UNIVERSITY OF SOUTHERN MAINE
Office of Research Integrity & Outreach

Procedure #:	HRPP-042
AAHRPP:	Element II.3.B.
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Reviewed By:	IRB Chair; IRB; ORIO
Procedure Title:	Data Safety Monitoring

1.0 Objective

1.1. To describe the Institutional Review Board (IRB) review of data and safety monitoring plan(s) (DSMP) to ensure adequate protection is in place for human subjects in research.

2.0 Responsibility

2.1. It is the responsibility of the Office of Research Integrity and Outreach (ORIO) staff, Research Protections Administrator (RCA), IRB, and Principal Investigators (PI) to execute this SOP.

3.0 General Description

3.1. PIs develop data and safety monitoring plans as a mechanism for assuring the safety of human subjects and human research data, the validity of data, and the appropriate termination of studies.

3.2. The IRB requires review and approval of data and safety monitoring plans for greater than minimal risk research, or clinical investigations funded by the National Institutes of Health (NIH) or regulated by the Food and Drug Administration (FDA).

4.0 Procedure

4.1. At initial review, PIs conducting greater than minimal risk research, or NIH funded/FDA regulated clinical investigations include a description of the proposed data and safety monitoring plan in the IRB application.

4.2. During initial review in accordance with HRPP 025 Initial and Continuing Review at IRB Meetings, the IRB reviews the general description of the DSMP to determine that adequate protections for human subjects are in place.

4.3. The IRB recognizes that the elements of a monitoring plan may vary depending on the potential risks, complexity, and nature of the trial.

4.4. The IRB reviews several elements of the DSMP, which may include but are not limited to:

4.4.1. Plans and reports for monitoring the progress of trials and the safety of subjects;

4.4.2. Plans for assuring compliance with requirements regarding the reporting of adverse events;

4.4.3. Plans for review or analysis of cumulative safety data to determine whether harm is occurring;

4.4.4. Plans for assuring that any action resulting in a temporary or permanent suspension of a clinical trial is reported to the appropriate agencies;

4.4.5. Plans for assuring data accuracy and protocol compliance; and

4.4.6. Plans for assuring communication among multi-center sites adequately protect the subjects.

4.5. The IRB may request additional information regarding the DSMP at initial review.

4.6. After reviewing the plan, the IRB may determine that a formal DSMP is not necessary or that the study may require an independent individual or independent body for monitoring.

4.6.1. For example, in studies of small numbers of subjects, toxicity may more readily become apparent through close monitoring of individual subjects while in larger studies risk may better be addressed through statistical comparisons of treatment groups.

4.7. If an external sponsor or funding agency has the responsibility for data and safety monitoring, the Research Service Center negotiates the provision of data and safety monitoring plans and reports by the sponsor to the PI in the funding agreement or contract.

4.8. If the IRB (or an external entity) determines the DSMP of an investigator-initiated protocol must include a Data and Safety Monitoring Board (DSMB), the IRB evaluates the DSMB for membership, charter, and DSMB responsibilities, all of which include, but are not limited to, the following:

4.8.1. DSMB Membership

4.8.1.1. Multidisciplinary representation from relevant specialties;

4.8.1.1.1. This may include experts such as bioethicists, biostatisticians and basic scientists;

4.8.1.2. Membership limited to individuals free of apparent significant conflicts of interest, whether financial, intellectual, professional, or regulatory in nature; and
4.8.1.3. Size appropriate to the type of study.

4.8.2. DSMB Charter

4.8.2.1. Detailed presentation of the membership composition, including qualifications and experience;
4.8.2.2. Roles and responsibilities of the DSMB and, if relevant:
4.8.2.3. Authority of the DSMB (e.g., advisory to the sponsor, PI);
4.8.2.4. Timing and purpose of DSMB meetings;
4.8.2.5. Procedures for maintaining confidentiality;
4.8.2.6. Format, content, and frequency of DSMB reports;
4.8.2.7. Specific data to be monitored and statistical procedures, including monitoring guidelines, to monitor the identified primary, secondary, and safety outcome variables;
4.8.2.8. Decision rules and actions to be taken upon specific events, outcomes or end points; and
4.8.2.9. Plans for changing frequency of interim analysis as well as procedures for recommending protocol changes.

4.8.3. DSMB Responsibilities

4.8.3.1. Initial review of the proposed research to assure quality study conduct;
4.8.3.2. Procedures to review and assure quality of study conduct including data management and quality control procedures;
4.8.3.3. Evaluation of the quality of ongoing study conduct by reviewing the study accrual, compliance with eligibility, subject adherence to study requirements, and accuracy and completeness of data;
4.8.3.4. Consideration of factors external to the study when relevant information becomes available, such as scientific or therapeutic developments that may have an impact on the safety of the subjects or the ethics of the study;
4.8.3.5. Recommendations of early termination based on efficacy results;
4.8.3.6. Recommendations of termination due to unfavorable benefit-to-risk or inability to answer study questions;
4.8.3.7. Recommendations for continuation of ongoing studies;
4.8.3.8. Consideration of overall picture, primary and secondary analysis;
4.8.3.9. Modification of sample sizes based on ongoing assessment of event rates; and
4.8.3.10. Review of final results.

4.9. The PI submits documentation evidencing DSMP or DSMB activities (i.e., summary report, meeting minutes) to the IRB prior to continuing review if provided to the PI by the sponsor or prepared by the PI, as described in the DSMP.

4.9.1. The IRB reviews DSMP or DSMB materials received prior to continuing review as a modification request in accordance with HRPP 040 IRB Review of Modifications.

4.10. The PI is responsible for acquiring evidence that DSMB activities have occurred if the sponsor has not been providing the documentation.

4.11. At the time of continuing review of the study, the PI submits documentation representing DSMP or DSMB activities (i.e., summary report, meeting minutes) not previously submitted to the IRB.

4.12. During the continuing review of the study, in accordance with HRPP 025 Initial and Continuing Review at IRB Meetings, the IRB reassesses the risk category and determines whether the PI should provide additional information in the informed consent document based on the information provided in the DSMP or DSMB materials.

5.0 References

5.1. 45 CFR 46.111(a)(6);

5.2. 21 CFR 56.111(a)(6);

5.3. NIH Policy for Data and Safety Monitoring