The following DSMB template is only to be used after scheduling a regulatory consult with the DSMB Program Manager at The Ohio State University CCTS. Please email April Green at April.Green2@osumc.edu or call at 614-366-7367. Scheduling a consult will allow for the use of the CCTS DSMB service, without completing a consult the DSMB service cannot be used.

THE OHIO STATE UNIVERSITY
CENTER FOR CLINICAL AND TRANSLATIONAL SCIENCE

Data and Safety Monitoring Board (DSMB) Charter

[Protocol title or DSMB name]

C o n f i d e n t i a l

Name of Sponsor:	The Ohio State University/Center for Clinical and Translational Science (CCTS)
ClinicalTrials.gov ID:	[Clinicaltrials.gov ID]
Protocol Number:	[Insert protocol number]
Contacts at OSU/CCTS:	[Name of PI] [Name of DSMB Chair] [Name of DSMB Program Manager]
Date of Charter:	[Date that the Charter is issued]

Confidential

This is an OSU/CCTS document that contains confidential information. Nothing herein is to be disclosed without written consent from OSU/CCTS.

Note: This Charter will serve as the Standard Operating Procedure (SOP) for the DSMB.

OSU/CCTS Signature Page

[Protocol title or DSMB name]

Reviewed and Accepted at OSU/CCTS by:

[Name of OSU/CCTS Representative]	Date

Table of Contents

1 INTRODUCTION

[Provide a brief introduction to the protocol.]

An independent Data and Safety Monitoring Board (DSMB) has been convened to assess the progress of a clinical study, the safety data, and critical efficacy endpoints (if appropriate) and provide recommendations to OSU/CCTS. The members of the DSMB serve in an individual capacity and provide their expertise and recommendations. The DSMB will review cumulative study data to evaluate safety, study conduct, and scientific validity and data integrity of the study. This Charter will outline the roles and responsibilities and serve as the Standard Operating Procedure (SOP) for the DSMB.

2 COMPOSITION OF THE DSMB

The Committee will be composed of <insert number> members (inclusive of the DSMB Chair). The DSMB includes experts in or representatives of the fields [protocol specific areas of expertise] and/or clinical trials methodology. The DSMB requires at least one biostatistician for each meeting review. Optional additional members may include but are not limited to: patient subject advocate, ethicist or both based upon trial risk complexity.

Refer to the Dynamic Reference entitled 'DSMB Membership List', maintained by DSMB Program Manager, OSU/CCTS, for the list of DSMB members with their corresponding contact information and area of expertise. This list is considered a 'dynamic reference' because it can be updated without requiring an amendment to the charter.

Quorum – A quorum will occur when [#] members are present. Without a quorum a meeting will not be held, unless alternate arrangements have been made by the Chair in agreement with OSU/CCTS that documents can be reviewed remotely and review comments will be provided to the Chair.

If a member misses a meeting, the Chair should ensure the member is available for the subsequent meeting. If a member misses a second meeting, the Chair should ask the member about his or her ability to remain on the DSMB. If a third meeting is missed,

the member should be replaced. The OSU/CCTS DSMB Program Manager or designee will serve as an ex-officio member of the DSMB.

Each member will serve a term of [#] of years.

3 INDEPENDENCE OF THE DSMB

It is essential that the judgment of members of the DSMB not be influenced by factors other than those necessary to maintain subject safety and to preserve the integrity of the study. Persons who have an apparent financial, intellectual, or other interests with a drug, device, or procedure should not be a DSMB participant for the evaluation of that product. Independence is essential to ensure that DSMB members are objective and capable of an unbiased assessment of the study's safety and efficacy data. The following will ensure the independence of the DSMB:

- Members of the DSMB will not participate as investigators in any study under review and will not be supervised by study investigators.
- Members of the DSMB must not have a direct interest in knowing or influencing trial outcome or have a financial or intellectual interest in the outcome of any studies under review.
- DSMB members must disclose all pharmaceutical companies, biotechnology companies, and Clinical Research Organizations (CROs) in which they hold financial interest. Members must disclose all consultancies (direct or indirect) with pharmaceutical companies, biotechnology companies, and CROs.
- Members who have served initially on protocol review teams may participate in the open sessions of the DSMB meeting when that protocol is under review. However, they will be excused from the closed sessions reviewing that protocol.

The OSU/CCTS will be responsible for deciding whether consultancies or the disclosed interests of the members materially affect their objectivity. Members of the DSMB will be responsible for notifying the DSMB Chair and OSU/CCTS of any changes of interest in pharmaceutical companies, biotechnology companies, or CROs, including consultancies. In such cases, the DSMB meeting minutes will document the disclosure

of the potential conflict of interest and the outcome of the discussion (e.g., abstention of member from voting, recusal from discussion). OSU/CCTS will decide whether any of these relationships results in a conflict of interest which would preclude involvement on the DSMB. Members of the DSMB who develop potential or significant perceived conflicts of interest will be asked to resign from the DSMB. Members will be polled at the beginning of each DSMB meeting to disclose whether status has changed.

4 RESPONSIBILITIES OF THE DSMB

[When the DSMB is constituted for a single protocol, DSMB members should only agree to serve if they are generally supportive of the study's overall aims and general design. This is because the study has already been through a scientific review. The DSMB will consider study-specific data as well as current relevant background knowledge about the disease, test agent, or patient population under study.]

4.1 Objectives

The primary objective of the DSMB is to monitor the safety of the interventions and the validity and integrity of the data from the clinical study. Additionally, the DSMB will evaluate the pace of recruitment and will make recommendations to OSU/CCTS regarding the continuation, modification, or termination of any or all arms of the study.

4.2 General Responsibilities

The general responsibilities of the DSMB are:

- To evaluate, on an ongoing basis, the accumulating safety assessments to ensure the ongoing safety of study subjects
- To 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
- To review all documents provided in the data and safety monitoring meeting report upon receipt
- To review the conduct of the study, including protocol violations

- To review data on participant recruitment, accrual, and retention, as well as assessments of data quality, completeness, and timeliness
- Protect the confidentiality of the study data and the DSMB discussions
- To make recommendations to continue, modify, or terminate the study

5 DSMB CHAIR RESPONSIBILITIES

The following responsibilities are those of the DSMB Chair:

- Serves as a voting member contingent on the requirements of the committee
- Facilitates the meetings, assists in the development of the agenda, and ensures that the meeting minutes and recommendation(s) are appropriately documented
- Serves as the additional contact person for the DSMB
- Reviews and approves the Charter
- Ensures that those involved in the day-to-day management of the study are excluded from DSMB voting procedures
- Discusses DSMB recommendations with OSU/CCTS and appropriate members of the project team via meetings. This responsibility may be delegated to the DSMB Program Manager.
- Takes and maintains minutes from open/closed sessions of DSMB meetings in coordination with DSMB Program Manger

5.1 DSMB PROGRAM MANAGER RESPONSIBILITIES

The following responsibilities are those of the DSMB Program Manager:

- Serves as DSMB Chair in the event that the Chair of Record is absent
- Facilitates the meetings, assists in the development of the agenda, and ensures that the meeting minutes and recommendation(s) are appropriately documented
- Serves as the primary contact person for the DSMB

- Develops, reviews, and revises the Charter
- Ensures that those involved in the day-to-day management of the study are excluded from DSMB voting procedures
- Discusses DSMB recommendations with OSU/CCTS and appropriate members of the project team via meetings when delegated to by chair.
- Takes and maintains minutes from open and closed sessions of DSMB meetings

6 PRINCIPAL INVESTIGATOR RESPONSIBILITIES

The following activities are the responsibility of the PI/trial statistician responsible for analyzing the study data:

- Provides DSMB regularly scheduled reports 2 weeks prior to scheduling meetings
- Provides ad hoc reports requested by the DSMB in a timely manner
- Provides statistician to explain reports

7 OSU/CCTS RESPONSIBILITIES

The following activities are the responsibility of OSU/CCTS or, as clarified herein, its designee(s):

- Approves selection of DSMB Chair and members
- Reviews and approves DSMB Charter
- Reviews and implements the DSMB recommendation(s), as appropriate
- Advises appropriate individuals of DSMB recommendations, and notifies regulatory authorities, other agencies, and investigators when required or necessary
- Reviews conflict of interest information and has authority for actions taken based on findings of conflicts
- Polls for and arranges DSMB meetings (or OSU/CCTS designee)

- Posts appropriate review materials for DSMB members (or OSU/CCTS designee)
- Writes minutes from open/closed sessions of DSMB minutes (or OSU/CCTS designee)
- Distributes minutes to DSMB members (or OSU/CCTS designee)
- Billing

8 MEETINGS OF THE DSMB

8.1 Organizational Meeting

The first meeting of the DSMB will be an organizational meeting. This meeting will formally establish the DSMB and begin to acquaint the DSMB members with the protocol or types of protocols that this DSMB will be charged with monitoring. It affords the DSMB an opportunity to recommend final revisions to the Charter and the communication plan between the DSMB, the project team, and OSU/CCTS.

The attendees for this organizational meeting will include DSMB members and [representatives from OSU/CCTS and or project team].

At the beginning of the DSMB meeting, the Chair will initiate the organizational session of the meeting, which will include calling the meeting to order and assuring a duly constituted Board.

Meeting objectives will include:

- the introduction of the DSMB
- review of the DSMB Charter
- defining the roles and responsibilities of the DSMB
- developing procedures for conducting business (e.g., voting rules and quorum, attendance, etc.)
- brief discussion of the upcoming protocol(s) and the development of possible standard study status tables and listing shells

8.2 Scheduled Protocol and Data Review Meetings

Each protocol and data review meeting will be classified as one or more of the following: Open Session, Closed Session, or Closed Executive Session.

8.2.1 Open Session

This will begin with an introductory session that includes introductions, roll call, assurance of a quorum, a reminder about the confidential nature of the proceedings and corresponding documentation, and a review of conflict of interest for all DSMB members.

Following the introductory session, the DSMB will move into the open session. Attendees will include the DSMB members, voting and *ex officio* members, the Principal Investigator and other required study staff personnel, and OSU/CCTS staff members. This session may also be open to Center PIs, representatives for industrial collaborators, and representatives from the Food and Drug Administration (FDA) and OSU/CCTS program as appropriate.

The open session will serve as a general study update. The PI will be called upon to present study status and known relevant findings. Others with specific safety experience or concerns may also be called upon to present. The session will provide a forum for an exchange of information among the various groups involved in the conduct of the study. It will afford the DSMB members an opportunity to question the project team about the study and to seek additional information deemed relevant to the data review. Discussions may include progress of the study, including adverse events, disease status of participants, comparability of groups with respect to baseline factors, protocol compliance, site performance, current accrual metrics, quality control, and timeliness and completeness of follow-up. Only masked data will be reviewed and/or discussed during the open session.

8.2.2 Closed Session

Following the open session of the meeting, a closed session involving the DSMB members and a PI representative will be held to review grouped safety data, discuss

findings, develop recommendations, and obtain agreement on voting. During this session, any issues related to subject safety will be discussed. Requests by DSMB Members for the unmasking of data may be made at this time. Interim efficacy analysis planned a priori will be addressed in closed session.

8.2.3 Closed Executive Session

A brief meeting will be held between the DSMB Chair, OSU/CCTS representative (DSMB Program Manager), and the Prinicipal Investigator to discuss the recommendations of the DSMB.

A brief summary that describes the individual findings, overall safety assessment, and DSMB recommendations will be agreed upon by the Chair and forwarded to the OSU/CCTS DSMB Program Manager within one week of the meeting for approval. The DSMB Program Manager, upon approval, will forward to the Principal Investigator.

8.3 Unscheduled Meetings/Reports

Unscheduled meetings can be requested by any party with the responsibility of overseeing the study. Requests can be made to the DSMB Chair, PI, or DSMB Program Manager project. The Chair, in collaboration with the DSMB Program Manager, will schedule any unplanned meetings.

The DSMB may request special reports on an as needed basis. These requests will be made to the Principal Investigator, who will direct the study team or study statistician as appropriate.

9 COMMUNICATION

This DSMB will meet via meeting/teleconference call [frequency]. An agenda will be provided detailing the protocol(s) to be discussed. It is estimated that the meeting/teleconference will be scheduled for [#] hours.

9.1 Reports to the DSMB

- Associated SAEs and AEs of special interest will be provided to the DSMB yearly or as requested by the Board.

- Data and safety monitoring meeting report will be provided to the DSMB at least two weeks prior to each scheduled meeting.

9.2 DSMB Minutes

The DSMB meetings may be audio taped for the purpose of documenting meeting minutes. Once the Chair approves the minutes, the tapes will be backed up on a secure server behind the OSUMC firewall.

The DSMB Chair and/or DSMB Program Manager will prepare the draft meeting minutes of the open session and forward to the DSMB Chair and committee for review within two (2) weeks following the DSMB meeting. Minutes of the open session will describe the proceedings. Draft minutes will be distributed to [Dynamic Reference] for review and comment.

Minutes of the closed session will describe the proceedings of the closed session. Minutes will be taken by the DSMB Chair and/or DSMB Program Manager. If unmasked information is reviewed during the closed session, minutes containing unmasked information will be marked as “Confidential” and distributed to the members of the DSMB only.

At the conclusion of the study, a complete set of the minutes of the closed sessions and the closed reports will be sent to the DSMB Chair and DSMB Program Manager.

9.3 Recommendations

Following the closed session, a brief meeting/teleconference will be held between the DSMB Chair and the specified Principal Investigator to discuss the recommendations of the DSMB. This brief unofficial meeting/teleconference will take place within one (1) week of the DSMB official meeting

A brief summary that describes the individual findings, overall safety assessment, and DSMB recommendations will be agreed upon by the Chair and forwarded to the DSMB Program Manager for distribution to the Principal Investigator within two (2) weeks of the meeting.

The DSMB can recommend to the Principal Investigator that the current study continue without modification, continue with specified modifications, discontinue one or more arms of the study, or halt or modify the study until more information is available.

10 REVISIONS TO THE CHARTER

A draft of the Charter will be provided to the DSMB prior to the organizational meeting. During the organizational meeting, the Charter will be reviewed and revised as needed. The Chair and DSMB Program Manager will approve all changes to the Charter. The version date will be displayed as a footer on all pages.

As needed, the Charter may be revised after the organizational meeting, with the Chair and DSMB Program Manager providing sign-off. Changes to the Charter will be clearly delineated in a tracked changes document, and this document will be associated with the new version.

11 COMPLETION OF DSMB ACTIVITIES

The DSMB will remain active until written notification is received from the Principal Investigator.

12 DOCUMENT RETENTION

The DSMB members will maintain a copy of any relevant correspondence, meeting packets, DSMB reports, and meeting minutes in a secure area prior to the meeting occurrence.

The PI and study team will maintain DSMB project files in a secure area with limited access.

The OSU/CCTS will keep all meeting materials in electronic format on the OSUMC server for a period of 5 years after the DSMB termination.

13 REFERENCES

Department of Health, Education, and Welfare, Office of the Secretary, Protection of Human Subjects. Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, Report of the National Committee for the Protection of

Human Subjects of Biomedical and Behavioral Research. DHEW Publication No. (OS) 78-0013 and No. (OS) 78-0014. 18 April 1979.

Ellenberg, Susan S., Fleming, Thomas R., DeMets, David L. Data Monitoring Committees in Clinical Trials, A Practical Perspective. John Wiley and Sons, LTD, West Sussex, England, 2002.

The Greenberg Report (1988). Organization, review, and administration of cooperative studies: a report from the heart special project committee to the National Advisory Heart Council. Controlled Clinical Trials 9 (2): 137-148.

US Food and Drug Administration (2001) Guidance for Clinical Trial Sponsors on the Establishment and Operation of Clinical Trial Data Monitoring Committees. Rockville, MD: FDA. http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM12707.

UNICEF/UNDP/World Bank/WHO (31 March 2004). Operational Guidelines for the Establishment and Functioning of Data and Safety Monitoring Boards. Geneva, Switzerland.

Food and Drug Administration (March 1, 2006). Guidance for Clinical Trial Sponsors Establishment and Operation of Clinical Trial Data Monitoring Committees. https://www.fda.gov/OHRMS/DOCKETS/98fr/01d-0489-gdl0003.pdf

DAMOCLES Study Group (2005). A proposed charter for clinical trial data monitoring committees; helping them do their job well. Lancet 365:711-22.

Appendix A: DSMB Member Signature Page

Member Information

Role: DSMB Chair _____ Member ____

Voting Rights: Yes ____ No ___

Name:

Affiliation:

Phone: Fax:

E-mail address:

Re: DSMB Charter Version Date: _____

I have reviewed the attached DSMB Charter and approve it as written. I understand my role as a member of this DSMB.

Signature: _____ Date: _____

Appendix B: Dynamic Reference List

DSMB Membership List

Members of the DSMB are:

1. [Name], Chair of the DSMB
2. [Names of each other member along with his/her title and area of expertise]