

Guidance - Data and Safety Monitoring

A criterion for IRB approval of research is that risks to subjects are minimized. This may be partly accomplished by monitoring the data collected while research is in progress. There are a number of aspects that are considered when determining the type of monitoring required for the study. It could be as simple as protecting the data (how data is protected, who has access, are you collecting the minimum necessary, etc.) in a retrospective record review or more complicated in clinical trials which would include some of the actual tests and procedures used for monitoring. Therefore, Data and Safety Monitoring (DSM) provisions should be tailored to the nature, size, complexity, and risks of the research and should be described in the protocol submission to the IRB.

- Many studies (e.g., if more than minimal risk) need a **DSM Plan**
- The **DSM Plan** *might* need to include a **Data Monitoring Committee**

A Data Monitoring Committee or Board (DMC or DSMB), *if required*, is described in the DSM Plan. (DMC and DSMB are generally used interchangeably.)

1. When is a Data and Safety Monitoring Plan (DSMP) required?

A Data and Safety Monitoring Plan (DSMP) is required for:

- More than minimal risk studies, for example:
 - Phase III clinical trials
 - New, unfamiliar interventions not otherwise categorized as phase III clinical trials
 - Multi-site research where Geisinger is the coordinating site
 - Research that is blinded, multi-site, enrolls vulnerable populations, or employs high-risk interventions
- NIH sponsored Phase I, II, and III clinical trials, and multi-site clinical trials involving interventions that entail potential risk to the participants
- Studies with an NIH or FDA requirement for a plan
- Other studies when required by the IRB

2. Components of a Data and Safety Monitoring Plan (DSMP)

The plan - *as appropriate to the risks, size, and complexity of the study* - might include:

- (i) **Types of data or events** captured, for example:
 - **What** safety information will be collected (including serious adverse events)?
 - **How** safety information will be collected (e.g., via case report forms, at study visits, by telephone calls with participants)?
 - **When** data will be collected (e.g., frequency; when collection starts)?
- (ii) **Roles and responsibilities for gathering, evaluating and monitoring the data**
 - Roles of investigators, research staff, sponsor, and monitoring committee/entity
 - Who will verify data accuracy, by what method?
 - Who will verify compliance with the protocol?

- (iii) **Information about the monitoring entity**
 - Description (e.g., individual Medical Monitor, Data Monitoring Committee (DMC) consisting of <number> members)
 - Information about each member's expertise
 - Mechanisms to assure independence of judgment
- (iv) **Timeframes for reporting adverse events and unanticipated problems to the monitoring entity**
- (v) **Frequency of monitoring entity's assessment of data or events**
For multicenter clinical trials involving high risk to subjects, frequent DSMB/DMC monitoring may be appropriate
- (vi) **Specific triggers or stopping rules:**
Conditions that would trigger an immediate suspension of the research.
If not using a data monitoring committee, the plan should describe statistical tests for analyzing the safety data to determine whether harm is occurring.
- (vii) **Procedures for communicating** the outcome of the reviews to the IRB, the study sponsor, and other appropriate entities.

3. Who or What is the Monitoring Entity?

Monitoring entity (ME): An identified individual or group who will conduct interim monitoring of accumulated data from research activities to assure the continuing safety of participants, relevance of the study question, appropriateness of the study, and integrity of the accumulating data. The ME should include expertise in the relevant field of study, statistics, and research design. A monitoring entity might be:

- PI
- Data Monitoring Committee (DMC)
- NIH sponsored cooperative group
- Coordinating or statistical center
- Medical Monitor (an individual)

4. Data Monitoring Committees (DMC)

- **NIH:**
 - Phase III clinical trials require a DMC
 - For phase I and II trials, a DMC may be appropriate.
- **FDA:**
 - Planned emergency research requires a DMC
 - A DMC is generally recommended for controlled trials of any size that will compare rates of mortality or major morbidity
 - A DMC may be useful for certain early clinical studies, e.g., when risk to participants appears unusually high
- **Other studies when required by the IRB**

5. Investigator Responsibilities

New Study Submission

When applicable, the study design should include procedures to monitor data to ensure the safety and well-being of participants. A DSM Plan, described in the study submission and must be commensurate with the level of risk, size, and complexity of the study.

Continuing Review – Reporting to the IRB

The continuing review report must include all reports. Even when a DMC has not identified any problems and simply recommends continuation of the research study as designed, the IRB should be informed of this recommendation. The report must be uploaded and attached to the continuing review report.

Multi-center Trials Monitored by a DMC or sponsor: Submit a current report from the monitoring entity including:

- A statement indicating what information (e.g., project-wide adverse events, subject withdrawals, complaints about the research, interim findings, and any recent literature that may be relevant to the research) was reviewed by the monitoring entity
- The date of the review and
- The monitoring entity's assessment of the information reviewed

6. IRB Responsibilities

To approve research, the IRB must determine that, when appropriate, the research plan makes adequate provisions for monitoring the data to ensure the safety of research participants [[45 CFR 46.111\(a\)\(6\)](#), [21 CFR 56.111\(a\)\(6\)](#)].

The IRB has authority to observe or have a third party observe the research [[45 CFR 46.109\(e\)](#)].

Review of the Data Monitoring Plan

The reviewer(s) review and evaluate the proposed DSM Plan and the administration and composition of the monitoring entity (ME) when applicable. The DSM Plan should include the appropriate elements and address required reporting.

If additional expertise is needed, the IRB consults with individuals with appropriate clinical, scientific, or biostatistical knowledge.

Setting the Timeframe for Reporting Data Monitoring Findings to the IRB

The IRB may specify the timeframe for reporting the findings to the IRB, for example, for continuing review in less than a year, after a specific number of participants are enrolled, or after a serious adverse event has been reported.

IRB Continuing Review and Data Monitoring Findings

The IRB considers relevant information since the previous IRB review and approval.

The IRB pays particular attention to risk assessment and monitoring, and ensures that the conditions satisfied in order for initial IRB approval of the research are still fulfilled.

It also may be appropriate for the IRB to confirm that any previously approved provisions for monitoring the research data have been implemented and are working as intended.

Multi-center trial monitored by DSMB/ DMC/sponsor/etc. if Geisinger is not lead site:

The IRB may require a report be submitted by the investigator and also may ask the monitoring entity directly to provide such a report ([45 CFR 46.102\(h\)](#), [109\(a\)](#)).

7. Sponsor Responsibilities

When sponsors are responsible for monitoring the research, Geisinger has a written plan or agreement with the sponsor that the sponsor promptly reports to Geisinger findings that could influence the conduct of the study, affect participants' safety or willingness to continue participation, or alter the IRB's continuing approval.

See HRPP Section 17.

Resources: Regulations and Guidance

FDA

- [21 CFR 56.111\(a\)\(6\)](#)
- [Establishment and Operation of Clinical Trial Data Monitoring Committees](#)

OHRP

- [45 CFR 46.111\(a\)\(6\)](#)
- [Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events](#)
- [Guidance on Continuing Review](#)

NIH & NIH Institutes and Centers

- [NIH Policy for Data and Safety Monitoring](#)
- [Further Guidance on Data and Safety Monitoring for Phase I and Phase II Trials](#)
- [Guidance On Reporting Adverse Events To Institutional Review Boards For NIH-Supported Multicenter Clinical Trials](#)

Resources: Other References

- Data Monitoring Committees –based on FDA March 2006 “Guidance for Clinical Trial
- Sponsors: [Establishment and Operation of Clinical Trial Data Monitoring Committees](#)”
- Data Monitoring Plans and Data Monitoring Committees - NIH and NCI Policies
- Events and Information that Require Prompt Reporting to the IRB
- Section 9.2