical trials.New York: Springer; 2006.

[412]Data Monitoring Committee (DMC) Charter for the Eurother3235 Trial (version 1.0 27/04/2009).