TEMPLATE

DATA MONITORING COMMITTEE (DMC) CHARTER FOR PRAGMATIC CLINICAL TRIALS

TITLE OF PROTOCOL:

PROTOCOL NUMBER:

SPONSOR OF PROTOCOL:

DATE OF DOCUMENT:

[***Delete explanatory text before finalizing Charter:*** This template is provided by the NIH Health Care Systems Research Collaboratory Regulatory/Ethics Core as a customizable Charter for data monitoring committees (DMCs) for pragmatic clinical trials. In addition to procedures and guidance for DMCs generally, it contains suggested practices specifically for DMCs for pragmatic clinical trials. Throughout the template, text in italics is intended to be replaced by the user with specific details. For more information on data and safety monitoring for pragmatic clinical trials, please see the NIH Collaboratory Data and Safety Monitoring Living Textbook chapter. This template was last updated August 22, 2017.]

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1. INTRODUCTION

This Charter is for the Data Monitoring Committee (DMC) for **[*protocol number, protocol title*]**.

This Charter defines the primary responsibilities of the DMC, its relationship with other trial components, its membership, and the purpose and timing of its meetings. The Charter also provides the procedures for minimizing conflicts of interest and ensuring confidentiality of emerging data and deliberations of the DMC, as well as statistical monitoring guidelines to be considered by the DMC, if any. It will also address the content of the Open and Closed Reports that will be provided to the DMC.

2. PRIMARY RESPONSIBILITIES

The DMC will be responsible for safeguarding the interests of trial participants by assessing the safety and efficacy of the interventions during the trial, and for monitoring the overall conduct of the clinical trial to ensure that trial results will be interpretable and of value to medical practice. The DMC will provide recommendations to **[*study sponsor, study leadership*]** about stopping or continuing the trial, or making modifications to enhance safety of trial participants and/or the value of the information collected, or to protect the integrity of the study.

To meet its responsibilities, the DMC will:

a. Prior to study activation, review the relevant study documents [***study protocol, statistical analysis plan, site monitoring procedures, informed consent template, and/or any other materials used to provide information about the study to potential participants***] and recommend any modifications deemed important to enhance safety of participants, to improve the integrity of study results, or to better ensure privacy of data.

   Note: The study investigators and/or study sponsor hold primary responsibility for study design; the institutional review board(s) hold primary responsibility for evaluating the informed consent documents. Nevertheless, should the DMC identify important flaws in any of these documents, they should bring them to the attention of the study leadership. It is important that DMC members have a full understanding of the study and its potential risks and benefits, and establish that they can support the goals and procedures of the study prior to taking on the responsibilities of interim review of emerging data.

b. Contribute to the development and finalization of the DMC Charter.

c. During trial conduct, review the DMC reports that present interim efficacy and safety data as well as data addressing trial progress and data quality, and make recommendations pertinent to safety of trial participants and/or the ability of the study to yield information of value.

3. MEMBERSHIP OF THE DMC

The DMC members will be appointed by the study sponsor, with input from study investigators. Once appointed, members cannot be removed except for chronic nonattendance at meetings, development of an unacceptable conflict of interest, or following determination by the DMC Chair that the member cannot contribute constructively to discussion and development of recommendations. In the latter case, the DMC Chair will apprise the sponsor of the need to remove the member from the committee.

3.1 List of Members

DMC Chair:	***Address*** ***Telephone/FAX*** ***Email address***
DMC Biostatistician(s):	***Address*** ***Telephone/FAX*** ***Email address***
DMC Clinicians:	***Address*** ***Telephone/FAX*** ***Email address***

Minimally, clinical and biostatistical expertise are needed for a DMC. Bioethicists and patient representatives are also frequently included on a DMC. Any other required discipline should be added. Expertise in clinical informatics and/or use of healthcare–based data systems may be needed for trials utilizing electronic health records. All members, with contact information, should be listed.

It is desirable that one or more members of the DMC (ideally the Chair) have prior experience in conducting and interpreting data from pragmatic clinical trials.

Agreement to serve as a DMC member carries a high commitment to attend all meetings except under rare circumstances.

3.2 Conflicts of Interest

The DMC membership should be restricted to individuals free of apparent significant conflicts of interest. The fundamental principle underlying conflict of interest determinations is as follows: no DMC member should have any basis for preferring the study outcome to be in one or the other direction (other than preferring that treatments that improve outcomes be identified), and no DMC member should have any means of influencing the conduct of the study in ways other than as a DMC member.

Conflicts that would generally preclude DMC membership include the following:

a. Employment by the sponsor of this trial, or by manufacturers of any products that are being evaluated or that are competitive with those being evaluated; or

b. Ownership of stock in the companies having products being evaluated by the clinical trial or that have products competitive with those being evaluated, other than diversified mutual funds not focused on medical products and with choice of stocks not under control of the committee member; or

c. Having had a leadership role in the scientific development of the products being evaluated by the clinical trial; or

d. Potential to be providing clinical care for participants in the trial; or

e. Participating as a subject in the trial, or having a close relative or friend who is participating as a subject in the trial; or

f. Potential to have regulatory responsibilities for the trial products.

Newly arising activities that could potentially pose a conflict of interest should be reported annually. [***Specify to whom the report should be made and who is responsible for making decisions in regards to the level of conflict.***] Potential conflicts that do not rise to the level of requiring resignation from the committee should be disclosed to other DMC members.

3.3 Indemnification of DMC Members

DMC members [***will, will not***] be provided indemnification by the trial sponsor against any legal action that might be taken as a result of their service on the DMC.

4. SCHEDULING OF DMC MEETINGS

The DMC will meet prior to trial initiation to discuss the protocol, the Charter, and any other relevant documents, and make recommendations to the sponsor and study team regarding possible modifications. Future meetings will review the accumulating data on safety, efficacy, and study quality and will be scheduled approximately **[*insert schedule*]**. Meetings will be **[*by teleconference or in-person*]**.

A DMC meeting must have a quorum, usually requiring participation of the Chair and **[*list any other member—e.g., statistician, patient representative—who must be present*]** and at least [***number to be inserted***] other members.

5. MEETING FORMAT

Meetings will include Open Sessions at which study investigators and/or study sponsor will present information on study progress and conduct, and Closed Sessions, in which only the DMC members and statistician presenting to the DMC will participate. (For government-sponsored trials, the funder policy may require a sponsor representative to participate.)

Data in Open Sessions will be presented in aggregate, not by study arm, and will focus on data related to the progress and quality of study conduct, such as accrual progress, timeliness of data submission, study withdrawals, adherence to assigned treatment, site-specific issues,

and any emerging problems related to study conduct. During this session, the DMC should be notified of all major changes to the protocol or to study conduct planned or implemented by the study sponsor and/or study investigators. In addition, the study sponsor/investigators should inform the DMC of any external information relevant to the trial.

During the Closed Session, interim data on safety will be presented by study arm. Additionally, data on study quality presented in aggregate during the Open Session will be presented by treatment arm. Interim efficacy data by arm will also be presented, even if no provision for early termination for efficacy has been made, to permit the DMC to make risk-benefit assessments. In cluster-randomized trials, it is particularly important to monitor the comparability of the clusters with respect to prognostic variables, and the interim estimates of the intraclass correlation coefficient, which is typically difficult to estimate accurately prior to the trial but which is very important in assessing the power of the trial to address the primary hypothesis.

An Executive Session, including only DMC members, should also be scheduled to permit the DMC to discuss aspects of the review process without the presence of statistical center or sponsor staff. Such sessions may not always be needed, but it is best to schedule them routinely to avoid speculation on the part of the sponsor or investigators about the reason for calling the session.

6. MEETING REPORTS, MINUTES, AND RECOMMENDATIONS

6.1 Meeting Reports

For each DMC meeting, Open and Closed Reports, containing the interim data to be presented in the Open and Closed Sessions, respectively, will be prepared by the trial statistical center. **[*If different statisticians are designated to prepare Open and Closed reports, that should be specified.*]**

The Closed Session report will typically show data by coded treatment arms, but DMC members should have access to the treatment codes used in the presentation of data.

The reports should provide information current up to within 6 to 9 weeks of the date of the DMC meeting. Updated information on accrual and on serious adverse events should be presented at the meeting.

For trials relying on electronic health records, a schedule for availability of updated safety information should be developed. Every effort should be made to retrieve safety information that is as up-to-date as possible for presentation and discussion at DMC meetings.

6.2 Meeting Minutes

Meeting minutes will be prepared by **[*the DMC Chair, a sponsor representative, a statistical center representative, DMC Chair delegate, other*]**.

The minutes will describe the proceedings in the Open Session of the DMC meeting, and will

summarize the recommendations of the DMC. These minutes can be the basis of a report to be circulated to study investigators and institutional review boards.

Draft minutes will be circulated to all DMC members for their review and approval prior to being finalized and circulated to investigators.

6.3 Recommendations to the Sponsor and/or Study Leadership

At each meeting of the DMC during the conduct of the trial, the DMC will make a recommendation to the sponsor and/or steering committee to continue, modify, or terminate the trial. For trials comparing alternative treatment approaches that are both in wide use, early stopping for either efficacy or futility is generally not warranted because if many practitioners believe one or the other of the treatment approaches is best, changing clinical practice will require a substantial data set. Early termination considerations will generally apply only to emerging safety issues of major concern, or problems with trial conduct that suggest the trial could not be completed successfully with a reliable conclusion in a feasible time frame.

The DMC may make additional recommendations regarding trial conduct. These recommendations may relate to changes in treatment delivery to improve safety, need for increased attention to data timeliness and/or quality, frequency of review, or any other aspect of the trial for which a modification seems warranted.

Ideally, DMC recommendations will be arrived at by consensus, after a full discussion of the committee. The DMC Charter should anticipate the possibility that consensus will not be reached and delineate where possible how such a situation will be managed. Possibilities include providing a majority vote of DMC members, advising the study leadership about the lack of consensus and/or additional actions that might be taken. These additional actions may include convening a separate committee of experts to review the materials and the concerns of the DMC or adding members to the DMC with expertise specific to the matter(s) under debate.