8 Participant Protections: 8.3 Data Safety Monitoring	Effective Date: **10/15/2010** Revised:

Research studies may require monitoring of ongoing data collection to ensure the safety of subjects. Preliminary analysis of data may signal the need to change study design, information presented to subjects, or halt the research. In its review of research, the IRB requires a data monitoring plan, when appropriate for the protocol.

1.0 Applicability.

Clinical trials involving behavioral or biomedical interventions, or any research involving more than minimal risk will generally require a data safety monitoring plan. The IRB, or a sponsoring agency, may also require a data monitoring plan when determined appropriate to protect the welfare of subjects.

2.0 Data monitoring plan.

The monitoring of data collection on an ongoing basis ensures that continuation of a study remains justified on the basis of safety and scientific integrity. For example, a study may require modification or early termination when the data indicate that risks are higher than anticipated, the benefits do not justify the risks, or the benefits of the experimental intervention have been established. The research protocol should include a description of the data monitoring plan, including the following elements.

2.1 Data collection.

The plan describes the type of data to be monitored, which may include:

- participant enrollment, retention and withdrawals
- adverse events, including serious adverse events
- unanticipated problems involving risk to participants
- primary and secondary outcomes
- any other data related to risks and benefits
- new information (e.g., external data) affecting safety or willingness of participants to remain in study

2.2 Frequency.

The plan describes the scope and timing of data monitoring, commensurate with risk, size and complexity of the research. For example, interim data analysis could occur within a specific time period, upon enrollment of a certain number of subjects, or in response to adverse events.

2.3 Responsibility.

The plan describes the entity (individual or group) responsible for monitoring the study for safety and efficacy.

2.3.1 Principal investigator.

The principal investigator may be designated to monitor a short term, single site study, including reporting and resolving adverse events and unanticipated problems.

2.3.2 Sponsor.
A qualified individual employed by the study sponsor may have responsibility for ongoing monitoring of the trial.

2.3.4 Data monitoring committee.
An independent data safety monitoring committee (DMC) may be required for oversight of long-term trials involving high risk interventions, multiple sites, and/or a particularly vulnerable population. DMC membership should generally include a biostatistician, knowledgeable experts in the relevant clinical discipline, as well as other members with relevant expertise; and may be appointed by a sponsor.

2.4 Stopping rules.
The plan describes the circumstances under which the study will be halted for either safety or scientific reasons. It may designate that a study should be terminated, for example, when the frequency of serious adverse events in the treatment arm greatly exceeds that in the control arm; or, if sufficient data has already been collected to prove efficacy of the treatment.

2.5 Coordination of multi-site studies.
As applicable, the plan describes the process for coordination of data collection, including adverse event reports, from multiple sites involved in a trial.

2.6 Recommendations and reporting.
The plan describes the process for providing periodic reports and recommendations to the IRB, sponsor, FDA, or other applicable entities. Reports include summaries of adverse events, and prompt reporting of serious adverse events. Recommendations may include: continuation of study as planned; continuation with major or minor changes; temporary suspension of study; or termination of study.

DEFINITIONS:
Adverse event: any untoward or unfavorable medical occurrence (physical or psychological) in a human subject, including any abnormal sign, symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to their research participation.

Clinical trial: any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Health-related interventions include any intervention used to modify a biomedical or health-related outcome (for example, drugs, surgical procedures, devices, behavioral treatments, dietary interventions, and process-of-care changes). Health outcomes include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events. *(as defined by the World Health Organization)*

Minimal risk: the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Sponsor: an individual or entity that initiates a clinical investigation, but that does not actually conduct the investigation.

Unanticipated problem: an unanticipated problem that involves risks to subjects or others is any incident, experience, or outcome that meets all the following criteria: is unexpected (in terms of nature, severity, or frequency) given the characteristics of the subject population and the research as described in the IRB approved protocol and consent document(s), is related, or possibly related to participation in the research, suggests the research places subjects or others at greater risk of harm (physical, psychological, economic, or social harm) than previously known or recognized.

REFERENCES:

45CFR46.111(a)(6) and 21CFR56.111(a)(6) Criteria for IRB Approval of Research
45CFR46.102 and 21CFR50.3 Definitions
Office of Human Research Protections (OHRP) IRB Guidebook, Chapter III, E. Monitoring and Observation
Guidance on Data and Safety Monitoring of Clinical Trials, National Institutes of Health (NIH)
Policy for Data and Safety Monitoring, NIH
Further Guidance on Data and Safety Monitoring for Phase I & II Trials, NIH
Guidelines for Developing a Data and Safety Monitoring Plan, National Institute on Drug Abuse
The Establishment and Operation of Clinical Trial Data Monitoring Committees, Food and Drug Administration (FDA) Guidance
Definition of 'Clinical Trial', World Health Organization (WHO)

RELATED FORMS:

IRB Protocol Form

RELATED STANDARD OPERATING PROCEDURES:

7.2 Criteria for IRB Approval
7.7 Reports of Unanticipated Problems
11.6. Review of FDA-Regulated Research
11.7 Review of Planned Emergency Research