I. PURPOSE

The purpose of this SOP is to outline the requirements for monitoring research data to ensure the safety of participants, and to describe when such plans are necessary. All research involving human subjects requires a plan calibrated to the anticipated risks associated with the research. Ensuring the integrity of the data collected and monitoring the study for emerging safety concerns ensures that the benefits derived from the research are maximized and the risk of harm to subjects and society are minimized.

II. POLICY STATEMENT

In order to ensure the safety of research participants and the integrity of research, the IRB will ensure that each study includes a plan for data and safety monitoring appropriate to the risks presented by the research.

III. SCOPE

This SOP applies to all Investigators involved in conducting Human Subjects Research.

IV. DEFINITIONS

DSMB or DMC or DMB: Data Safety Monitoring Board, Data Monitoring Committee, or Data Monitoring Board.

DSMP: Data and Safety Monitoring Plan. The DSMP includes all aspects for ensuring the integrity of the data and for protecting the safety of current and future participants.

Independent DMC: A committee composed of individuals with no other connection or conflicts of interest related to the current study or its sponsor(s) and organized to provide oversight of the emerging data and safety during the progress of a clinical trial. One of the primary purposes of the Independent DMC is to preserve the integrity of a randomized blinded trial.

Internal DMC: A committee composed of representatives of the study investigators and sponsors who are empowered to monitor the progress, safety and integrity of a study.

Medical Monitor: An individual assigned to provide oversight of the medical aspects of a study.

Serious Adverse Event (SAE): Any adverse event that meets any of the following conditions:

- results in death;
- is life-threatening (places the subject at immediate risk of death from the event as it occurred);
- requires inpatient hospitalization or prolongation of existing hospitalization;

(hospitalization for a protocol-specified activity or for an elective, pre-planned procedure is not considered an SAE.)
- results in persistent or significant disability/incapacity;
- results in a congenital anomaly or a birth defect; or
- based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse).

V. PROCEDURES

A. Description and Objectives of the DSMP

Investigators are required to develop a DSMP appropriate in scope to the anticipated risks of the research. The DSMP should at a minimum address the following issues:

1. A description of the plan to ensure the integrity of the data including:
   (a) A description of the systems for storing the data;
   (b) A listing of who will monitor and review the data, and a description of the monitor's qualifications; (note: it may be appropriate for the PI to serve as the monitor)
   (c) The frequency of review (e.g., specific points in time, or after a specific number of participants have enrolled);
   (d) A description of the data to be monitored;
   (e) Procedures for analysis and interpretation of the data;
2. Procedures for communication from the data monitor to the IRB and other sites;
3. Protection of the rights and welfare of subjects during the recruitment, consenting process and study participation;
4. Protection of subject privacy and confidentiality;
5. A description of the mechanisms for detecting, reviewing and reporting unanticipated problems involving risks to subjects or others by the investigative team at a frequency and intensity sufficient to ensure the safety of participants. (**SOP 408**);

(a) If there are external reporting responsibilities, the plan should describe the processes and oversight the investigator has in place to report unanticipated problems and SAEs to the following as applicable: the FDA and the study sponsor or funder;

6. Assurance that research responsibilities delegated by the principal investigator to investigative team members are carried out in accordance with the protocol, federal regulations, federal, state and local laws and institutional policies and procedures.

B. Assignment of Responsibility for Data and Safety Monitoring

The complexity of the study, the number of sites, the seriousness of the disease or condition and the risks inherent in the study intervention determine whether a single individual, several individuals or an independent group of individuals should take responsibility for execution of the DSMP. The responsibility may be shared by several individuals or groups of individuals. For example, the Principal Investigator, the study Sponsor and an Independent DMC may all play a role in the DSMP.

In reviewing the DSMP, the IRB may consider a range of options as appropriate, including but not limited to the following:

1. The principal investigator will have sole responsibility for monitoring; or
2. A group of designated CHOP faculty/staff will have responsibility for monitoring; or
3. An independent individual or group of non-CHOP individuals will have responsibility for monitoring; or
4. A combination of CHOP faculty/staff and non-CHOP individuals will share responsibility; or
5. A designated medical monitor, or group of monitors, for commercially funded or for not-for-profit sponsored studies will have responsibility for monitoring; or
6. A formal Internal or Independent DMC will have responsibility for monitoring.

C. Independent DMCs

The IRB will determine when to require a formal DMC to provide data and safety monitoring oversight.

1. An Independent DMC is generally not required for:

(a) Early phase studies which involve the investigative use of an open-label intervention, test article or device; or

(b) When the study involves non-serious conditions or when the outcomes are limited to symptom relief.

2. Generally, an Independent DMC is required for controlled trial of any size that will compare rates of mortality or major morbidity, or that involve a study population that is at increased risk for morbidity or mortality, or where the risks of the study intervention places subjects at risk of morbidity or mortality.

   (a) Names of specific members of a DMC need not be provided to the IRB provided the description of the DMC contains sufficient information about the criteria for selecting the individuals who will serve on the DMC.

3. Description of the DMC (Internal or Independent)

   (a) DMC membership and their qualifications (if available);

   (b) The frequency of DMC review of data;

   (c) Description of data to be reviewed;

   (d) Plans for interim analysis that might impact continuation of the protocol; and

   (e) Any pertinent stopping rules.

4. Scope of the DMC responsibilities including:

   (a) Reviewing the research protocol, informed consent documents and plans for data and safety analysis;

   (b) Role in evaluating the progress of the intervention, including periodic assessment of data quality and timeliness, participant recruitment, accrual and retention and other factors that affect study outcome;

   (c) Considering factors external to the study when relevant, such as scientific or therapeutic developments that may have an impact on the safety of the subjects or the ethics of the trial;

   (d) Reporting on the safety and scientific progress of the trial;

   (e) Making recommendations to the PI and/or the sponsor, and, if required, to the FDA concerning continuation, termination or modification of the trial based on observed beneficial or adverse effects;

(f) If appropriate, conducting interim analyses of efficacy in accordance with pre-specified stopping rules;

(g) Ensuring the confidentiality of the trial data and the results of monitoring

D. IRB Review of the DSMP

As part of its review process, the IRB will review the information contained in the protocol to ensure that plans for data and safety monitoring have been developed in accordance with the guidelines above, and are adequate for the protocol under review.

The IRB's decision regarding the adequacy of the plan will be recorded.

VI. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.111(a)(6)	21 CFR 56.111(a)(6)
FDA Guidance for Clinical Trial Sponsors: Establishment and Operation of Clinical Trial Data Monitoring Committees	OHRP Guidance on Continuing Review: (2010)
NIH Guide: Further Guidance on Data and Safety Monitoring for Phase I and Phase II Trials	NIH Guide: NIH Policy for Data and Safety Monitoring

VII. REFERENCES TO OTHER APPLICABLE SOPS

SOP 408: Unanticipated Problems Involving Risks to Subjects	SOP 801: Investigator Responsibilities

VIII. RESPONSIBILITIES

Title	Responsibility
Principal Investigator	The investigator is responsible for developing a DSMP appropriate to the risks inherent in the research.
IRB Reviewer	The primary reviewer is responsible for reviewing the DSMP and making a recommendation to the IRB regarding the appropriateness of the plan

XI: REVISIONS:

06-10-2010 Revised to correct minor grammatical issues for consistency across SOPs.

03-07-2013 Minor administrative edits to update definitions and CHOP IRB SOP titles

09-25-2018 Revised to update definitions.

12-13-2022 Revised to update reflect current processes.

IX. APPROVAL:

Approval Indicator: Approved by Amy Schwarzhoff and Barbara Engel on 12/13/22

Amy Schwarzhoff, Director, Human Subjects Research and Barbara Engel, Chair, CPHS