Data and Safety Monitoring Board (DSMB) Charter
[name of study or consortium]

This charter defines the roles and responsibilities of the Data and Safety Monitoring Board (DSMB) for the *[name of study/consortium]* which is funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

The DSMB will serve in accordance with the guidelines set forth in this charter. Typically DSMB members review and agree to the charter at the initial meeting. If changes to the charter are necessary, the DSMB reviews and affirms their agreement with the changes. Their concurrence will be noted in the DSMB meeting summary.

DSMB RESPONSIBILITIES

Generally, the first responsibility of the DSMB will be to approve the final protocol of the clinical study named above, or the study/studies being undertaken by the research network named above so that the study/studies can begin enrolling patients. After initial approval, and at periodic intervals during the course of the study, the DSMB responsibilities are to:

- Provide input to assist the investigator(s) in protecting the safety of the study participants;
- Provide input to the investigator(s) on major changes to the research protocol, informed consent documents and plans for data and safety monitoring;
- Provide input to the investigator(s) on the progress of the study, including periodic assessments of data quality and timeliness, participant recruitment, accrual and retention, participant risk versus benefit, performance of the study sites, and other factors that may affect study outcomes;
- Review areas of concern regarding the performance of individual sites and provide comment to the investigator(s) on actions to be considered regarding sites that perform unsatisfactorily;
- Consider factors external to the study when relevant information becomes available, such as scientific or therapeutic developments that may have an impact on the safety of the participants or the ethics of the study;
- Provide input to the investigator(s) on modification of the study protocol or possible early termination of the study because of attainment of study objectives, safety concerns, low likelihood of showing a benefit of the intervention, or inadequate performance (such as enrollment and retention problems);
- If appropriate, review the interim analysis of efficacy in accordance with stopping rules which are clearly defined in the protocol and have the concurrence of the DSMB;
- Provide input to the investigator(s) on the desirability of proceeding to the full-scale study at the completion of a feasibility phase, if appropriate;
- Provide input to the investigator(s) on the potential impact of ancillary studies on the integrity of the parent study; and
- Monitor clinical ancillary studies unless an independent monitoring is established.

MEMBERSHIP

The members have been appointed by the investigator(s) and approved by NIDDK. Members of the DSMB shall have no financial, scientific, or other conflict of interest with the study.

Collaborators or associates of the investigators in this study are not eligible to serve on the DSMB. Written documentation attesting to absence of conflict of interest is required at least annually, and each time there is a change in site investigators and/or institutions involved in the study.

The investigator(s) will appoint a DSMB chairperson. S/He is responsible for overseeing the meetings and developing the agenda in consultation with the investigator(s).

DSMB MEETINGS

The DSMB will typically meet twice a year, or as deemed necessary. A quorum of more than half of the DSMB members is required in order to convene a meeting of the DSMB.

Meetings shall be closed to the public because discussions may address confidential patient data. Meetings are attended, when appropriate, by the principal investigator and members of his/her staff, as well as the study statistician. Meetings may be convened as conference calls or webinars, as well as in person. In special circumstances, the meetings may also be conducted by email. An emergency meeting of the DSMB may be called at any time by the DSMB chairperson should questions of patient safety arise.

MEETING FORMAT

An appropriate format for DSMB meetings consists of an open, closed (if the DSMB is monitoring a study in which the investigators are masked in any way), and executive session. This format may be modified as needed.

Open Session

Members of the DSMB, the principal investigator and members of the steering committee, including the study biostatistician may attend the open session. Issues discussed will include the conduct and progress of the study, including patient recruitment, data quality, general adherence and toxicity issues, compliance with protocol, and any other logistical matters that may affect either the conduct or outcome of the study. Proposed protocol amendments will also be presented in this session. Patient-specific data and treatment group data may not be presented in the open session.

Closed Session

The closed session will be attended only by DSMB members, and the unmasked study biostatistician. The discussion at the closed session is completely confidential. All materials from the closed session will be destroyed at the end of the meeting.

Analyses of outcome data are reviewed by masked intervention groups, including baseline characteristics, primary and secondary outcomes, adverse events, adherence and dropouts, and examination of any relevant subgroups. The DSMB may request unmasking of the data for either safety or efficacy concerns. Procedures to accomplish unmasking of either individual or treatment group data are to be specified in the Data and Safety Monitoring Plan.

Executive Session
The executive session will be attended by DSMB members only, who will discuss the information presented during the closed and open sessions and provide input on the continuation or termination of the study, protocol modification or other changes to the conduct of the study. The DSMB can be unmasked at any time if trends develop either for benefit or harm to the participants.

The DSMB will make a recommendation for either continuation or termination of the study. Termination may be suggested by the DSMB at any time. Reasons for early termination include:

- Serious adverse effects in entire intervention group or in a dominating subgroup;
- Greater than expected beneficial effects;
- A statistically significant difference by the end of the study is improbable;
- Logistical or data quality problems so severe that correction is not feasible.

Sound rationale for either decision (continuation or termination of the study) should be presented.

REPORTS TO THE DSMB
Reports will be prepared by the unmasked biostatistician on a quarterly or semi-annual basis as decided by the investigator(s) and the DSMB. The reports will be distributed to the DSMB at least 10 days prior to a scheduled meeting. These reports shall be provided in sealed envelopes within an express mailing package, by secure email, or by access to a secure website, as the DSMB prefers.

Data reports for randomized clinical studies or any study in which the investigators are masked generally consist of two parts: an Open Report and a Closed Report.

Open Session Report: This portion of the report provides information on study aspects such as accrual, baseline characteristics, and other general information on study status. This report is generally shared with all investigators involved with the clinical study. The reports contained in this section generally include:

- Comparison of Target Enrollment to Actual Enrollment by Month;
- Comparison of Target Enrollment to Actual Enrollment by Site;
- Overall Subject Status by Site, including: Subjects Screened, Enrolled, Active, Completed and Terminated;
- Demographic and Key Baseline Characteristics by Group;
- Treatment Duration for Subjects who Discontinue Therapy;
- Adverse Events/Serious Adverse Events by Site and Subject.

Closed Session Report: This report may contain data on study outcomes, including safety data. Data will be presented by masked treatment groups; however, the DSMB may request that the treatment groups be unmasked to ensure that there are no untoward treatment effects. The Closed Session Report is considered confidential and should be destroyed at the conclusion of the meeting. Data files to be used for interim analyses should have undergone established editing procedures to the extent possible. This report should not be viewed by any members of the clinical study except the designated unmasked study statistician.

DOCUMENTATION OF DSMB MEETINGS

Meeting summary

A formal summary containing the DSMB's input on the conduct of the study and their recommendation regarding continuation of the study will be prepared by the DSMB Executive Secretary. Each DSMB summary will include the DSMB's recommendation regarding continuation or termination of the study. The DSMB meeting summary will not include unmasked data, discussion of the unmasked data, or any other confidential data. Once completed, the summary is sent to the DSMB members for their review and concurrence. When the summary is satisfactory to the DSMB members and concurrence with the summary is received, the summary will be sent to the PI. It is the responsibility of the PI to distribute the summary to all co-investigators.

It is the responsibility of the study investigators to assure that the DSMB summary is submitted to all the Institutional Review Boards (IRBs) associated with the study.

CONFIDENTIALITY AND OBJECTIVITY

All materials, discussions and proceedings of the DSMB are completely confidential. Members and other participants in DSMB meetings are expected to maintain confidentiality. Closed session meeting materials should be destroyed in a secure manner (shredding) following each meeting.

In order to maintain their objectivity, DSMB members are expected not to discuss the study/studies with the investigators except during DSMB meetings.