

**PRINCIPAL INVESTIGATOR RESPONSIBILITIES RELATED TO THE
NIAMS Data and Safety Monitoring Boards (DSMBs) or
Observational Study Monitoring Boards (OSMBs)**

**The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS),
National Institutes of Health (NIH)**

INTRODUCTION

This document describes the roles of the clinical study Principal Investigator with respect to a Data and Safety Monitoring Board (DSMB) or Observational Study Monitoring Board (OSMB). The role of the DSMB/OSMB is to provide ongoing, independent study review and assure the study is conducted according to the highest scientific and ethical standards.

PRINCIPAL INVESTIGATOR SAFETY MONITORING RESPONSIBILITIES

The Principal Investigator's Safety Monitoring responsibilities throughout the study are outlined in the following sections and appear in *bold italics*.

Prior to the First DSMB/OSMB Meeting

- ***Submit a monitoring plan to the NIAMS Program Director for approval*** - The plan should address how data and safety monitoring activities will be implemented.
- ***Submit the clinical protocol to the NIAMS Program Director for approval*** – This document must be reviewed and approved by the NIAMS prior to beginning enrollment.
- ***Develop the study Manual of Operating Procedures (MOOP)***. This document should be sent to the NIAMS and the DSMB/OSMB for review.
- ***Submit the IRB approved consent form(s), Food and Drug Administration (FDA) approval(s), if applicable, and IRB approval letter(s) to NIAMS for record.***
- ***Suggest members for the DSMB/OSMB to the NIAMS Program Director*** - Potential candidates should possess appropriate expertise in the relevant scientific and methodological areas and may include clinicians, statisticians, ethicists and patient advocates. Members must be completely independent of the Principal Investigator and have no financial, scientific, or other conflicts of interest with the trial.
- ***In consultation with the study statistician, propose routine reports to present at DSMB/OSMB meetings*** – Reports include a brief narrative description of the study background, status, significant problems, and proposed resolutions. The narrative is followed by a series of tables. These reports must be customized to meet the needs of each particular study. Report templates can be found on the NIAMS public website.

- ***Provide the Executive Secretary with the protocol, safety monitoring plan, MOOP, study forms, proposed DSMB/OSMB meeting reports, and any other meeting materials at least two weeks before the meeting.***
- ***Prepare a presentation about the study protocol to give at the first DSMB/OSMB meeting*** – A presentation, using slides or other materials and limited to no more than 45 minutes to one hour, should be prepared and presented at the first meeting. The presentation should include a brief summary of the study, follow-up and analysis plan(s), etc. Presentation materials should be sent to the Executive Secretary at least one week prior to the meeting for immediate posting to the website. The presentation should touch on significant areas of the protocol and should not repeat the entire protocol.
- ***Review the DSMB/OSMB Charter*** – The DSMB/OSMB Charter outlines the charge to the DSMB/OSMB and is dynamic throughout the study. The DSMB/OSMB members will provide suggestions for amending the Charter at the first meeting and/or vote for its approval.

The First DSMB/OSMB Meeting

The first meeting generally takes place in an in-person format prior to study initiation and will last approximately four hours. Attendees include the Principal Investigator, the study statistician, the DSMB/OSMB members, the NIAMS officials and the Executive Secretary. Any additional study staff must be approved by the NIAMS officials. The Executive Secretary will gather calendars, facilitate the meeting and distribute study materials that are prepared by the study personnel to the DSMB/OSMB members and NIAMS officials. Travel arrangements for the study staff attendees will be the responsibility of the study staff, per the [grant/contract].

- ***The DSMB/OSMB members vote to approve the Chairperson appointed by the NIAMS*** - The Chairperson is responsible for overseeing and leading the DSMB/OSMB meetings. In addition, the Chairperson works with the NIAMS and/or the Executive Secretary to prepare the agenda and summarize the meeting. The Chairperson is the primary contact person for the DSMB/OSMB.
- ***The DSMB/OSMB members vote to approve the designated Safety Officer appointed by the NIAMS*** – Serious Adverse Events (SAEs) should be sent to the designated DSMB/OSMB Safety Officer, the NIAMS officials and the Executive Secretary within 48 hours of the event. The Executive Secretary will follow up with the Safety Officer, if needed, and inform the PI, NIAMS and the DSMB/OSMB Chair what action, if any, has been recommended. *Please note: Adverse Events will be reported to the DSMB/OSMB in aggregate summaries and listings.*
- ***The PI gives a presentation about the study protocol*** – The purpose of this presentation is to provide the DSMB/OSMB members with background about the study and explain the basics of the study protocol. Please limit this presentation to 45 minutes to one hour.
- ***DSMB/OSMB members decide on the content of DSMB/OSMB reports*** – The DSMB/OSMB reviews the reports proposed by the study statistician and Principal

Investigator and provides instructions on what information they would like the study coordinating center/statistical office or statistician to include in future reports. Requirements for an interim analysis, if applicable, will also be determined by the DSMB/OSMB at this meeting. Reporting requirements may be augmented as the study progresses.

Subsequent DSMB/OSMB Meetings – Subsequent meetings are usually held biannually, once via teleconference (approximately two hours) and once in-person (approximately four hours). Additional meetings may be held ad-hoc or routinely, if determined necessary.

- ***The PI/study statistician provides the Executive Secretary with the DSMB/OSMB report at least two weeks before a meeting*** - Once a study begins, the study coordinating center, statistical office or statistician will prepare reports as agreed upon with the DSMB/OSMB. The reports should be clearly labeled to identify open and closed session reports, as relevant. It is preferred that the reports be sent electronically to the Executive Secretary for immediate posting to the NIAMS Safety Monitoring Website. The Executive Secretary will distribute the reports to the DSMB/OSMB and the NIAMS representatives.
- ***The PI/study statistician distributes the DSMB/OSMB report to all study staff members who will attend the DSMB/OSMB meeting***
- ***The changes to the report(s) since the last meeting should be highlighted*** – Presentation for subsequent, routine meetings should be streamlined and highlight changes to the report(s) since the last meeting. Please limit this presentation to 45 minutes to one hour.

Below is the general format of DSMB/OSMB Meetings:

General (Open) Session

- Includes the Study Staff, DSMB/OSMB members, the NIAMS and the Executive Secretary
- The Principal Investigator presents the study's key points, progress, and issues to the DSMB/OSMB

Closed Session

- Includes the DSMB/OSMB, the Study Statistician (if needed), the NIAMS and the Executive Secretary
- Safety data is presented by the Study Statistician
- Efficacy data is also presented, if it is requested by the DSMB/OSMB members

Executive Session

- Includes the DSMB/OSMB members, the NIAMS and the Executive Secretary
- Study status (advise NIAMS to start, stop or modify the protocol)
- Closed and executive sessions may be combined if the study statistician is not needed during the closed session.

Open Session (optional)

- Includes the Study Staff, the DSMB/OSMB members, the NIAMS and the Executive Secretary
- Discuss the DSMB/OSMB recommendations with the Principal Investigator

Follow-up after a DSMB/OSMB Meeting

- ***The PI submits a written response to the meeting recommendations within a specified timeframe*** - Recommendations are prepared by the Executive Secretary within 48 hours of the meeting and are submitted to the NIAMS and the DSMB/OSMB for review and approval. Once approved, the recommendations are submitted to the Principal Investigator, who is required to submit a written response to the recommendations within a specified timeframe (typically 30 days).
- ***The study staff attendees review and send comments through the PI to the Executive Secretary about the open session minutes (if applicable)*** - A formal report that provides the rationale for the recommendations is prepared by the Executive Secretary and submitted to the NIAMS and the DSMB/OSMB for initial review and comment. Once approved, the open session minutes are sent to study staff participants for review and comment. If applicable, closed session minutes, absent the executive session, will be sent to the study statistician. Closed session minutes must be held in confidence and must not be shared with persons who do not attend the closed session portion of the meetings.

Executive Secretary

The Principal Investigator and the study staff may only communicate with the DSMB/OSMB through the NIAMS or the Executive Secretary. The Executive Secretary is identified by the NIAMS and facilitates communication and distribution of safety materials to the DSMB/OSMB and the NIAMS. The Executive Secretary coordinates DSMB/OSMB meetings and teleconferences and provides logistical arrangements and support for the DSMB/OSMB. The agenda, recommendations and minutes for DSMB/OSMB meetings are prepared by the Executive Secretary, who will seek input and approval from meeting participants. NIAMS officials and the Executive Secretary serve as ex-officio DSMB/OSMB members.