

Institutional Review Board (IRB) Policies & Procedures Manual



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Data and Safety Monitoring Plans

Purpose

The purpose of this policy is to define the requirements for inclusion of a Data and Safety Monitoring Plan in clinical research protocols submitted to the Boston Children's Hospital IRB for review and approval.

It also provides guidance for investigators in establishing an appropriate Data and Safety Monitoring Plan for their research.

Policy

Boston Children's Hospital IRB requires the inclusion of a Data and Safety Monitoring Plan (DSMP) in all clinical research protocols that involve more than minimal risk to subjects.

The DSMP must be described in sufficient detail for the IRB to determine whether the plan is appropriate for the research.

This policy complies in part with the requirement for IRBs to determine "where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects" [45 CFR 46.111(a)(6) and 21 CFR 56.111(a)(6)]

Procedure

Data and Safety Monitoring: The regular evaluation of data and documentation collected during a study to ensure adherence to the approved investigative plan, the validity of data, continued scientific merit, and safety of the subjects.

Minimal risk: The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. [45 CFR 46.102(j) and 21 CFR 56.102(i)]

Content of a DSMP

The Data and Safety Monitoring Plan (DSMP) should include the following:

1. The type of data or events that are to be captured under the monitoring plan.
2. Who will be responsible for monitoring the data collected and their respective roles (i.e., investigators, the research sponsor, a coordinating or statistical center, an independent medical monitor, a Data Safety Monitoring Board (DSMB)/Data Monitoring Committee (DMC), and/or some other entity), including data related to unanticipated problems and adverse events

3. Unanticipated problems and adverse events: The following should be established:
 - a. Procedures to report.
 - b. Time frames for reporting.
 - c. Plans for assuring compliance with requirements regarding reporting.
4. The frequency of assessments of data or events captured by the monitoring plan, such as points in time or after a specific number of participants are enrolled.
5. Plans for review or analysis of cumulative safety data to determine whether harm is occurring.
6. Definition of specific triggers or **stopping rules** that will dictate when some action is required.
 - a. **Stopping rules:** Predetermined guidelines that are used to determine that the study should be altered or stopped, based on review of study data and related events that occur during the conduct of the study.
 - b. Stopping rules should be specific about the endpoints that will be used and the decisions that will be made. Studies may be stopped, for example, when there is a greater than expected rate of morbidity or mortality or when the experimental arm of a head-to-head comparison study is shown to be better or worse statistically than the standard care arm.
7. Plans for assuring data accuracy and protocol compliance.
8. As appropriate, procedures for communicating to the IRB, the study sponsor, and other appropriate entities the outcome of the reviews by the monitoring entity.
9. Plans for assuring communication among multi-center sites adequately protect the subjects for multicenter studies where a BCH PI is responsible for the single IRB review of the protocol or is when BCH is the coordinating institution.

Types of DSM Plans

A Data and Safety Monitoring Plan should be tailored to the nature, size, and complexity of the research protocol, the expected risks of the research, and the type of subject population being studied.

Appropriate DSMPs may fall anywhere along a continuum from monitoring by the Principal Investigator (PI) or group of investigators to the establishment of an independent Data and Safety Monitoring Board (DSMB)/Data Monitoring Committee (DMC).

1. Investigator

A PI could perform the monitoring function, if the study involves a small number of subjects; the study is conducted only at one site; and the range of possible study events that could have an important impact on the risks and benefits of research participants is narrow. In such cases, continuous monitoring of events by the PI, and prompt reporting to the IRB and when applicable, the FDA, NIH, or others, may be adequate.

2. Monitor/Monitoring Group

A qualified and objective individual or group not directly involved with the design and conduct of the study (i.e., safety officer, designated medical monitor or monitoring group) could perform the monitoring function, if the study is a clinical trial that involves the following:

Endpoints that are not serious irreversible events;

- An intervention (i.e., to relieve symptoms) that is not high risk and the effects would not generally be so compelling as to ethically warrant early termination for effectiveness;
- Short term treatments where effects are evaluated over periods of a few days to a few months; and
- A smaller number of subjects where the study is completed quickly, and the risk can be adequately assessed through simple comparisons.

These individuals may or may not be employees of Boston Children's Hospital or the study sponsor. However, conflict of interest is an important consideration when employees of the study sponsor have the primary responsibility for monitoring data from the standpoint of scientific integrity and participant safety.

3. Data and Safety Monitoring Board (DSMB)/Data Monitoring Committee (DMC)

A DSMB/DMC is a formal committee that is established specifically to monitor data throughout the life of a study to determine if it is appropriate, from both the scientific and ethical standpoint, to continue the study as planned.

In general, an independent DSMB/DMC is the most appropriate way to monitor data and safety for studies that involve:

- Large numbers of subjects where risk may better be assessed through statistical comparisons of treatment groups.
- Blinded study treatment groups where the validity and integrity of the study may be adversely affected by having an individual or group associated with the design and conduct of the study break the blind.
- Multiple clinical sites where there is a need for investigators to submit reports of adverse events to a central reporting entity, such as a coordinating center or statistical center, responsible for preparing timely summary reports of adverse events for distribution among the clinical sites, and to the IRBs;
- High risk interventions where death or severe disability is a major risk of research participation; and/or
- Controlled trials with mortality or major morbidity as a primary or secondary endpoint where increased morbidity or mortality may better be assessed through statistical comparisons of morbidity or mortality among treatment groups.

DSMB/DMC Composition

DSMBs/DMCs are typically made up of individuals who:

- Have expertise in the field
- Experience in the conduct of clinical trials
- Statistical knowledge
- Who do not have any conflicts of interest, such as:

- Financial interests that could be substantially affected by the outcome of the trial
- Strong views on the relative merits of the interventions under study,
- Relationship with the sponsor or those in trial leadership positions that could be considered reasonably likely to affect their objectivity.

Schedule and Oversight

DSMBs/DMCs meet at least annually depending on the nature of the trial being monitored. DSMBs/DMCs can monitor the timeliness of accrual, the quality of data collection and management, and the accumulating outcomes to assure the safety of participants and the scientific integrity of the study.

Overall PI Responsibility

Regardless of data and safety monitoring plans by the sponsor or others, the Principal Investigator is ultimately responsible for protecting the rights, safety, and welfare of subjects under their care and for ensuring that the study is conducted at their investigative site in accordance with the IRB-approved protocol, and applicable regulations and requirements of the IRB.

NIH Sponsored Research

It is the policy of the NIH that each Institute and Center should have a system for the appropriate oversight and monitoring of the conduct of clinical trials to ensure the safety of participants and the validity and integrity of the data for all NIH-supported or conducted clinical trials.

The establishment of the data safety monitoring board (DSMB) is required for multi-site clinical trials involving interventions that entail potential risk to the participants. The data and safety monitoring functions and oversight of such activities are distinct from the requirement for study review and approval by an IRB.

Related Content

Federal Guidance

NIH Data and Safety Monitoring: Policy and Guidance, Institute/Center Procedures and Guidance: http://grants.nih.gov/grants/policy/hs/data_safety.htm

FDA Guidance for Clinical Trial Sponsors: Establishment and Operation of Clinical Trial Data Monitoring Committees, March 2006:
<http://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm127073.pdf>

Document Attributes

Title	Data and Safety Monitoring Plans		
Author	Susan Kornetsky	Dates	04/01/2005

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