Wayne State University Human Investigation Committee	
Subject	Data and Safety Monitoring in Research
Form Date	11/2008 (Rev. 03/07/11)
Approvals	General Counsel 12/21/2006; Steering Committee 02/05/2007; Administrative Approval 03/19/2007; Administrative Approval 10/30/2008; General Counsel 11/07/2008; Administrative Approval 03/07/11

Background

In order to ensure the safety of human participants throughout research studies, the scientific validity and integrity of data generated during the research, and compliance with federal mandates, the Institutional Review Board (IRB) at Wayne State University (WSU) must determine whether or not a data and safety monitoring board and/or plan is necessary for a protocol under review, and if required, whether or not the plan is adequate for these purposes [38 CFR 16/111(a)(6), 45 CFR 46.111(a)(6), 21 CFR 56.111(a)(6), and VHA Handbook 1200.05 17 e].

Scope

This HIC Policy/Procedure applies to all research being proposed at Wayne State University and its affiliate institutions. The criteria that may be used to determine if a data and safety monitoring plan would be required include:

- A large study population is being studied and there is the potential for many participants to be harmed before problems are recognized;
- The study is blinded, includes vulnerable participants or employs high risk interventions;
- Multi-site studies where no one Principal Investigator (PI) studies more than a few participants and it is more difficult to recognize a pattern of increased or unusual problems;
- Where the research involves highly toxic therapies or dangerous procedures;
- When the study population is such that high morbidity and mortality rates are expected and where that could mask adverse events and unexpected problems that occur from a research intervention;
- There is a high likelihood that the study may be terminated for reasons of safety, efficacy, or futility; and
- A data and safety monitoring plan is required by the NIH or FDA.

For research that does not meet any of the criteria cited above, the IRB will determine if the submission of a data safety and monitoring plan is required on a case-by-case basis.

Definitions

Data and Safety Monitoring Board (DSMB) or Committee – A group typically comprised of experts including scientists, physicians, statisticians, bio-ethicists, and others that meet periodically throughout the course of a research study to monitor: (1) the disease, drug, device, procedure, or outcome measures of the research; and (2) methodological issues including design, data management and statistical analysis. These groups are usually external to the research team. Its primary functions are to monitor outcomes to assure the safety of participants and the scientific integrity of the research study. The results of their reviews determine whether or not a study must continue or be closed. At each meeting, the group reviews summary reports of related studies, adverse events, cumulative toxic summaries, interim data, major protocol amendments, safety and efficacy outcomes, and other compliance issues. The PI should receive a written report from the DSMB regarding the significant findings or concerns for safety.

Data and Safety Monitoring Plan – A written description of the PIs plan to monitor the data and safety of participants enrolled during the course of a study. This should include:

- Who will be involved in the monitoring (PI, medical monitor, independent committee, sponsor's DSMB committee) and the composition of the committee/board;
- At what intervals during the research will data monitoring occur (specified intervals and when harm is first identified);
- If appropriate, how many persons will be enrolled prior to interim analyses;
- Plan for collection and storage of data and security measures for the data must be included;
- What type of monitoring will be done;
- How will the data be analyzed and by whom (comparing character, incidence, and actual harm to that expected, comparing the magnitude and probability of benefits to that expected, or determining causality of unexpected harm);
- Who will be responsible for monitoring and reporting the occurrence of adverse events and unexpected problems throughout the study; and
- Outcomes that will be used to stop the study.

HIC Policy

A description of the data and safety monitoring plan, if required for research study, must be submitted to the IRB for review. It may be a formal board that is required and organized by a sponsor, a local independent board organized by the PI, or a plan for monitoring the data and safety by the PI and his/her research staff.

The protocol will only be approved after the IRB can be satisfied that:

- An adequate plan is in place;
- The individuals involved in the monitoring plan have the appropriate scientific and statistical expertise;
- The data management and statistical analysis sections of the protocol submission are adequate;
- The IRB will be notified of significant findings (safety reports, adverse events and/or unexpected problems) throughout the course of the research; and

- The research plan makes adequate provisions for monitoring the data collected to ensure the safety of participants.

If the IRB determines that a data and safety monitoring plan is adequate, parallel review of the safety data may not be needed. However, the results of the ongoing data and safety monitoring throughout the research must be submitted to the IRB at intervals throughout the study (at continuation) or more frequently when the findings of the monitoring have changed the risk/benefit ratio of the study. See the HIC Policy/Procedure "Reporting of Unexpected Problems, Suspensions and Terminations, Serious and Continuing Non-Compliance and the Institutional Official's Responsibilities" for guidance on timelines and how to report any significant findings that result from safety monitoring.

If the PI requires assistance from the IRB in negotiating the formation of a DSMB by the sponsor, or if the PI does not agree with the IRB's request the IRB will provide written rationale to the PI explaining:

- Why the IRB feels a DSMB is needed;
- Specific reports that will be needed from the DSMB;
- What adverse events and/or unexpected problems that should be reported to the IRB; and
- Criteria for stopping study participation, if needed.

HIC Procedures

The PI should provide as much in-depth information in the Protocol Summary Form, the informed consent documents, and the proposal or scientific protocol as is necessary for the IRB to provide an in-depth review in order to determine the adequacy of the DSMB or monitoring plan.

The IRB will review each Protocol Summary Form and the complete scientific protocol to determine if the DSMB or plan is sufficient for the nature of the study. If the PI has not submitted sufficient information for the IRB to use in analyzing whether or not the data and safety monitoring plan is adequate, the protocol will not be approved.

Once approved, the PI should submit all safety reports that are generated by the DSMB or committee to the IRB for review.

The IRB will review all safety reports generated by the DSMB or committee that are submitted by the PI as amendments to the protocol, reported at the time of protocol renewal, and/or with the submission of an Unexpected Problem Report. This review assures that the PI is taking appropriate actions to safeguard the participants enrolled in the research study.

At all IRB reviews (initial submission, continuations, and amendments) the IRB reviewers will utilize the appropriate reviewer checklist to document the review of the monitoring of data and participant safety in the protocol.

As part of the IRB review process, the WSU IRB will assess the appropriateness and adequacy of a study's proposed data oversight and safety monitoring plan (or the justification as to why such plan is not possible) based on the following criteria:

1. Whether the proposed plan is commensurate with the nature, size, and complexity of the clinical trial, as well as the degree of risk involved in the study.

2. The timeliness of the planned monitoring (annual monitoring for low risk studies vs. quarterly monitoring for high-risk studies).
3. How the monitoring conclusions are reported to the IRB, as well as how often they are reported.
4. Whether the PI or entity conducting the monitoring activities has the expertise to accomplish the monitoring mission. For studies requiring a monitoring group, the group should consist of clinical trial experts, biostatisticians, bio-ethicists, and/or clinicians knowledgeable about the disease and treatment under study.
5. The planned mechanisms for reporting adverse reactions/unexpected events to the IRB, OHRP, FDA, ORO, NIH, as applicable.
6. When WSU serves as the Lead Institution in a multi-site study or the PI provides services such as data coordination, the IRB will determine whether the PI has submitted an adequate plan to communicate information among the sites that may affect the health or safety of participants or their willingness to continue to participate in the study. Examples include: unexpected problems and adverse events, protocol modifications, and interim study results.

NOTE: It is the responsibility of the PI to be familiar with the sponsor's specific policies regarding data and safety monitoring.