Policy for Data and Safety Monitoring of Human Subject Research Studies

Purpose

The National Institutes of Health (NIH) requires the monitoring activities of all NIH-sponsored or -conducted clinical studies to be commensurate with their risks, nature, size, and complexity.

It is recognized that Institutes (I) and Centers (C) within NIH may have varying guidelines for DSM activities that are mandated for receipt of NIH IC specific funding. Hence, it is the PIs responsibility to check with individual institutes and centers for specific requirements. This policy presents broad guidelines and related definitions and procedures to follow when a DSM protocol is needed for an NIH study.

Definitions

Data and Safety Monitoring Plan (DSMP) - A written description of the procedures for reviewing accumulated data in an ongoing research protocol to ensure the safety of research participants and the continuing validity and scientific merit of the protocol.

NIH Definition of a Clinical Trial - A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

Data and Safety Monitoring Board (DSMB) (also known as a Data and Safety Monitoring Committee [DSMC] or Data Monitoring Committee [DMC]) - A formal committee made up of experts, who are not the trial organizers or investigators, which reviews on a regular basis accumulating data from one or more ongoing clinical trials.

Policy Details

Human Studies Requiring a DSMP

Appropriate mechanisms for data and safety monitoring may range from monitoring by the Principal Investigator (PI) or co-investigator (Co-I), to monitoring by an independent DSMB.

For example:

1. Monitoring by the PI or Co-PI or other designated individual may be appropriate for protocols involving no more than minimal risk or a minor increase over minimal risk and that are conducted at a single site.

2. Monitoring by an individual or team that is independent of the protocol may be appropriate for protocols that pose more than minimal risk to the subjects, for multi-site protocols, for studies where an investigator has a potential conflict of interest, or for some FDA-regulated research.

3. Because individual ICs may have varying requirements for DSMPs, PIs and UT Tyler IRB must refer to that specific IC for outlining protocol-specific DSMP.

4. When required as part of a protocol the DSMP shall be part of the IRB application materials as a separate Word document.

Implementation

Broad Requirements for a DSMP include:

1. Monitoring study safety;
2. Minimizing research- associated risk;
3. Protecting the confidentiality of participant data; and
4. Identifying, reviewing, and reporting adverse events and unanticipated problems to the IRB(s), NIEHS, and Food and Drug Administration (FDA) (if applicable).

Specific Requirements for a DSMP will address the following as appropriate:

1. Monitoring mechanism

    a. The individual(s) who will be responsible for the data and safety monitoring should be identified.
    b. When a DSMB is the monitor, the PI will provide the names of the DSMB chair, secretary and members and who is establishing the DSMB.

2. Frequency of monitoring: Monitoring should be performed on a regular basis at intervals determined before the study begins.

3. Stop or change rules: Specific criteria to be used for interrupting enrollment or administration of study products or procedures and formal guidelines to be used for stopping one or more study arms should be provided.

4. Advanced plans for any interim analyses and/or futility analyses.

5. Information to be monitored: In describing what information will be monitored, consideration will be given to the following, as appropriate:

    a. An evaluation of the progress of the research study, including assessments of data quality and timeliness and participant recruitment,

accrual and retention consistent with plans for diversity and generalizability.

b. A review of adverse event and outcome data to determine whether there is any change to the risk/benefit ratio of the study, if a stop rule has been invoked, a study endpoint has been reached, and whether the study should continue as originally designed, be changed, or be stopped.

c. An assessment of external factors or relevant information (e.g., developments in the literature, results of related studies, etc.) that may have an impact on the safety of participants or on the ethics of the research study.

6. Communication:

a. The lines of communication between the PI, the study sites, research teams, the data and safety monitor/committee, the IRB, the FDA, and other individuals at the NIH should be identified.

b. PIs for studies must submit, at a minimum, annual progress reports to the PO for extramural studies or to the CD for intramural studies that:

1. Confirm adherence to the DSMP.
2. Include a summary of any data and safety monitoring issues that occurred since the previous reporting period.
3. Describe any changes in the research protocol or the DSMP that may or does affect risk.
4. Provide all new and continuing IRB approvals.

Functions and Operations for DSMBs

DSMBs:

1. Are convened to protect the interests of research subjects and ensure that they are not exposed to undue risk.
2. Are advisory to the sponsor of the study and operate without undue influence from any interested party, including study investigators, UT Tyler IRB staff, or any IC.
3. Must be informed by the relevant IC of their ability to access unmasked data.
4. Are encouraged to review interim analyses of study data in an unmasked fashion as needed to assess the risks and benefits in the study.

For an extramural protocol, certification of IRB approval(s), and the DSMB plan if needed, must be sent electronically to the appropriate PO and approved before a proposed human subject research project may begin at a site. All other related

documents for an extramurally funded study will also be sent to the PO and archived in the main grant file as a permanent repository of study decisions and progress.

For intramural studies, all supporting documents will be sent to the NIH IRB of record after approval by the CD.

For multi-site studies, the study sites initiating a protocol and the Data Coordinating Center (DCC) must submit certification of IRB approval as well as assurance that IRB approvals have been obtained from all study sites, are on file, and are available to the appropriate IC upon request.

For extramural studies, the DSMB members will be proposed, after PI consultation, by the awardee institution, who will assure that there are no conflicts of interest.

For intramural studies, board members will be proposed, after PI consultation, by the CD. The DSMB will meet after IRB approval of the study but before enrollment of subjects.

Each DSMB must operate according to the provisions of a formal charter (see the National Institute of Aging Template, attached). Charters should address appointment and responsibilities of members, terms of appointment, scheduling and format of meetings, quorum requirements, distribution and disposition of meeting materials, preparation of meeting summaries and written recommendations, management of conflict of interest, voting rights, and other procedural matters.