Data & Safety Monitoring Plan (DSMP)

I. Statement

According to OHRP (45 CFR 46) and FDA (21 CFR 56) regulations, one of the determinations an IRB must make to approve non-exempt, human subjects research is: "*when appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of subjects.*"

Researchers are required to develop a Data and Safety Monitoring Plan appropriate in scope to the anticipated risks of the research. The method and extent of monitoring may vary across different types of studies, depending on multiple factors, including the experimental design and complexity of the study (e.g., Phase I vs. Phase III trial vs. a descriptive psychosocial interview study), and the degree of risk to subjects. Various funding sources also may have additional requirements related to data and safety monitoring which must be considered.

II. What is a Data & Safety Monitoring Plan (DSMP)?

A DSMP is the portion of a protocol that describes the steps the research team will take to identify, address, and report any physical, social, or psychological events that may result from participation in a study. This can be incorporated in the protocol or in a stand-alone document. The DSMP establishes a system for the appropriate oversight and monitoring of the conduct of the human subjects research to ensure the safety of participants and the validity and integrity of the data.

III. Why is a DSMP important?

- To protect the safety of the individual participants in research studies
- To ensure the validity of research results and scientific integrity of a study
- To help ensure that risks to subjects are minimized

Risks actually encountered in a study may be different from risks projected in research design. Monitoring the data allows the study team to make adjustments as necessary.

IV. What studies are required to have a DSMP?

Almost all research studies approved by the IRBs are expected to have a DSMP, although the contents of the DSMP will vary from study to study. The planned monitoring activities and their frequency depend on the risks of the study.

- The oversight provided by the IRB provides one element of study monitoring in ensuring human subject safety and protection. There are also other entities (sponsor, investigators, DSMBs, monitors, etc.) who play a role in ensuring human subject safety and protection.

- Study teams must submit communications to the IRB from entities that provide additional monitoring as part of the DSMP according to the IRBs (ORIO reporting guidance: IRBMED & IRB-HSBS.)

- Study teams must submit AE and SAE reports to the IRB according to the approved AE/SAE reporting plan for the study.

- If study teams plan to conduct self-monitoring activities as part of their DSMP, they must keep records of their monitoring activities and have the documents available for oversight bodies to review.

    - The U-M IRBs recommend using the ORCR Self-Assessment Tools for Investigators for documentation of team monitoring activities.

V. What should a study's DSMP look like?

- A section of the protocol should address the DSMP
- Researchers at U-M also use section 7-1.10 in eResearch to indicate their study will have a DSMP

- Researchers describe their DSMP in sections 32, 32-1, and 32-2 of the eResearch application.

eResearch section	Scope of questions/information requested
32. Data Safety Monitoring Plan	32. Use the checkboxes to show which study team member(s) are involved in the informed consent process, and which member(s) obtain information on adverse events
32 Data Safety Monitoring Plan - Multi site Research	32. Refer to sIRB and Multi-Site Research • IRBMED - Single IRB (sIRB) and Cooperative Multi-Site Research • HSBS - Single IRB (sIRB) of Record Process • Multi-Site Research Reporting Plan
32-1. Data and Safety Monitoring Plan - AE Reporting	32-1. Add details on Adverse Event Reporting including selecting a Standard or a Study-specific reporting timetable: • IRBMED: Adverse Event reporting • IRB HSBS: Adverse Event Reporting: Flowchart and Guidance
32-2. Data Safety and Monitoring Plan - Monitoring the Study	32-2. Add details on the monitoring plan, including who reviews data and at what frequency

VI. Content of a DSMP:

- Description of monitoring activities

- Frequency
- Tools and methodology
- Reporting to oversight bodies, including the IRBs

- Roles of internal and/or external monitors
- Procedures for treatment or resolution of any issues identified during monitoring
  - Data collected on adverse events and potential unanticipated problems (UaPs)
  - Circumstances that would result in halting or terminating research.

Example DSMPs: Appropriate monitoring plans, depending on study characteristics, may include:

Study characteristics	Entities providing additional monitoring	Consider:
• Small study with low risks	• PI/study team	• Appropriately report toxicities and AEs; ensure that the protocol-approved risk minimization procedures are followed. • Needs to have records of monitoring activity done by the PI/study team • Consider conflict of interest

• Industry-sponsored • Moderate to high risk • Death/severe disability is not a risk. • See guidelines for assessing risk level: IRBMED & IRB-HSBS	• Internal committee through the study sponsor or CRO • May also have a clinical research associate/clinical study monitor (CRA/CSM)	• Consider conflict of interest • Items reportable to the sponsor or coordinating center may not always be reportable to the IRB
• Studies that should have a Data Safety Monitoring Board (See next section)	• Formally chartered, independent DSMB/DMC • May also have a clinical research associate/clinical study monitor (CRA/CSM)	• Items reportable to the sponsor or coordinating center may not always be reportable to the IRB

VII. What is a Data Safety & Monitoring Board/Data Safety & Monitoring Committee (DSMB/DSMC)?

The Data Safety & Monitoring Board (NIH) is an 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 research participants, 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. Also known as a Data & Safety Monitoring Committee (DSMC). (Data and Safety Monitoring Board (DSMB Guidelines - NIH)

VIII. What studies should have a DSMB/DSMC?

As part of a DSMP, some studies have a more formal DSMB/DSMC. Since DSMB and DSMC are interchangeable naming conventions, DSMB will be used as the standard reference going forward. There are no regulatory requirements on when a DSMB is required; however, there may be specific funding requirements. (NIH Policy for Data and Safety Monitoring)

Trial characteristics that may make a DSMB more important include:

- Multiple clinical sites
- Blinded study arms
- High risk interventions
- Vulnerable populations (especially monitoring for safety of participants)
- Trial is designed to provide definitive information about effectiveness and/or safety (especially monitoring for data integrity)

IX. How does a DSMB work?

A formal DSMB charter contains a detailed description of the membership, which usually consists of three to six scientific experts, and often at least one biostatistician, and their experience. None of the members will have any affiliation or interest in the study outcome. The DSMB has the authority

to stop the study for reasons that may include unacceptable toxicity. The DSMB will provide recommendations on changes to the study, frequency of reports for other oversight bodies, and provisions for protecting the confidentiality of data. The DSMB has greater access to the study data than the IRB, and the IRB can use the DSMB's reports to inform the ongoing risk/benefit assessment for a study, especially at the time of continuing review. The IRB may rely on DSMB monitoring reports for external site AEs and interim findings.

X. References and Further Guidance

- HRPP Operations Manual Part 7.III
- OHRP (45 CFR 46)
- FDA (21 CFR 56) regulations
- U-MIC "Post Approval Study Monitoring: Understanding the Investigator's Role" parts 1 and 2
- MICHR Research Management, Study Monitoring service
- ORCR Study start-up consultation and compliance reviews
- ORCR Self-Assessment Tools for Investigators
- U-M Rogel Cancer Center Data and Safety Monitoring Committee
- DSMP guidance for studies with devices that are non-significant risk.
- NIH Data and Safety Monitoring Policies
- FDA Oversight of Clinical Investigations — A Risk-Based Approach to Monitoring (2013 guidance)
- FDA A Risk-Based Approach to Monitoring of Clinical Investigations -- Questions and Answers (expands on 2013 guidance)
- AHRQ Data and Safety Monitoring Policy
- National Cancer Institute (NCI) – Phase III randomized trials
- Rogel Cancer Center Policy - Interventional cancer clinical trials initiated by U-M investigators must either use the UMCCC Data and Safety Monitoring Committee (DSMC), or an independent trial-specific DSMB.
- FDA guidance - A DSMB is particularly important in situations in which subject safety concerns may be unusually significant, including where the study:
    - May ethically require early termination based on a highly favorable or unfavorable result, or even a finding of futility, at an interim analysis;
    - Involves use of a drug that may induce an unacceptable toxicity;

- Compares rates of mortality or major morbidity; or
- Is being performed in a fragile population, such as children, pregnant women or the very elderly.