Procedure Title: Safety Monitoring

Associated Policy:	Human Research Protection Policy (OSA Policy 1.0)		
Responsible Unit:	Office of Scholarly Activity		
Created:	10/25/2017	**Executive Lead:**	Chief Research Officer
Effective:	10/25/2017	**Revision History:**	.01 – 10/25/2017; .02 – 10/07/2019; .03 – 3/22/2023
Approved by:	Institutional Review Board		
Procedure Number:	SOP 125.03		
Key Words:	Data Safety Monitoring Plan, DSMP, Data Safety Monitoring Board, DSMB		
Purpose:	To meet the responsibilities for protecting human subjects as issued by the Office for Human Research Protections (OHRP) requirement for individuals involved in the conduct or review of human subjects research at institutions holding OHRP-approved Federal Wide Assurances (FWAs)		

Process:
This SOP serves to inform all agents, offices, departments, and affiliate sites of PNWU regarding the requirements for inclusion of a data and safety monitoring plan in human subject research protocols.

This SOP must be used as a guide in parallel with OSA Policy 1.0 to comply with proper reporting of events. SOPs are not intended to supersede existing institutional policies, and local, state, and federal laws and regulations.

Responsible Parties

The Institutional Review Board (IRB) is responsible for:

- Reviewing and approving the data safety monitoring plan (DSMP), as applicable.
- Evaluating data and safety monitoring entity's reports including:
  - Information regarding any unanticipated problems that have occurred since the previous IRB review will be pertinent to the IRB's determinations regarding the risk/benefit ratio of the study.
  - Any provisions for monitoring the data to ensure safety of research subjects, contained in the previously approved protocol, have been implemented and are working as intended (45 CFR 46.111(a)(6)).
- Assessing the principal investigator (PI) proposed actions, based on monitoring report findings.

The Office of Scholarly Activity (OSA) is responsible for:

- Providing oversight support of the study consistent with the IRB-approved DSMP.
- Ensuring a process is in place for appropriate monitoring of the conduct of studies to assure the safety of research subjects and the validity and integrity of the data.
- Providing adequate resources and staff support to support the DSMP.

- Establishing a data safety monitoring board (DSMB), as applicable, consistent with federal polices (e.g. the NIH Policy for Data and Safety Monitoring (see References).
- Appointing medical monitors or members to a DSMB.
- Ensuring that conflict of interest requirements are addressed for DSMB members, as applicable.
- Addressing the data and safety monitoring entity recommendations.
- Monitoring compliance with this SOP.
- Posting this SOP for the PNWU community.
- Providing the necessary support to investigators and the IRB.

The Investigator is responsible for:

- Establishing a DSMP in an applicable IRB protocol that is consistent with the requirements in this SOP.
- Implementing the IRB-approved DSMP
    - This includes, but not limited to:
        - providing the data and safety monitoring entity with all the data and information needed to monitor the study.
        - promptly notifying the data and safety monitoring entity of any IRB-approved protocol amendments.
        - protecting the rights, safety, and welfare of research subjects under his/her care.
        - ensuring that the study is conducted at his/her investigative site in accordance with the IRB-approved protocol, and applicable regulations and requirements of the IRB.
- Promptly submitting all data and safety monitoring entity's reports and recommendations to the IRB.
- Addressing the data and safety monitoring entity's recommendations.
- Responding to the data and safety monitoring entity's reports.
- Ensure that all FDA-required data and safety monitoring requirements are met (21 CFR 50.24(a)(7)(iv)).

Definitions

Please reference the Glossary for complete definitions of the following terms and additional terms not listed.

- Adverse Events
- Adverse Reactions
- Clinical Trials of Investigational Medicinal Products (CTIMPs)
- Corrective And Preventive Action (CAPA) Plan
- Data and Safety Monitoring
- Data and Safety Monitoring Board (DSMB)
- Data and Safety Monitoring Plan (DSMP)
- Federal Wide Assurance
- Good Clinical Practice (GCP)
- Institutional Review Board
- Institutional Official
- Medical Monitor
- Minor Protocol Deviation/Protocol Noncompliance
- Non-Medical or 'Data' Monitor
- Principle Investigator
- Protocol Deviation/Protocol Noncompliance

- Reportable Event
- Resolution
- Serious Adverse Events
- Sponsor
- Stabilize
- Suspected Serious Adverse Reactions
- Suspected Unexpected Serious Adverse Reactions

Procedure:

1. Upon review of a submitted study protocol to the IRB, the IRB Chair, Vice-Chair, and members may request a DSMP and the formation of a DSMB. All sponsored clinical trials submitted to the IRB are required to have a DSMP and appropriate DSMB.
    a. Studies may have various monitoring schedules depending on the status of the study such as: a reduced monitoring plan, regular monitoring plan or increased monitoring plan. The number and frequency of monitoring assessments shall be determined by the DSMB and detailed in the DSMP.
    b. Members of the DSMB should include experts in the relevant field of study, the conduct of the study, statistics and/or research design. DSMBs meet at least annually or more often depending on the nature of the study.

2. The DSMP process is designed to ensure that active studies with investigational products, devices, procedures, methods, etc. conform to the requirements of Good Clinical Practice (GCP) and relevant legislation. The DSMP should include, but not limited to:
    a. The method and degree of monitoring commensurate with the expected risk involved in participation, the nature, size and complexity of the study, and the populations involved in the study.
    b. Depending on study needs and sponsor resources, one study may have a 'data' monitor, a medical monitor, a DSMB, or some combination of these. If a 'data' monitor(s) is being assigned specifically to verify data accuracy and compliance with the protocol, along with the inclusion of a medical monitor or DSMB, that individual/entity should be described in the plan.
    c. For FDA-regulated research, the sponsor is responsible for ensuring proper monitoring of the investigation, including selecting monitors qualified by training and experience. The FDA has issued a guidance document called "The Establishment and Operations of Clinical Trial Data Monitoring Committees for Clinical Trial Sponsors (2006)" which addresses the types of trials that may warrant use of a DSMB. This document is intended to assist clinical trial sponsors in determining when a DSMB is needed and how such boards should operate. It addresses the roles, responsibilities and operating procedures of DSMBs and describes reporting and recordkeeping responsibilities including: sponsor notification of DSMBs regarding waivers of expedited reporting; DSMB delivery of meeting minutes and other reports to sponsors; sponsor reporting to the FDA on DSMB safety-related recommendations; standard operating procedures for DSMBs; and DSMB meeting records.
    d. Type of data or events that must be captured as part of monitoring. In describing what information will be monitored, consideration should be given to the following, as applicable:
        i. An evaluation of the progress of the research study, including assessments of data quality and timeliness, and whether participant recruitment, accrual and retention are consistent with plans for diversity and generalizability.
        ii. A review of unanticipated problem, adverse event and outcome data to determine whether there is any change to the risk/benefit ratio of the study. In addition, the DSMP should address whether the study should continue as originally designed, be

changed, or be stopped if a stopping rule has been invoked or a study endpoint has been reached.

iii. An assessment of external factors or relevant information (e.g. developments in the literature, results of related studies, etc.) that may have an impact on the safety of research subjects or on the ethics of the study.

iv. Reporting schedule for notifying the sponsor and, as applicable, the data and safety monitoring entity about adverse events and unanticipated problems.

v. Frequency of assessments of data or events. This can be points in time (3 months, 6 months etc.) or after a specific number of research subjects are enrolled depending on the level of risk and the schedule for study visits, i.e. according to the planned accumulation of new data.

vi. Stopping rules should be specific in terms of the endpoints that will be used and the decisions that will be made. Studies may be stopped, e.g. when there is a greater than expected rate of morbidity or mortality or when the experimental arm is shown to be better or worse statistically than the standard of care arm.

vii. Plans for interim and/or futility analyses, designed and timed so as not to adversely impact the power of the study.

viii. Procedures for communication between the PI, research team members, the study sponsor, the coordinating or statistical center, the medical monitor, the DSMB, the IRB, the FDA, other study sites, and others as applicable.

3. An effective monitoring plan set-up by the designated DSMB should ensure that:
    a. the rights, wellbeing and safety of the trial participants are protected.
    b. the study data are secure, of high quality, accurate, complete and verifiable from source documents.
    c. the conduct of the trial is in compliance with the currently approved protocol / amendments and conducted by approved personnel.
    d. research misconduct and fraud are deterred and inadequate research practices are identified before they escalate to research misconduct
    e. Good Clinical Practice is promoted and compliance with the guidelines for research governance, including applicable regulatory requirements, is achieved.

4. DSMP Follow-up Procedures - In accordance with their training, qualifications, and designated study responsibilities, the DSMB and PI will assess potential medical safety and social harm issues affecting participants. Social harms are defined as non-medical adverse consequences that occur as a result of the participants' involvement with the study. DSMB members and the PI will identify appropriate follow-up, treatment, and/or referral requirements in the event that safety concerns arise, whether medically or socially related. If study staff members do not have sufficient knowledge or skills to adequately assess a participant's medical or social issues, they will contact the PI for advice or assistance, with the PI being ultimately responsible for ensuring adequate and appropriate clinical management of all participants.

5. Any medical or social harm emergencies will be managed per the DSMP.

6. Reporting, tracking, and documenting of adverse events (AEs), whether medical or social harm, should be managed per OSA SOP: 131.

7. All medical issues and social harms events must be followed to "resolution" or "stabilization", with the current status and further action plans (if applicable) documented at each study visit until resolution or stabilization occurs.

8. Quality Assurance practices should be conducted by the study staff with the PI. By routinely reviewing random selections of participant study records, it ensures that protocol specifications related to participant safety are being followed and that appropriate clinical and social harm management is being provided and properly documented. The frequency and number of selections should be outlined in the DSMP and reported to the DSMB, as applicable.

References:

1. Code of Federal Regulations, Title 45, Public Welfare, Department Of Health And Human Services Part 46, Protection of Human Subjects, Revised January 15, 2009, Effective July 14, 2009. https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/investigator-responsibilities/index.html

2. The Establishment and Operation of Clinical Trial Data Monitoring Committees for Clinical Trial Sponsors: http://www.fda.gov/RegulatoryInformation/Guidances/ucm127069.htm

3. NIH Policy for Data and Safety Monitoring: http://grants.nih.gov/grants/guide/notice-files/not98-084.html

4. The Federal Advisory Committee Act: http://www.gsa.gov/portal/content/100916

Revision History:

Version/ Effective Date	Author	Section Changed & Reason for Revision
.00 / 10-25-2017	M. McCarroll	Original SOP
.01 / 10-25-2017	M. McCarrroll	Minor revisions throughout after consult with HRP
.02 / 10-07-2019	C. Case	Put into new PNWU SOP Format
.03 / 3-22-2023	C. Case	Removed reference to the L: Drive in the footer of the SOP as all SOPs are now stored in the electronic IRB management system; minor format and grammar changes.

Appendices:

None