



Guidance:

Approval criteria #6 – Monitoring plan to ensure subjects' safety

Overview

Approval criteria #6 is as follows: **When appropriate the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects. (45 CFR 46).**

Data monitoring is required for all IRB protocols, regardless of risk level, and must include methods for monitoring and ensuring the accuracy, security, and validity of the data.

Safety monitoring includes the methods to ensure the safety of the subjects. The details and protections for this part of the plan should be calibrated to the likely harms associated with the research.

“When appropriate” allows an IRB to determine when a safety plan may not be required; however, there are definitive times when such plans are required. This guidance details data safety monitoring plans and boards, components, and requirements. It can be used when determining criteria #6 have been met.

What is a data safety monitoring plan (DSMP)

A data safety monitoring plan (DSMP) establishes procedures for the appropriate oversight and monitoring of participant safety in research by outlining the steps taken to review the validity and integrity of research data, tracking the progress of the research and safety of participants, and outlining the mechanism for reporting unanticipated problems involving risk to subjects and adverse events.

When is a DSMP needed?

All interventional studies¹ deemed more than minimal risk must include a data safety monitoring plan. This plan can be an attachment to the IRB application or include key components filtered throughout the IRB application itself. The substance and complexity of the data safety monitoring plan may differ depending on the risk to participants and the nature of

¹ A type of clinical study in which participants are assigned to groups that receive one or more intervention/treatment (or no intervention) so that researchers can evaluate the effects of the interventions on biomedical or health-related outcomes. The assignments are determined by the study's protocol. Participants may receive diagnostic, therapeutic, or other types of interventions.



the research. It is the responsibility of the PI to ensure there is an appropriate DSMP included with the IRB application and implemented throughout the life of the research protocol.

Regardless of risk level, a DSMP may be requested by an expedited reviewer or convened IRB.

Components of a DSMP

- A detailed plan to monitor study progress and participant safety.
- A description of the research staff that will conduct the monitoring and at what frequency the review will occur.
- The type of data and events (i.e., efficacy data, adverse events, unanticipated problems involving risk to participants or others) that are to be captured under the monitoring plan.
- Procedures for communicating the outcome of reviews to the IRB, the study sponsor and/or other appropriate entities.

When appropriate, the following may be required:

- A plan for conducting and reporting analysis
- Clearly defined rules for stopping or suspending a study based on monitoring.
- Clearly defined rules for withdrawing participants from study intervention(s)

What is a Data Safety Monitoring Board (DSMB)?

A Data Safety Monitoring Board (DSMB) consists of outside experts who monitor participant safety and/or the efficacy of a study product for a clinical trial. A DSMB is typically composed of three to ten people who are not directly involved in the conduct of the study and have no financial stake in the research. A DSMB will typically include ethicist, statistician, and medical personnel who specialize in the disease being studied and any possible adverse events (side effects) related to the experiment. Many studies also include a community or patient advocate – a representative from the primary target population for the study drug.

When is a DSMB required?

1. The study is intended to provide definitive information about the effectiveness and/or safety of a medical intervention.
2. Prior data suggests that the intervention under study has the potential to induce a potentially unacceptable toxicity.
3. The study is evaluating mortality or another major endpoint, such that inferiority of one treatment arm has safety as well as effectiveness implications.



4. It would be ethically important for the study 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.

What is the composition of a DSMB?

1. Multidisciplinary representation, including physicians from relevant medical specialties and biostatisticians. This may include other experts such as bioethicists, epidemiologists, and basic scientists.
2. Members who are free of significant conflicts of interest (i.e., financial, intellectual, professional, or regulatory).
3. The appropriate size depending on the type of study and types of expertise needed.

What information about a DSMB must be included in the IRB application?

If the protocol requires a DSMB, the following information is to be detailed in the protocol application form or as a standalone document.

1. **Composition:** Description of the expertise represented by the members of the DSMB. DSMBs generally include members with expertise in biostatistics, clinical trials, and the disease and treatment being studied. Other areas of expertise such as bioethics may also be useful.
2. **Independence:** Confirmation that DSMB members are independent of the study sponsor and will not participate in the study as investigators, nor will they have conflicts of interest regarding the study, the study sponsor, or any study drugs or devices being tested.
3. **Data:** Briefly description of the data the DSMB will review, e.g., data for primary or secondary endpoints (safety and efficacy), data for early termination of trial (stopping rules), or adverse events.
4. **Frequency of Review:** Description of how often the Board will meet, whether based on the calendar or accrual targets. If formal interim analyses are planned, describe when they will occur.
5. **Authority:** Description of the actions the DSMB is authorized to take. DSMBs should have authority to recommend changes in the study, including discontinuation, if significant trends in safety or efficacy are identified earlier than expected.

References & Resources

- [Common Rule, 45 CFR Part 46](#)
- [NIH Policy on Data and Safety Monitoring](#)
- [Data Safety Monitoring for Phase I and Phase II Trials](#)
- [Individual Funding Agency Requirements](#)
- [Example of a Data Safety Monitoring Plan](#)



- [\(16\) An NIH Data Management and Sharing \(DMS\) Policy Primer for the PRIM&R Community | LinkedIn](#)