# National Center for Complementary and Integrative Health (NCCIH)

# Data and Safety Monitoring Board Charter

**TRIAL NAME (ACRONYM)**

It is the National Institutes of Health (NIH) policy that all clinical trials require data and safety monitoring, with the method and degree of monitoring being commensurate with the risks posed by study participation ([NOT-98-084](http://grants.nih.gov/grants/guide/notice-files/not98-084.html) and [NOT-99-107](http://grants.nih.gov/grants/guide/notice-files/not99-107.html)). The following document summarizes National Center for Complementary and Integrative Health (NCCIH) guidelines concerning the establishment, responsibilities, and operating procedure of a data and safety monitoring board (DSMB).

The DSMB will act in an advisory capacity to NCCIH, to monitor patient safety, evaluate the efficacy of the intervention and the performance of the clinical trial in meeting its stated objectives. Dr. (PI NAME) at (INSTITUTION) is conducting a clinical trial entitled, TRIAL NAME AND ACRONYM. This study is being funded by the National Center for Complementary and Integrative Health (NCCIH) {IF APPLICABLE, ADD OTHER CO-FUNDING ENTITIES HERE}.

# DSMB RESPONSIBILITIES

The initial responsibility of the DSMB will be to approve the initiation of this clinical trial, which includes review and approval of the research protocol, informed consent and plans for data safety and monitoring After this approval, and at periodic intervals during the trial, the DSMB responsibilities are to:

* review all proposed revisions to the research protocol, informed consent documents and plans for data safety and monitoring, including;
* evaluate the progress of the trial, including periodic assessments of data quality and timeliness, participant recruitment, accrual and retention, participant risk versus benefit, performance of the trial site(s), and other factors that may affect study outcome;
* 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, the ethics of the trial or a subject’s willingness to participate;
* protect the safety of the study participants;
* report on the safety and progress of the trial;
* make recommendations to the NCCIH, the Principal Investigator (PI), and, if required, to the Food and Drug Administration (FDA) and the Institution Review Board (IRB) concerning continuation, termination or other modifications of the trial;
* if appropriate, conduct interim analysis of efficacy in accordance with stopping rules which are clearly defined in advance of data analysis and have the approval of the DSMB;
* ensure the confidentiality of the trial data and the results of monitoring;
* assist the NCCIH by commenting on any problems with study conduct, enrollment, sample size and/ or data collection.

# MEMBERSHIP

The DSMB will consist of at least X members. X members will constitute a quorum. The members have been appointed by the NCCIH and will include at least one member with human subject research monitoring expertise, at least one member with relevant disease expertise (such as an M.D. or equivalent), at least one member with expertise in the intervention or observation technique under study and a biostatistician.

Members of the DSMB shall have no financial, scientific, or other conflict of interest with the study. Current or past collaborators (within the past three years), including any individual involved in the design, conduct or analysis of the trial, associates and direct reports of the PI are not eligible to serve on the DSMB. Written documentation attesting to absence of conflict of interest is required. Additionally, DSMB members will be queried at the beginning of each DSMB meeting to ensure accurate and updated accounting of any conflicts of interest.

Dr. (DSMB CHAIR NAME) of the (INSTITUTION) has been selected by the NCCIH to serve as the DSMB Chair. Dr. (NAME) will serve as the NCCIH DSMB Executive Secretary (ES). The DSMB ES is an NCCIH employee with relevant clinical trials expertise who is not otherwise involved in the study or the study team, and is impartial in DSMB interactions.

While the Chair will lead all meetings of the DSMB, the Chair and the DSMB ES will cooperate on development and execution of all logistic activities associated with the DSMB including 1) oversight and coordination of all meetings and communications; 2) development of the agenda; 3) identification and review of substantive materials; and 4) production of meeting minutes and reports. In addition, the DSMB ES ensures that the DSMB complies with all NIH and PHS DSMB policies and procedures and communicates DSMB comments and recommendations to relevant NCCIH staff. NCCIH shall oversee the logistical management and financial support for the DSMB.

*If Applicable:* The safety officer, [name] M.D., will be the contact person for any safety issues related to the trial, including adverse event reporting. Procedures for notifying the DSMB Chair and the DSMB ES will be discussed and approved by the DSMB. Those procedures will be part of the DSMB written plan and the NCCIH approved Data and safety Monitoring Plan. The DSMB written plan can be revised, as needed, with the approval of the Board.

# BOARD PROCESS

The DSMB will meet (SPECIFY PLANNED FREQUENCY (no less than annually) at the call of the Chair, with advance approval of the DSMB ES. The DSMB ES or designee will be present at every meeting. Prior to the first meeting, the DSMB Chair and DSMB ES will develop a plan for the recording of meeting minutes and recommendations for each meeting, and a plan for how NCCIH will send DSMB communications to the study team.

Meetings shall be closed to the public because discussions may address confidential patient data. Meetings are attended, when appropriate, by the trial investigators and members of the study team. Meetings may be convened as conference calls as well as in person. An emergency meeting of the DSMB may be called at any time by the Chair or by NCCIH should questions of patient safety arise. The DSMB Chair should contact the DSMB ES prior to convening a meeting.

# MEETING FORMAT

An appropriate format for DSMB meetings consists of an open, closed and executive session. A final joint open session is optional for DSMB meetings, and will be included if requested by the DSMB.

# Open Session:

The open sessions are attended by the DSMB, the DSMB ES, study PI (s), study team members, including the study biostatistician, and designated NIH staff. The DSMB may limit the number of non-board members in attendance. The number of non-DSMB members (study team and NIH representatives) in attendance should be limited, as they are observers to the proceedings, so as not to overwhelm free and open exchange among DSMB members. Typically, NIH Program Official (s) for the study will attend open sessions. Issues discussed in open sessions usually include conduct and progress of the study, including patient accrual, compliance with protocol, general safety issues, and any other problems encountered. **Patient-specific data and treatment group data will not be presented in the open session.**

# Closed Session:

Closed sessions are attended by the DSMB. NIH staff participation in closed sessions is restricted to the DSMB ES and the NCCIH biostatistician.

All study progress and safety data, as well as planned interim analyses are presented at this session. The DSMB may choose to review masked group data, or may request review of unmasked data during the trial. Access to unmasked data must be limited to DSMB members and a small group of additional individuals who are to be determined at the onset of the study. Generally, these data are prepared by and presented to the DSMB by the unmasked trial biostatistician and the DCC statistical PI. The discussion at the closed session is completely confidential.

# Executive Session:

Executive sessions are attended by the DSMB members. NCCIH staff is not required to attend the executive session; however, the DSMB Chair may ask the DSMB ES to remain in the executive session at their discretion. On occasion, and by request, the DSMB Chair may request other NIH Staff participate in the Executive Session. The DSMB Chair will record minutes/recommendations during the executive session, when the DSMB ES is not present. In the executive session, the DSMB will discuss the general conduct of the trial and all outcome results, including adverse events.

DSMB recommendations are developed and finalized in the executive session.

The DSMB will discuss information presented during the closed and open sessions and provide comments and recommendations regarding study progress and continuation. The DSMB will specifically discuss whether to recommend continuation or termination of the study. The DSMB will also discuss whether protocol modification or other changes should be implemented in the study.

Should a DSMB member make a recommendation for trial termination, a full vote of the DSMB will be required. The final results of the vote will be presented to the NCCIH Director for consideration in binding decisions made by NIH with regard to the continuance of the trial. In the event of a split vote, majority vote will rule and a minority report should be appended.

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.

# Final Open Session (optional):

The final open session may be attended by voting DSMB members, the DSMB ES, the trial PI(s), the study biostatistician or other study members, and other relevant NIH staff.

The Chair of the DSMB shall report on the recommendations of the DSMB regarding study continuation and concerns regarding the conduct of the study. Requests regarding data presentation for subsequent meetings will be made. Scheduling of the next DSMB meeting may also be discussed.

# DATA PRESENTATION

At the first DSMB meeting, the DSMB will be informed by the DSMB ES that study data in closed reports during the trial can be presented by either masked intervention groups (e.g. Group A vs.

Group B) or in an un-masked format. The DSMB may routinely review data in a masked fashion to prevent any potential compromise to the study blind. The DSMB may request access to unmasked data throughout the duration of study oversight, on a one time or continuous basis. The DSMB can request unmasking by the unmasked study statistician if a majority vote of the DSMB agrees that data trends warrant further information on group assignment. Generally, these data would be prepared by and presented to the DSMB by the unmasked trial biostatistician. Discussion and deliberation of the unmasked data should be limited to members of the DSMB along with select attendance by unmasked members of the study team, as requested.

# REPORTS

**Interim Reports**: Interim reports will be prepared by the Data Coordinating Center for the trial at (INSTITUTION). The reports will be distributed to the DSMB and the designated NIH staff at least 14 days prior to a scheduled meeting. The contents of the report are determined by the DSMB. Additions and other modifications to these reports may be directed by the DSMB on a one-time or continuing basis. Interim data reports generally consist of two parts:

Part 1 (**Open Session Report**) provides information on study aspects such as accrual, baseline characteristics, and other general information on study status. The Open session Report should begin with an Executive Summary of the Study Progress and outline the specific issues to be discussed with the DSMB. This report is generally shared with all investigators involved with the clinical trial. The reports contained in this section will 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
* Treatment Duration for Subjects who Discontinue Therapy
* Report on Intervention Fidelity and Treatment Adherence
* Adverse Events/Serious Adverse Events by Site and Subject (this includes severity, classification by organ system, and by relationship to intervention).
* Unanticipated problems.

Part 2 (**Closed Session Report**) may contain data on study outcomes (if pre-specified by the DSMB), safety data, serious adverse events or termination. The Closed Session Report should begin with an Executive Summary of the Report, and specific items to be discussed with the DSMB. Data will be presented by masked treatment groups; however, the DSMB may request that the treatment groups be unmasked. The Closed Session Report is confidential and should be destroyed at the conclusion of the meeting. This report should not be viewed by any members of the clinical trial team, except the designated unmasked study biostatistician.

**Reports from the DSMB:** A formal report containing the recommendations for continuation or modifications of the study will be prepared by the DSMB and submitted to NCCIH, via the DSMB ES. After review of the DSMB recommendations in NCCIH, the DSMB ES will provide a final set of recommendations to the trial PI (s). This report may also contain recommendations of the NIH in reference to the DSMB recommendations.  Each report should include a recommendation about whether to continue or to terminate the study. The report should not include unmasked data, discussion of the unmasked data, or any other confidential data.

It is the responsibility of the trial PI (s) to distribute this report to all co- investigators and to ensure that copies are submitted to all the IRBs associated with the study.

**Communications to the DSMB:** On a scheduled basis, [usually on a quarterly basis] (as agreed upon by the DSMB) masked safety data should be communicated to DSMB members or the Chair (as agreed upon by the DSMB), the DSMB ES and, if applicable, the designated safety officer. Any concerns noted by the DSMB or the safety officers should be brought to the attention of the DSMB ES.

# CONFIDENTIALITY

All materials, discussions and proceedings of the DSMB are completely confidential. Members and other participants in DSMB meetings are expected to maintain confidentiality.

# NCCIH CONTACT FOR DSMB QUESTIONS AND COMMENTS

DSMB member concerns related to designated NIH staff attendance or participation at DSMB meetings should be directed to the NCCIH Deputy Director.

**APPENDIX A**

# Data and Safety Monitoring Board Roster

**TRIAL NAME (ACRONYM)**