UNIVERSITY OF SOUTH ALABAMA

IRB SOP 1204
Data Safety Monitoring Plan

Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe Institutional Review Board review of data and safety monitoring plans (DSMP) to ensure adequate protection is in place for study participants.

Scope

This SOP applies to all clinical research in which the USA Institutional Review Board is the IRB of record.

Applicability

This policy applies to all research studies (i) involving greater than minimal risk, or NIH funded/FDA regulated clinical trials and (ii) all investigator-initiated clinical research studies, regardless of risk.

Definitions

Data Safety Monitoring Plan (DSMP): A DSMP describes how the Lead Researcher plans to oversee the research participant's safety and welfare, and how adverse events will be characterized and reported.

Data Safety Monitoring Board (DSMB): A DSMB (or DMC) is a formally appointed group that will conduct interim monitoring of accumulating data from research activities to assure the continuing safety of research participants, relevance of the study question, appropriateness of the study and integrity of the accumulating data.

Policy

It is the responsibility of the IRB to ensure the study site has appropriate measures to monitor the data in order to maintain the safety of the patients and the integrity of the study data. The IRB should review all studies for the presence and adequacy of the PI's monitoring plan.

1.0 Data Safety Monitoring Plan

A Data Safety Monitoring Plan (DSMP) is a written procedure that describes how the Principal Investigator plans to oversee the human subject's safety and welfare throughout the course of the study. The level of detail in the plan should be based upon the degree of risk to the subjects. The intensity and frequency of monitoring should be tailored to fit the expected risk level, complexity, and size of the particular study. Review of safety reports and trial data by a Data Safety Monitoring Board (DSMB) or medical monitor may be part of a DSMP, but it is not the entire DSMP. A DSMP is required for all research that is not exempt under Federal Regulations applicable to Human Subjects Research.

A Data and Safety Monitoring Plan (DSMP) is unique to a particular study. Appropriate DSMPs may fall anywhere along a continuum from monitoring by the principal investigator or group of investigators to the establishment of an independent Data and Safety Monitoring Board (DSMB). Safety monitoring may be accomplished as follows:

- The investigator performs the safety monitoring. (This would be appropriate for a single site open label trial.)
- An uninvolved expert in the research topic performs the safety monitoring. (This would be appropriate for a single site blinded trial.)
- The sponsor's medical monitor performs safety monitoring.
- The sponsor's safety monitoring committee performs safety monitoring.
- An independent data and safety monitoring board (DSMB) performs safety monitoring. Regardless of the type of DSMP, the individuals participating in the monitoring plan must be objective.

2.0 Data Safety Monitoring Board

A Data and Safety Monitoring Board (DSMB) is an independent group of experts that advises the sponsor and the study investigators. The members of the DSMB serve in an individual capacity and provide their expertise and recommendations. The DSMB evaluates research data on an ongoing basis to assure participant safety and study integrity. The DSMB periodically reviews study data and unanticipated problems and makes recommendations based on their reviews along with assessing the performance

of overall study operations and any other relevant issues, as necessary. The following is a list criterion for the use of a DSMB:

- Multi-site clinical trials with interventions that entail risk(s) to participants
- If the trial is evaluating mortality or another major endpoint, such that inferiority of one treatment arm has safety as well as effectiveness implications.
- Any research done in an emergency setting where the informed consent requirement is waived.
- All phase III clinical trials with the exception of behavioral and nutritional studies
- Phase I or II trials that involve blinding
- The trial includes vulnerable population and is greater than minimal risk
- When it would be ethically important for the trial to stop early if the primary question addressed has been definitively answered, even if secondary questions or complete safety information were not yet fully addressed.
- When there is prior information suggesting the possibility of serious toxicity with the study treatment
- Studies that do not meet the above criteria, but are required by the funding source to be reviewed by a DSMB.

Most industry sponsored trials will have an established DSMB. If a central DSMB is established by the sponsor, then the University of South Alabama will defer safety monitoring to that Board. Regular reports from the DSMB will need to be submitted to the governing IRB.

Procedures

1.0 IRB Responsibilities

Federal regulations [45 CFR 46.111(a)(6) and 21 CFR 56.111(a)(6)] stipulate that the IRB must determine that: “When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects. Consequently, it is the responsibility of the IRB to ensure a DSMP is in place for all research that is not exempt under Federal Regulations applicable to Human Subjects Research. This can be present in various formats including but not limited to a separate DSMP report or a section(s) in the protocol.

Studies that do not meet the criteria listed under Section 2.0 of the Policy (listed above) are not required to utilize a Data Safety Monitoring Board (DMSB). However, a Data Safety Monitoring Plan (DSMP) may still be required. The DSMP should be submitted with the initial IRB submission. A DSMP template can be found on IRBNet under Forms and Templates.

The IRB will determine whether the DSMP makes adequate provisions for monitoring the data collected to provide for the safety of subjects during initial review, continuing review, and review of modifications to research.

At the time of continuing review, the IRB will review the summary provided by the Investigator as part of the continuing review submission. The IRB will determine if the Investigator is adhering to the DSMP and if the DSMP is still adequate. Modifications to the DSMP may be requested by the IRB as part of the continuing review process.

1.1 Central Data Safety Monitoring Board

It should be indicated on the initial IRB application if the study sponsor is utilizing a central DSMB. The IRB will determine if the protocol, or any supplemental documents, makes adequate provisions for monitoring the data collected to provide for the safety of subjects.

At the time of continuing review, the IRB will review the recommendation of the central DSMB provided by the Investigator as part of the continuing review submission. The IRB may use the central DSMB's recommendation in their decision of continuing renewal.

1.2 USA Data Safety Monitoring Board

It should be indicated on the initial IRB application if the study sponsor is utilizing the USA DSMB. The IRB will determine if the protocol, DSMP, and/or any supplemental documents, makes adequate provisions for monitoring the data collected to provide for the safety of subjects.

The IRB administrative staff will notify the USA DSMB that a study requires review. Initial submission to the USA DSMB will be coordinated by the IRB administrative staff. DSMB review is independent of IRB review. In order to optimize processes for the USA IRB and USA DSMB committee review, both reviews will be carried out concurrently, to the extent possible.

Refer to the University of South Alabama, *SOP: Data Safety Monitoring Board* for more information regarding the responsibility of the IRB and the IRB administrative staff.

At the time of continuing review, the Investigator should submit the most recent USA DSMB recommendation. This recommendation should not be older than one year from the continuing review date.

Any recommendation made by the USA DSMB that references concerns for subject safety or data integrity should be submitted to the IRB within five (5) business days of receipt.

2.0 Investigator Responsibilities

Investigators will submit the DSMP in writing as part of the initial IRB submission. The elements that encompass a DSMP may be incorporated in the protocol. If placed in the protocol, a separate DSMP is not needed as long as the protocol adequately addresses the essential elements of a DSMP.

Depending on the extent and severity of expected harms in a research study, the DSMP should include provisions to determine whether the character, incidence, and severity of harms match expected harms and should describe the stages of research at which monitoring will occur (e.g., specific points in time, after a specific number of subjects have been recruited, upon recognition of harms). Monitoring may be conducted by investigators themselves, a medical monitor, a data safety monitoring committee, or other appropriate mechanism for the research activity. The Investigator should also include the process to unblinding and the criteria, if any, to stop administration of the product due to safety concerns.

2.1 Central Data Safety Monitoring Board

The Investigator should indicate on the initial IRB application that a central DSMB will be utilized.

At the time of continuing review, the Investigator should submit the most recent DSMB recommendation. This recommendation should not be older than one year from the continuing review date.

Any recommendation made by the DSMB that references concerns for subject safety or data integrity should be submitted to the IRB within 5 business days of receipt.

2.2 USA Data Safety Monitoring Board

The Investigator should indicate on the initial IRB application that the USA DSMB will be utilized.

At the time of continuing review, the Investigator should submit the most recent DSMB recommendation. This recommendation should not be older than one year from the continuing review date.

Any recommendation made by the DSMB that references concerns for subject safety or data integrity should be submitted to the IRB within five (5) business days of receipt.

Regulated Documents

45 CFR 46.101(b)
45 CFR Part 46, Subpart C 46.301-46.306

University Related Documents

SOP 1206: USA Data Safety Monitoring Board

Related Forms

Data Safety Monitoring Plan Template (Located in IRBNet forms and templates)

References

FDA: Guidance for Clinical Trial Sponsors- Establishment and Operation of Clinical Trial Data Monitoring Committees
NIH Policy for Data and Safety Monitoring

HISTORY
Effective Date:
Revisions: November, 2018