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What is a DSMB?

The Emory IRB Policies and Procedures define a DSMB as a formally appointed independent group consisting of at least three (3) members assigned to conduct interim monitoring of accumulating data from research activities to assure the continuing safety of human subjects, relevance of the study question, appropriateness of the study, and integrity of the accumulating data. Membership should include expertise in the relevant field of study, statistics, and research study design.

In a 2001 draft guidance document, the FDA defines a DSMB as “a group of individuals with pertinent experience that reviews on a regular basis accumulating data from an ongoing trial. The DSMB advised the sponsor regarding the continuing safety of current participants and those yet to be recruited, as well as the continuing validity and scientific merit of the trial.” <http://www.fda.gov/cber/gdlns/clindatmon.htm#1>

There are other names for committees that monitor accumulating data (e.g., Data Monitoring Committee).

What is the Purpose of a DSMB?

- Identify unacceptably slow rates of accrual
- Identify high rates of ineligibility determined after randomization
- Identify protocol violations that suggest clarification of changes to protocol are needed
- Identify unexpectedly high dropout rates that threaten the trial’s ability to produce credible results
- Ensure the credibility of the study
- Ensure the validity of study results
- Protect the safety of trial participants

Regulatory Considerations

The regulations provide minimal insight on DSMBs. In 2001, the FDA released draft guidance which can be found at: <http://www.fda.gov/cber/gdlns/clindatmon.htm#1>

This guidance discusses the roles, responsibilities, and operating procedures of DSMBs. This document is helpful in determining whether a DSMB is needed and how DSMBs should function.

Though it is not required, the FDA generally expects the use of DSMBs for randomized trials with mortality or major morbidity as primary endpoints.

The only mention of DSMBs in the Code of Federal Regulations is found in 21 CFR 50.24 (a)(7)(iv), the section on “Exception from informed consent requirements for emergency research.” This regulation mandates that the establishment of an independent data monitoring committee to exercise oversight of the clinical investigation for studies where human subjects are in a life-threatening situation and the investigation meets the criteria in 21 CFR 50.24.

The Code of Federal Regulations indirectly address data safety monitoring in [45 CFR 46.111 \(a\)\(6\)](#) which states “When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.”

Do I need a DSMB?

While it is important to remember that all studies require careful monitoring, it is also important to know that not all studies require DSMBs. The following questions are designed to help make a determination as to whether or not a DSMB may be needed.

- Is there a large study population, or are there multiple study sites?
- Is the trial intended to provide definitive information about effectiveness and/or safety of a medical intervention?
- Do prior data suggest that the intervention being studied has the potential to induce unacceptable toxicity?
- Does the trial evaluate mortality or another major endpoint, such that inferiority of one treatment arm has safety and effectiveness implications?
- Would it 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?

A DSMB usually should be implemented if two or more answers to the above questions are yes.

Who should the DSMB consist of?

The PI or trial sponsor generally appoints the DSMB. When appointing individuals to a DSMB, the following should be considered: relevant expertise, experience in clinical trials, experience as a member of other DSMBs, and a lack of conflict. A DSMB may consist of as few as 3 members, but this number should be large enough to include a representation of all needed skills and experience.

Who is typically included in a DSMB?

- Clinicians with expertise in relevant clinical specialties
- At least one biostatistician knowledgeable about analysis of trial data

Who might be included in a DSMB?

- Medical ethicist
- Other types of scientists (i.e., clinical pharmacologist, toxicologist, epidemiologist, laboratory scientist, etc.)
- Appropriate representation of gender and ethnic groups

What are the responsibilities of the DSMB?

The primary responsibility of the DSMB is to safeguard the interest of study participants. Therefore, the DSMB must approve the safety measures in the protocol to preserve the study credibility and facilitate the availability of timely and reliable findings to the broader clinical community.

In addition, the DSMB should:

- Provide written documentation confirming review of the protocol and agreement with the study design and the data safety monitoring plan (DSMP).
- Review the progress of the study carefully and diligently. At a minimum, each enrolled subject's research chart should be reviewed monthly for side effects and tolerability.
- Review the adverse event reports.
- Be available to the Investigator for consultation concerning any adverse study events.
- Consider the impact of newly published findings bearing on the safety profile of the study.
- Provide a written report to the IRB which summarizes oversight activities and recommendations, and any concerns regarding subject safety.

DSMB Charter Template:

http://www.niams.nih.gov/Funding/Clinical_Research/dsmb_charter.asp

Do all studies need an independent DSMB?

Some studies have too few subjects to support statistical analysis by a DSMB, but must have a clinical safety monitoring mechanism.

Some trials do not require a DSMB; for example, early phase non-randomized trials with limited safety concerns. Additionally, studies with rapid recruitment and short-term endpoints may not be long enough for a DSMB to be of any use. **All studies posing more than minimal risk should have a data safety monitoring plan (DSMP).** It is the policy of the Emory IRB that each research application that involves a medical intervention or procedure must include a plan to assure the safety and welfare of its participants.

What is a DSMP?

A DSMP describes how the Principal Investigator plans to oversee the human subject's safety and welfare. The Emory Policies and Procedures reporting apply to any DSMP, at least to impose the minimum requirements. Sponsors may impose stricter requirements. The intensity and frequency of monitoring should be tailored to fit the expected risk level, complexity, and size of the particular study.

What are the essential elements of the DSMP?

The plan should describe processes for dealing with the following:

1. Monitoring the Progress and Safety of the Trial
 - a. What are the potential risks and benefits for study participants?
 - b. What is the screening process and how it will be used to protect participants?
 - c. What are the measures to protect participants against risk?
 - d. Who will monitor the trials, what type of information will be reviewed, what are the parameters for defining abnormal values and what is the periodicity of review?
 - e. What are the stopping rules for the study?
 - f. What procedures are in place for multicenter trials, if applicable?
 - g. How will conflict of interest, or the perception of a conflict, be managed?
2. Reporting of Unanticipated Problems (Ups)
 - a. What constitutes a UP (include a definition, grading scale, and “study relatedness” criteria)?
 - b. What is the process for assuring that UPs are reported appropriately?
 - c. What are the timelines for UP collection and reporting?
3. Reporting of Suspensions or Terminations
 - a. Which actions (FDA, Sponsor, IRB, etc.) will be reported and who insures these actions are reported appropriately?

4. Assuring Data Accuracy and Protocol Compliance
 - a. How are data accuracy and protocol compliance assured?
 - b. What are the procedures to assure protocol adherence (i.e., protocol compliance checks, external data-audits, regular data verification, etc.)?
 - c. How are protocol deviations reported?
 - d. How is noncompliance reported?

Examples of DSMPs:

<http://www.cancer.gov/images/Documents/f69cebbb-fe0b-4f89-bee3-1609c2f5197b/StJudePLAN.pdf>

<http://www.cancer.gov/images/Documents/f69cebbb-fe0b-4f89-bee3-1609c2f5197b/DukeDSMPLAN.pdf>

<http://www.cancer.gov/images/Documents/f69cebbb-fe0b-4f89-bee3-1609c2f5197b/NorrisCottonDSMPlan.pdf>

<http://www.cancer.gov/images/Documents/f69cebbb-fe0b-4f89-bee3-1609c2f5197b/WisconsinDSMPlan.pdf>

What is the role of the IRB with regard to DSMBs and DSMPs?

The IRB is responsible for evaluating a study to determine, among other things, whether “risks to subjects are minimized” and “risks to subjects are reasonable in relation to anticipated benefits” [21 CFR 56.111\(a\)\(1\) and \(3\)](#). Additionally, the Code of Federal Regulations stipulates that “when appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects” [45 CFR 46.111 \(a\)\(6\)](#).

Reviewing the DSMP and all DSMB reports should be part of the IRB initial approval and subsequent approval. The IRB does not typically have access to the interim data, but the IRB may take action based on recommendations from the DSMB. The IRB must still review internal AEs and UPs involving risks to subjects or other and any information to ensure that the review is meaningful.

Where can I find more information about DSMBs and DSMPs?

[Guidance for Clinical Trial Sponsors On the Establishment and Operation of Clinical Trial Data Monitoring Committees](#) March (2006)

[National Cancer Institute Data and Safety Monitoring Guidelines](#)

[Policy for the National Cancer Institute for Data and Safety Monitoring of Clinical Trials](#)

[The Emory IRB Policies and Procedures: Section 47 Data and Safety Monitoring Plans](#)

[NIH/NIAMS DSMB Charter](#)

[NIH Guidance on Data and Safety Monitoring for Phase I and II Trials \(June 2000\)](#)

[Decision Tree for Data and Safety Monitoring Plan](#)

Ellenberg, Susan S., Thomas R. Fleming, and David L. DeMets. [Data Monitoring Committees in Clinical Trials: A Practical Perspective](#). Chichester, England: John Wiley, 2003.