

Policy Number: 44

Title: Data and Safety Monitoring

Date of Last Revision: 08/10/05; 08/04/10; 05/01/16; 09/28/20, 05/18/22

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board IRB that clinical investigations¹ involving greater than minimal risk to participants include a plan to assure the safety and welfare of its participants.

In addition, the IRB Chair retains the right to require a monitoring plan for a clinical investigation involving no more than minimal risk, should it be determined appropriate based on the type of risk involved in the study.

I. **Data and Safety Monitoring** - A Data and Safety Monitoring Plan (DSMP) should be developed based on the size, complexity, and types of potential of risk involved in the research. A DSMP is required when the research meets the definition of a clinical investigation. The IRB has the authority to request a DSMP for other clinical research studies with appropriate justification.

II. **Data and Safety Monitoring Plan**

A detailed plan is required for all clinical investigations involving greater than minimal risk to participants. The level of detail should be based on the research procedures and types of potential risk to the research participants. As noted above, the IRB Chair retains the right to require a monitoring plan for a clinical investigation involving no more than minimal risk, should it be determined appropriate.

All DSMPs must contain at least the following information:

- A. A description of how risks are minimized;
- B. A description of how risks are reasonable in relation to anticipated benefits;
- C. Identification of a Data and Safety Monitor or Data and Safety Monitoring Board (DSMB), if applicable;
- D. A description of the plan to monitor progress and safety;
- E. Depending on the complexity of the research, the plan may include assessments of data quality, timeliness, participant recruitment, accrual and retention.
- F. A description of the plan to assure compliance with reporting of unanticipated problems involving risk to participants or others. This may include:
 1. A description of the process for detecting and reporting unanticipated problems involving risk to participants or others;
 2. A description of who will be monitoring and collecting unanticipated problems (e.g., LR, Research Coordinator, Research Nurse, etc.);
 3. Specification of who will be notified of an unanticipated problems (e.g., IRB, NIH, FDA, LR, etc.);
 4. A reporting plan indicating the timing of reports; and

¹ 21 CFR 50.3(c)

- 5. A plan for annual reporting of unanticipated problems if the study will go on longer than one year.
- G. As applicable, an investigator must submit to the sponsor a report of any unanticipated adverse device effect per HRP Policy # 42.

III. **Research Activities that Should Include a DSMB**

- A. The study is intended to provide definitive information about the effectiveness and/or safety of a medical intervention;
- B. Prior data suggests that the intervention under study has the potential to induce a potentially unacceptable toxicity;
- C. The study is evaluating mortality or another major endpoint, such that inferiority of one treatment arm has safety as well as effectiveness implications; or
- D. It would be ethically important for the study 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.

IV. **DSMB Composition**

- A. The DSMB should have multidisciplinary representation, including physicians from relevant medical specialties and biostatisticians. This may include other experts such as bioethicists, epidemiologists and basic scientists.
- B. The DSMB should have membership limited to individuals free of apparent conflicts of interest, whether they are financial, intellectual, professional, or regulatory in nature.
- C. The appropriate size depends on the type of study and types of expertise needed.

V. **DSMB Responsibilities**

- A. The primary responsibility of the DSMB is to safeguard the interests of study participants. Therefore, the DSM or DSMB will approve the safety measures in the protocol:
 - 1. To preserve the study integrity and credibility; and
 - 2. To facilitate the availability of timely as well as reliable findings to the broader clinical community.
- B. The DSMB will review the progress of the study carefully and diligently.
- C. Each enrolled subject's research chart should be reviewed frequently for side effects and tolerability of the investigational drug.
- D. The DSMB will assure that all unanticipated problems are reported to the IRB according to policies and procedures.

VI. **DSMB Tasks**

Tasks may include, but not be limited to, the following:

- A. Conduct initial review of the proposed research to assure quality study conduct;
- B. Review procedures to assure quality of study conduct including data management and quality control procedures;
- C. Evaluate the quality of ongoing study conduct by evaluating the study accrual, compliance with eligibility, participant adherence to study requirements, and accuracy and completeness of data;
- D. Consider 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 participants or the ethics of the study;

- E. Recommend early termination based on efficacy results;
- F. Recommend termination due to unfavorable benefit-to-risk or inability to answer study questions;
- G. Recommend continuation of ongoing studies;
- H. Consideration of overall picture; primary and secondary analysis;
- I. Modify sample sizes based on ongoing assessment of event rates; and
- J. Review final results.

Procedure Number: 44.A

Title: Procedure for Data and Safety Monitoring Plans

Procedure:

This procedure outlines the use of data and safety plans to assure extra protections and safety in research involving humans.

I. Lead Researcher (LR) Responsibilities

- A. It is the responsibility to address the data and safety plan as part of the initial IRB Application and to provide a copy of the sponsor's DSMP, if applicable.
- B. DSMB reports are to be submitted to the IRB (per HRP Policy # 19) when the report identifies an unanticipated problem involving risk to participants or others. An Amendment referencing the UP report should also be submitted along with the revised documents as applicable (e.g., consent document, recruitment material).
- C. DSMB reports that do not identify new risks or change the risk-benefit profile must be submitted to the IRB at the time of renewal.

II. IRB Committee Responsibilities

- A. The IRB Committee will review the initial IRB Application to assure the adequacy of the DSMP in relationship to the size, complexity, and level of risk of the proposed research.
- B. A DSMP is required when the research meets the definition of a clinical investigation.
- C. The IRB Committee will review the qualifications of the composition of the DSMB including the qualifications of the individual members. The IRB may make recommendations regarding expertise, frequency of meetings, etc., to the Investigator for the enhancement of human participant protections.
- D. The IRB Committee may request additional information or clarification regarding the DSMP or DSMB.
- E. The IRB has the authority to request a DSMP for other clinical research studies with appropriate justification.

III. IRB Administrator Responsibilities

- A. The Administrator may conduct a pre-review of the IRB application.
- B. The Administrator will correspond with the LR if the protocol submitted lacks adequate plans for assuring proper data collection and participant safety, per the findings of the IRB and/ or based on their pre-review.
- C. The Administrator will provide the LR guidance in meeting the IRB requirements for a DSMP, when possible.

21 CFR 56.111(a)(6)

21 CFR 50.3 (c)

45 CFR 46.111(a)(6)

Establishment and Operation of Clinical Trial Data Monitoring Committees Guidance for Clinical Trial Sponsors, March 2006

NIH DSMB Guidelines - Webpage