WFSM INSTITUTIONAL DATA AND SAFETY MONITORING BOARD (I-DSMB) CHARTER

I. INTRODUCTION

Data and safety monitoring is required for all clinical research studies. An independent Data and Safety Monitoring Board (DSMB) is required for multi-site clinical trials involving interventions that entail potential risks to study participants (NIH Policy for Data and Safety Monitoring; (http://www.grants.nih.gov/grants/guide/notice-files/not98-084.html). DSMB oversight of lower-risk Phase III studies may also be warranted. DSMB monitoring of earlier-phase trials (Phase I and II) may be appropriate if they involve multiple clinical sites, are blinded, or employ particularly high-risk interventions or vulnerable populations (Further Guidance on a Data and Safety Monitoring [Plan] for Phase I and Phase II Trials; http://www.grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html).

II. I-DSMB MISSION AND RESPONSIBILITIES

- The WFSM Institutional Data and Safety Monitoring Board (I-DSMB) is a Dean-appointed standing committee that serves in an advisory capacity to the Dean. I-DSMB recommendations are reported to the study PI, who is responsible for forwarding them to the IRB and to the study sponsor.

- Prior to study initiation, I-DSMB members will review for approval purposes study protocols, informed consents, Data and Safety Monitoring Plans and other relevant documents as needed (case report forms, manual of procedures).

- Clinical trials being monitored by the I-DSMB will undergo periodic review of accumulating safety, endpoint and other relevant study data (e.g., participant recruitment, retention and compliance, data quality and timeliness, risk vs. benefit).

- I-DSMB oversight may include establishment of criteria for "early stopping," performance of interim analyses and recommendation for early termination, if there is significant evidence of benefit, harm or futility.

- Frequency of I-DSMB reviews for a particular study may be based on when early stopping rules are established for that study (e.g., after a pre-defined number of subjects have been enrolled and followed).

III. USE OF I-DSMB

- The I-DSMB will serve as the data monitoring body for select WFSM/WFSM-affiliated, IRB-approved studies meeting certain criteria (e.g., investigator-initiated, locally conducted [single- or multi-site], Phase I-IV clinical trials). Studies *not* requiring I-DSMB oversight typically include epidemiologic and observational studies that do not test interventions, or multi-site clinical trials utilizing a central DSMB.

- During the IRB review process, the IRB will decide if a study needs an independent DSMB, in which case the study team will be notified that they may make use of the I-DSMB or may develop their own DSMB. The institutional Conflict of Interest Committee may also recommend study oversight by the

I-DSMB. Investigators needing DSMB monitoring for their trials will be encouraged, but not required, to use the I-DSMB.

- Investigators considering using the I-DSMB are strongly encouraged to contact Dr. Abbie Eaton, abeaton@wakehealth.edu, phone: 336-716-9134, I-DSMB Managing Director, *before* submission of their grant or *before* IRB submission to discuss the specific monitoring needs of their respective studies.

- There is no charge for use of the I-DSMB for investigator-initiated, *pilot* research studies receiving NIH, departmental, or other non-industry support. Use of the I-DSMB for full-scale clinical research studies would involve charges.

- Studies originating at institutional affiliates of WFSM (WFU Reynolda campus, Translational Science Institute affiliates) may make use of the WFSM I-DSMB. Utilization of the I-DSMB by these affiliates will be evaluated on a case-by-case basis.

IV. MEETING FORMAT AND CONDUCT

While most I-DSMB reviews are conducted via electronic interactions, face-to-face meetings would occur as needed (e.g., for unplanned interim analyses, based on safety concerns):

- *Open-meeting sessions* could include, in addition to I-DSMB members, the study investigator, key study staff and the study statistician. These sessions would precede closed sessions, for purposes of discussing trial conduct and progress, subject accrual, compliance, retention, and challenges encountered.

- *Closed-meeting sessions* would include only I-DSMB members (voting and non-voting), who review the cumulative trial data either completely unblinded (data identified by intervention group) or partially unblinded (Study Group A vs. Study Group B). All data information and study related discussions remain confidential.

All individual study discussions (online or face-to-face) are preceded by inquiring if any I-DSMB members have either a *perceived* or *actual* conflict of interest that could bias their ability to objectively monitor and make judgments about the study. Actual conflicts would mandate recusal from all closed-session discussions and relinquishment of voting for the study, while perceived conflicts may be dealt with by having the member in question simply abstain from voting. Conflict of interest (COI) management of studies monitored by the I-DSMB will be determined on a case-by-case basis.

V. INTERIM REPORTS FOR I-DSMB REVIEW

- Contents and frequency of interim reports from the PI to the I-DSMB will be determined by the I-DSMB membership, with suggested input from the PI and her/his study team. Interim reports are generally prepared by the study statistician and other personnel. It is the PI's responsibility to arrange for a biostatistician to perform these analyses.

- I-DSMB members and statisticians preparing the interim reports will keep all trial data and results of study monitoring confidential.

VI. I-DSMB RECOMMENDATION REPORTS

- Subsequent to each I-DSMB review of a particular trial, the PI will receive in writing the I-DSMB's recommendations concerning trial continuation and any "action items" that need to be addressed. Such action items could, for example, include recommendations to amend the study consent form or modify the study protocol (e.g., revise eligibility criteria, Data Safety Monitoring Plan, study procedures or intervention[s]).

- Should the I-DSMB recommend closure of a study, the IRB will make the final decision regarding such recommendations.

- PIs must forward to the IRB all I-DSMB recommendations.

VII. I-DSMB MEMBERSHIP

- I-DSMB members will have expertise in clinical trial methodology and conduct, epidemiology, biostatistics, ethics, and clinical research. *Ad hoc* members may be invited to serve on the I-DSMB, based on a need for unique expertise not represented by regular members.

- I-DSMB members must be independent of the trials being monitored (no financial, scientific or other conflicts of interest).

- I-DSMB members will complete a Conflict of Interest Form that will be updated annually.

- I-DSMB members will serve either 2-year or 3-year terms (staggered membership), with the possibility of re-appointment.

- Current I-DSMB voting members include: Drs. Furberg, Kevin High, David Bowton, Nancy King, Shannon Mihalko, Michael Miller, Kaycee Sink, Haiying Chen, Kristen Hairston, Chadwick Miller

- *Ex officio* I-DSMB members include Drs. Jan Wagner and Richard Weinberg and Mr. Joseph Andrews and Ms. Paula Means.