

[INSERT NAME OF TRIAL]

[Insert name of PI]

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## Data and Safety Monitoring Board Charter

### 1. PURPOSE

The Charter defines the primary responsibilities of the Data and Safety Monitoring Board (DSMB) for the study [INSERT TITLE], which is conducted by the National Institute of Neurological Disorders and Stroke (NINDS). The DSMB will act in an advisory capacity to the study Principal Investigator (PI) and the NINDS Clinical Director (CD) to monitor participant safety, data quality and evaluate the progress of the study. The NINDS establishes DSMBs to provide independent, expert advice to the Institute regarding the safety and credibility of Institute-supported clinical trials. This charter will define the roles and responsibilities of the DSMB, delineate qualification of the members, describe the processes for conducting the DSMB meetings, and communication with the PI and NINDS Office of the Clinical Director (OCD). This charter will serve as the Standard Operating Procedure (SOP) for the DSMB. The DSMB will be independent of the sponsor, regulatory agencies, IRBs, and investigators. The DSMB will serve in accordance with the guidelines set forth in this charter.

### 2. DSMB RESPONSIBILITIES AND FUNCTIONS

The DSMB has the general charge of ensuring that the trial is conducted safely and ethically and that the trial meets its primary objectives. This includes the interests of currently enrolled participants and future participants, but also includes the interests of society. The DSMB is charged with making recommendations to the PI and CD with regards to the conduct of the trial. To these ends the DSMB has the following responsibilities and functions:

- review and acknowledge the protocol, including the data and safety monitoring plan (DSMP) and data analysis plan, before enrollment of the first subject; and provide opinion/advice on any substantial amendments to the protocol at any time, per the discretion of the PI or CD
- establish and confirm a DSMB Charter at the first DSMB meeting
- evaluate cumulative safety data; determine specific safety concerns that may arise during the conduct of the trial; and provide recommendations based on the DSMBs review
- perform periodic assessments of the following, as applicable: data quality, completeness and timeliness; performance of the study site(s), including participant recruitment, accrual and retention, compared to accrual targets; status of enrolled participants, overall and by treatment group (on/off study, on/off treatment, withdrawals/lost-to-follow-up, etc.); participants off-treatment, including the reason for discontinuation; participant baseline characteristics, overall and by treatment group; protocol deviations and Unanticipated Problems (UPs), including review of participant eligibility criteria and non-adherence to other protocol requirements; participant adherence to treatment

regimen (e.g., based on pill counts or diaries); overall risk versus benefit; and other factors that can affect study outcome

- consider factors external to the study when interpreting the data, such as scientific or therapeutic developments that may impact the safety of the participants or the ethics of the study
- evaluate data per a pre-specified interim analysis plan, if included in the protocol
- make recommendations to the investigators concerning continuation, termination, or other modification of the study based 1) on the observed benefits or adverse effects of any of the investigations under study (overall risk versus benefit); and 2) the unlikelihood that a meaningful assessment of treatment effect could be established by the planned end of the trial
- review the general progress of the study and to assist in resolving any problems which may arise

### 3. MEMBERSHIP

The DSMB members and Chairperson were appointed by the study PI and approved by the CD and IRB. The members reflect the disciplines and medical specialties necessary to interpret the data from the study and ensure participant safety. The voting member of the DSMB consists of **[LIST ALL MEMBERS (N ≥ 3) BELOW, ADD/DELETE LINES AS NEEDED]:**

Chair Name & Discipline/Specialty area:  
Voting member? Yes  No

Name & Discipline/Specialty area:  
Voting member? Yes  No

Name & Discipline/Specialty area:  
Voting member? Yes  No

Name & Discipline/Specialty area:  
Voting member? Yes  No

Name & Discipline/Specialty area:  
Voting member? Yes  No

**[INCLUDE THIS SECTION IF THE STUDY HAS AN INDEPENDENT MEDICAL MONITOR (IMM)]** At times the expertise of the IMM may also be required, at which point an invitation will be extended to review study data and/or attend DSMB meetings.

The IMM is: **[NAME]**.

The DSMB Chair, in addition to **his/her** responsibilities as a DSMB member, is responsible for chairing and overseeing all meetings, reviewing and approving meeting minutes and reports, and acting as the primary contact within the DSMB for the immediate reporting of Serious and Unexpected Adverse Events.

[CONSIDER IDENTIFYING AN ALTERNATE CHAIR IN THE EVENT THE DSMB CHAIR IS UNAVAILABLE. IF YES, INCLUDE THE FOLLOWING] In the event the DSMB Chair is unavailable, [INSERT NAME OF ALTERNATE HERE] will serve as the Acting DSMB Chair until the DSMB Chair is available to resume his/her duties. A quorum (based on the number of members including the DSMB Chair) will still be required for meetings to proceed.

DSMB members are appointed for the duration of the trial.

- DSMB members must make time for preparing and attending all scheduled DSMB meetings, as well as to devote time and attention to other matters deemed necessary, such as Serious Adverse Event (SAE) reviews.
- While attendance of all DSMB members is preferable, in order to conduct a DSMB meeting, a quorum of greater than 50% (i.e., 50% plus 1) of the voting members should be present to proceed. If the DSMB Chair is unable to attend, he/she may appoint another DSMB member to Chair the meeting.
- If any member leaves the Board or is dismissed during the course of the study, the reason(s) for their departure will be recorded and filed. If a member leaves the Board, the PI will propose a replacement to be approved by the CD and IRB.

#### 4. CONFLICT OF INTEREST (COI)

Each DSMB member must review the *Guide to Avoiding Financial and Non-Financial Conflicts or Perceived Conflicts of Interest in Clinical Research at NIH* (referred to as “the Guide”), and adhere to the rules set forth in the Guide. Specific examples of COI for DSMB members can be found in section III and IV of the Guide. Each DSMB member must sign the “*Guide to Avoiding Financial and Non-Financial Conflicts or Perceived Conflicts of Interest in Clinical Research at NIH*” Acknowledgement Form (Appendix C) prior to beginning review activities, and at least annually thereafter. The Acknowledgement Form should be kept in the study file.

Individuals invited to serve on the DSMB will disclose verbally and in writing any real or apparent COI at the initial DSMB meeting. Real and apparent COIs must be discussed by the DSMB to determine if/how the COI can be resolved. Those with COI are excluded from serving on NINDS DSMBs. Individuals with a COI may be present to provide information requested by the DSMB, but they cannot serve as voting members. The minutes will reflect the COI discussion, which individual(s) has a real or apparent COI, as well as the resolution.

At the beginning of every meeting, the [SPECIFY DSMB Chair, coordinating site, DSMB Secretary, or person responsible coordinating meetings/taking minutes] will ask members to disclose any changes to their COI. The COI discussion will be documented in the minutes.

#### 5. HALTING/STOPPING CRITERIA

The halting/stopping criteria (as determined by the study PI) include:

- INSERT HALTING/STOPPING CRITERIA FROM THE STUDY DSMP HERE

The PI, IRB, CD, the Sponsor [IF NOT NINDS], or the FDA may halt the study at any time following review of any safety concerns. The DSMB [ADD "or the IMM" IF APPLICABLE] may recommend a study halt.

Specific events that would lead to the halting of the study and potential termination will include:

- [LIST EXAMPLES HERE, IF NEEDED, BASED ON THE STUDY DSMP]

Reporting a Study Halt: The PI must inform the OCD, IRB and the DSMB that a halting rule has been met, including a description of the event(s) or safety issue(s). [EDIT AS NEEDED IF THE DSMB IS TO DETERMINE IF A HALTING/STOPPING CRITERIA HAS BEEN MET]

Resumption of a Halted Study: The PI, CD, DSMB, IMM and the IRB will determine if it is safe to resume the study. The conditions for resumption of the study [DEFINED HERE].

## 6. MEETINGS

The Board will meet at intervals specified by the needs of the trial, via [SPECIFY MEETING TYPE HERE: Face-to-Face meeting, conference call, web-meeting; IF NOT FACE-TO-FACE, STATE WHICHEVER APPLIES: a password protected phone line/secured webmeeting will be used], which include:

- [LIST MEETING TIMEPOINTS HERE; the DSMB should meet at least annually while the study is open to enrollment or has participants in active follow-up, and more frequently if needed.]

Additional meetings may be scheduled when necessary for adequate monitoring. Any member of the DSMB may request a meeting if they believe data provided within interim reports warrant an additional meeting.

### 6.1. Initial DSMB review

The DSMB will review and acknowledge the protocol, including the DSMP and data analysis plan, with recommendations as appropriate, as well as establish and confirm the DSMB Charter, as stated above in section 2. COI of each member will be reviewed, and the Conflict of Interest and Confidentiality Statements will be collected and retained (see section 4). The DSMB may provide expectations for the reports provided by the study investigator; however, these standards may evolve over the course of a study.

### 6.2. Subsequent DSMB review

Subsequent DSMB review will be convened as specified above. Prior to each DSMB review, the study investigators will submit [ADD OR DELETE THE BELOW AS APPROPRIATE FOR EACH STUDY]:

- Summary of accrual, overall and by study site, compared to accrual targets.
- Summary of baseline characteristics, overall and by treatment group.
- Summary of the data completeness (e.g., percentage of missing data).
- Summary and status of study participants, overall and by treatment group (e.g., proportion of subjects on- and off-study, on- and off-treatment, including screening failures, withdrawals and drop-outs).

- Assessment of participant adherence to the treatment regimen, overall and by treatment group (e.g., drug accountability report).
- List of individual SAEs, including PI's determination of relatedness.
- List of AEs by treatment group and body system including summary of cumulative rates, overall and by treatment group.
- If an interim analysis is scheduled, summary of outcome data by treatment group.
- List of protocol deviations, unanticipated problems (UPs), and non-compliance, if any.
- Summary of protocol amendments since the last DSMB review

[RECOMMENDED; INCLUDE AS APPLICABLE] Interim reports, which include safety data and/or comparative effectiveness data, should be reported by study group and be [coded by group/completely unblinded]. These reports should be available only to DSMB members (i.e. presented during closed session), and be withheld from the sponsor and investigators until the study is complete or the blind is broken. [ADD THE FOLLOWING IF THE RANDOMIZATION IS STRATIFIED (E.G., BY AGE)] These tables and figures [may/will] be presented by strata.

In addition to the above, the DSMB may request additional information to aid in their determination. This may include recommendations to include additional content or to change the format of the data provided.

### 6.3. DSMB meeting format

DSMB meetings will be divided into the below types of sessions [LIST ALL AS APPROPRIATE], with the expected attendees as listed:

- Open Session: may include PI, study statistician, study staff, DSMB members, DSMB/NINDS administrative staff, other parties at the discretion of the DSMB chair
  - Trial progress such as patient accrual, baseline characteristics, safety data, statistics and outcome data may be presented and discussed
- Closed Session: restricted to DSMB members, DSMB/NINDS administrative staff, and additional invited unblinded attendees ([ADD/DELETE AS APPROPRIATE:] unblinded pharmacist, unblinded statistician, IMM, or other may be requested to attend by DSMB)
  - Study progress is discussed, and the DSMB will vote/make recommendations
- Closed Executive Session: Only voting DSMB members and DSMB/NINDS administrative staff
  - Used only if non-DSMB members or non-voting DSMB members are present at the closed session; to allow the DSMB to reach an independent decision

### 6.4. DSMB Vote

The DSMB will vote and make recommendations and decisions to continue, modify or terminate the study during the closed session as described above. If there is a tie, the Chair will be the deciding vote. If there is not unanimous support for a decision, the recommendations will include a minority report.

## 7. DSMB ACCESS TO UNBLINDED DATA

For all blinded studies, DSMB members will have access to unblinded treatment assignments and data. [SPECIFY WHICH OF THE FOLLOWING WAYS THIS WILL BE ACCOMPLISHED]

1. DSMB members will be blinded, with access to unblinded treatment information upon request.
2. The majority of the DSMB will be blinded, with one member [SPECIFY; ideally a clinician] unblinded to treatment assignment. [SPECIFY NAME] will unblind the remaining members if warranted.
3. DSMB is fully unblinded. The study statistician(s) performing analysis to present to the DSMB may also be unblinded. In this case, the study statistician can be present in the closed session, followed by a separate executive closed session with DSMB members only.

## **8. DSMB RECOMMENDATIONS**

Following the meeting, formal minutes will be prepared by [SPECIFY: coordinating site, DSMB Secretary, or DSMB member] to record the proceedings of the meeting. [INCLUDE THE FOLLOWING 2 SENTENCES IF OPEN SESSIONS WILL BE CONDUCTED] Meeting minutes will be divided into open and closed sessions. Closed session minutes should not be circulated until the trial is terminated. The minutes will include the DSMB's recommendations concerning continuing, modifying, suspending or terminating the study. [SPECIFY NAME] will provide the minutes to the DSMB Chair, at minimum, for approval. Once the minutes are approved, closed session minutes will be distributed to study investigators and the OCD.

The PI should respond to the DSMB recommendations in writing prior to the next scheduled DSMB meeting, unless the DSMB requests an earlier response. Safety/serious concerns should be communicated immediately.

## **9. Confidentiality Procedures for DSMB Members**

Materials/information made available to the DSMB that are not in the public domain, as well as discussions that take place during the meetings, are strictly confidential. Each member of the DSMB, including non-voting members, will be required to sign a confidentiality agreement.