**Puerto Rico Clinical and Translational Research Consortium**

# DATA SAFETY MONITORING PLAN

**I. Procedure Title:** Data Safety Monitoring Plan at the Puerto Rico Clinical and Translational Research Consortium (PRCTRC)

**II. Introduction:**

Since1998, the National Institutes of Health (NIH) has required that all intervention studies have sufficient oversight and monitoring to assure participant safety and the validity of the study data. Further Guidance on Data and Safety Monitoring for Phase I and Phase II Trials was issued on June 5, 2000.

The study risks, whether from the intervention (medication or non-medication trial), tests, or study population, determine the type of monitoring required. The NIH requires data and safety monitoring, generally, in the form of Data and Safety Monitoring Boards (DSMBs) for phase III clinical trials. For earlier trials (phase I and II), a DSMB may be appropriate if the studies have multiple clinical sites, are blinded (masked), or employ particularly high-risk interventions or vulnerable populations. An Independent Safety Officer typically monitors small, single site studies with low risk interventions and populations. However, Phase I and II clinical trials with multiple clinical sites, masked design, high-risk intervention or vulnerable population require a Data and Safety Monitoring Board (DSMB).

**Data Safety Monitoring Plan (DSMP) –** is a written plan for monitoring study data and the safety of the study participants during the conduct of a clinical research study. A DSMP must be included as part of the protocol and submitted to the Institutional Review Board (IRB) for review. A DSMP has to be submitted to the PRCTRC for review and approval before the study begins.

**Data Safety Monitoring Board (DSMB)** – is a group of individuals charged with monitoring an ongoing clinical research study for study quality and for the safety of the study participants during the conduct of the study. A key feature of a DSMB is its independence from the study investigators. Other commonly used terms for a DSMB include Data Monitoring Committee (DMC), and Data and Safety Monitoring Committee (DSMC).

**Intervention study** is defined as testing a hypothesized epidemiological cause-effect relationship by intervening in a population and modifying a supposed causal factor and measuring the effect of the change.

**Observational studies** with large (i.e. greater than 1,000 participants) or vulnerable populations, or with risks associated with tests and/or standard of care are likely to require

monitoring oversight either through the Observational Study Monitoring Board (OSMB) or Safety Officer.

**III. Purpose**:

The purpose of this Standard Operating Procedure (SOP) is to provide guidelines for writing/answering the DSMP document to make sure that the all intervention studies have sufficient oversight and monitoring to assure participant safety and the validity of the study data. The Principal Investigator and staff members are responsible for the safety of study participants and the safety review of the data credibility and validity. However, ongoing, independent review of the data and the study helps to assure that a trial can continue without jeopardizing patient safety.

**IV. Area(s) of Responsibility:** Regulatory Knowledge and Support Core, Investigators and their collaborators

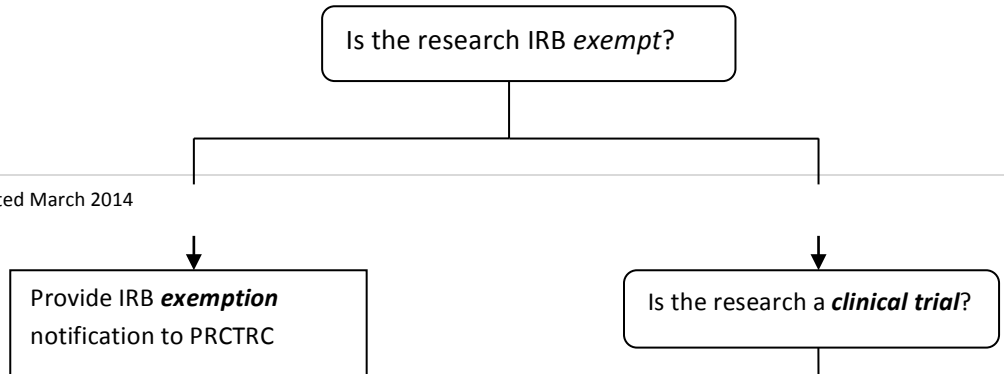
**V. Procedure Details:**

1. The Research Subject Advocate (RSA) is available to assist investigators and coordinators in identifying, developing, and overseeing risk-appropriate monitoring plan. Before human subject research can begin, the DSMP will be reviewed as follows: **As a first step,** The Regulatory Knowledge and Support Core Leader **(KFL)** will review and approve the DSMP. **As a second step,** The KFL will inform the PRCTRC Internal Advisory Committee **(IAC)** of his/her decision.

2. The **required elements** of a DSMP for a study dependent on the magnitude of risk to which research subjects are exposed, but all **must address:**

- Study risk assessment
- Adverse event grading and plans for reporting adverse events
- Description of whom will be performing the safety reviews
- Description of safety monitoring plan to assure:
    - Only subjects who meet the study eligibility criteria are enrolled
    - The informed consent process is conducted appropriately and that informed consent is obtained prior to proceeding with any study procedures;
    - Data is collected and analyzed as specified in the protocol;
    - Adverse events are reviewed promptly and reported as required; and
    - Privacy and confidentiality of study subjects is maintained.

**Figure1. DSM Decision Flowchart for Research Involving Humans or Human-Derived Materials**



**YES** **NO**

**YES** **NO**

**YES** **NO** **YES** **NO**

Adapted from NIH- http://www.nhlbi.nih.gov/funding/policies/dsmpolicy_flowchart.htm

## DATA SAFETY MONITORING PLAN:

## I-DESIGN

Choose among a list of research designs that apply to your investigation.

## II-DETERMINING LEVEL OF RISKS

Monitoring Guidelines Based on Level of Risk[1]

Safety monitoring must be appropriate for the level of risk identified. The combination of factors used in assessing the level of risk drives the intensity of monitoring required for a protocol. The requirements noted below represent the minimum necessary to assure subject safety. The PRCTRC Advisory Committee may require more frequent and/or additional monitoring. Consult the following sections.

**A- Subjects**

**Low Risk** - healthy participant. Adults able to understand risks and benefits and to sign consent. Use of databanks for secondary analysis, use of specimens/samples for Bio-repository

**Moderate Risk** – ill population. Adults with a disease or condition; able to understand risks and benefits and to sign consent; other treatment options available **OR** Vulnerable subjects (children, prisoners, pregnant women and their fetuses, elderly, institutionalized).

**High Risk -** seriously ill population. Vulnerable subjects (children, prisoners, pregnant women and their fetuses, elderly, institutionalized), **OR** subjects are unable to understand risks and benefits, cannot make decisions on their own, and cannot sign consent, **OR** subjects are critically ill patients with no other treatment options available

**B- Procedures/Interventions**

When determining this risk, think about the *possibility of harm* and consider both the *magnitude* of harm (from transient discomfort to death) and the *probability* that harm will occur (unlikely to highly likely). Risk may be psychological, social, or legal as well as physiological. Remember to consider the *research* interventions only. **Procedures that are standard of care that the subject would undergo whether in or out of the study should not be part of the risk consideration. Choose the safety level and then the corresponding procedure(s) listed in each one.**

**Safety Level 1 – Minimal Risk** means that the risk of harm anticipated in the proposed research is not greater, considering probability and magnitude, than that ordinarily encountered in daily life or during the performance of routine examinations, tests and treatments that might occur during a routine visit to a physician.

**Safety Level 2 – Moderate Risk** means that the risk of harm anticipated in the proposed research is somewhat greater than that encountered in a routine visit to a physician.

**Safety Level 3 – High Risk** means that the risk of harm anticipated with the proposed research is substantially greater than that encountered during a routine visit to their physician.

[1] All PRCTRC studies must have a Data Safety Monitoring Plan (DSMP). However, not all studies need a Data Safety Monitoring Board (DSMB).

**C-Overall level of Risks**

Identify the overall level of risk of this study, which will determine the frequency of safety monitoring**. This level must be the same as the highest level checked in the previous section.**

- Low
- Moderate
- High

## III-MONITORING PLAN

### A-Safety Monitoring

Answer the following questions:

1. **Who will monitor this study?**
    a. Indicate who will be performing the safety monitoring of research study subjects
2. **How often will data and safety be monitored?**
    a. The frequency of the safety review ddepends upon the risk of the trial. Regardless of the risk level, it is expected that study investigators will review safety data on each subject real-time to protect that individual safety. Safety reviews (or interim analyses) should be conducted as often as needed, based upon the risk level and the speed with which subjects are enrolled.
3. **What will be monitored?**
    a. Check the specific information to be monitored and provided in a report to the PRCTRC and IRB at the time of each continuing review. Select those appropriate for your study, add additional items as needed:
4. **Confidentiality:**
    a. Discuss how data confidentiality will be maintained: Please indicate your plan to protect the private health information from improper use and disclosure (e.g. assign study numbers, de-identification process, locked storage, etc.)
5. **Data integrity and security:**

a. Describe how data will be organized, managed, and stored. Security measures used to protect study data from loss or inappropriate use. (e.g. password protection, restricted access to database, database backup etc.)

6. **Informed consent process:**

   a. Describe your plan to assure that the consenting process will be conducted properly and in accordance with all federal regulations.

7. **Endpoints or stopping rules of the study**

   a. Which are the predetermined criteria (stopping rules) for stopping or modifying the study? (e.g. endpoints of the study)

## IV-ADVERSE EVENT REPORTING

### A. Definition of adverse events and serious adverse event

**Definition of Adverse Event (AE):** any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporarily associated with the use of a medical treatment or procedure regardless of whether it is considered related to the medical treatment or procedure.

- Anticipated (Expected) Adverse Events: these are risks or events reported in the Investigator's Brochure and listed in the consent form. The IRBs and the PRCTRC will consider an adverse event as "anticipated" or "expected" only if it is discussed in the Investigational Brochure, protocol and included in the Informed Consent document.

- Unanticipated (Unexpected) Adverse Events: an unanticipated adverse event is any unexpected untoward event or medical occurrence in a study subject that is not consistent with the known, predicted possible effects of the research protocol. An unanticipated adverse event can therefore be any unanticipated, unfavorable, and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the study that was not listed in the protocol, consent form or investigator's brochure. This includes any experience that suggests a significant hazard, contraindication, side effect, or precaution. In addition to this definition, the IRBs and the PRCTRC interpret any adverse event not included in the Informed Consent document as a risk to be "unanticipated" or "unexpected."

**Definition of Serious Adverse Event (SAE):** A serious adverse event (SAE) is defined as an adverse event that results in any of the following outcomes:

- death
- life-threatening event (an event that places the patient or subject, in the

- view of the investigator, at immediate risk of death from the experience)
- inpatient hospitalization or prolongation of existing hospitalization
- persistent or significant disability/incapacity
- congenital anomaly/birth defect

**B. Identification of Adverse Events**

Indicate how adverse events will be identified.

**C. Grading Methods for Adverse Events**

Investigators are encouraged to use a standardized scale to grade AE's by severity. There are several available designed for disease-specific trials, but are generalizable to other studies. Indicate which scale will be used to grade AE's.

**D. Attribution of Adverse Events Categories**

Indicate the scale to be used by the PI to attribute the relatedness of the experience to the study procedures/interventions: Choose among 3 or 5 points or specify any other attribution scales.

**E. Reporting of Adverse Events**

**Adverse event(s)** must be reported within a specific time frame to the corresponding IRB using the applicable report form. **A copy of all reports submitted to the IRB and or other entities must be sent to the RKS Core.**

## V. Signature

Ensure that the Principal investigator sign the document by committing to comply with the terms approved by PRCTRC.

**Help Page: Data Safety Monitoring Plan document**
**http://prctrc.rcm.upr.edu/researchers/requesting-services-from-the-prctrc**

**References:**


1. NIH 1998 notice: http://grants.nih.gov/grants/guide/notice-files/not98-084.html
2. NIH 2000 notice: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html
3. http://www.nhlbi.nih.gov/funding/policies/dsmpolicy_flowchart.htm
4. IRB policies on adverse event reporting: http://www.wfubmc.edu/or/IRB/ADVERSE%20EVENTS%20AND%20UNANTICIPATED%20PROBLEMS.pdf
5. The Belmont Report http://ohrp.osophs.dhhs.gov/humansubjects/guidance/belmont.htm
6. Office for Human Research Protections: http://ohrp.osophs.dhhs.gov
   45 CFR 46 (The Common Rules
   http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm
7. The Food and Drug Administration: http://www.fda.gov/
8. National Institutes of Health: http://www.nih.gov/
9. National Center for Research Resources: http://www.ncrr.nih.gov/
10. Office of Research Integrity: http://ori.dhhs.gov/