INSTITUTIONAL REVIEW BOARD
HUMAN SUBJECTS PROTECTION OFFICE

PENN STATE COLLEGE OF MEDICINE
PENN STATE MILTON S. HERSHEY MEDICAL CENTER

Guidance for Developing Data and Safety Monitoring Plans

Data and Safety Monitoring Plans

All clinical research studies require a data safety monitoring plan (DSMP) as a component of the proposed protocol. The purposes of the DSMP are to promote subject safety and to protect study integrity and validity. The specifics of a study-specific plan will be dependent on the type of study and the level of risk to subjects.

DSMPs will be reviewed by the IRB as a component of the protocol review. As a guideline, lower risk, less complex studies will generally require a briefer DSMP with less frequent review of cumulative adverse events and study progress. A Data Safety Monitoring Board (DSMB) may be required as a component of the DSMP for studies with large subject numbers, multiple sites, highly toxic therapies, dangerous procedures, high expected rates of morbidity and mortality in the study population, or high chance of early termination of the study. A study may utilize a DSMB established by the sponsor or the investigator.

Assess the risk level of the study (minimal, low, medium, high). See Appendix for guidelines. Then, develop a DSMP based on the level of assessed risk.

All monitoring plans must contain the following:

- A description and assessment of the study risks
- A description of anticipated adverse events (including the grading mechanism) and reporting mechanisms for adverse events (AEs), include timing and reporting structure (IRB, FDA, NIH, sponsor, etc.)
- Procedures (e.g. lab tests, evaluations, observations and their frequency) which will be utilized to monitor subject safety
- Identification of person(s) responsible for identification, documentation and reporting of AEs
- Mechanism to inform all pertinent groups of any actions taken by the PI in response to AEs and any actions taken or recommended by the IRB during continuing review
- Stopping rules which define critical thresholds for stopping or modifying the study
- A description of data and confidentiality protection mechanisms
- Defined frequency of review for summarized safety and aggregate analysis of adverse events information, and explanation of who will perform the review (PI, medical monitor, clinical trial team, DSMB, sponsor monitoring board, etc.)

For sample DSMPs based on risk level, see below.

DSMP Examples

Example I: Minimal Risk Study

This study involves minimal risk to subjects as the only interaction with human subjects involves _____ (e.g. collection of minimal amounts of blood (5 ccs) at the time of clinically indicated blood draws).

Oversight for the conduct of the study will be provided by the PI, _____. Adverse events are not anticipated, but any occurring will be documented and reported according to HSPO policies and procedures. The principal investigator will be solely responsible for data collection and verification, and review of cumulative adverse events. Confidentiality will be protected by utilizing a code number as the only identifier for each subject and the master list will be kept under lock and key with access limited to the PI. Cumulative adverse events and study progress summary will be communicated to the IRB at the time of continuing review.

Example II: Low Risk Study

This study involves low risk to subjects as it involves _____.

Oversight for the conduct of the study will be provided by the PI, _____ and the clinical research nurse, _____. They will ensure that all eligibility criteria and consent requirements are met prior to a subject's participation on study and that all study procedures and adverse event reporting occur according to the IRB approved protocol.

All data forms and study specific information will be kept in locked file cabinets and in a password protected computer database with access limited to the PI and clinical research nurse. Any presentation or publication of the data will be done in aggregate fashion without identifiers.

All adverse events will be documented on study specific case report forms and entered into a computer-based log. Anticipated adverse events for this study include the following: _____. The events will be graded according to _____ (e.g. the following scale, CTC criteria, etc.)

All deaths on study, not related to progression of underlying disease, will be reported to the IRB (FDA, sponsor, etc) immediately. All unanticipated AEs related or possibly related to the study will be reported by the PI to the IRB according to HSPO policies and procedures.

The PI and clinical research nurse will review cumulative adverse events, early termination of study participation, and accrual every six months and report any issues requiring modification of the study or alteration of the risk:benefit ratio to the IRB immediately. A summary of adverse

events, study progress and protocol modifications will be included for IRB review in the continuing review report.

Example III: Moderate or High Risk Study

Note: Many of these will be grant funded or industry sponsored, with a DSMP which contains a plan for a DSMB. Submission of the DSMP as delineated by the sponsor will be adequate for IRB review.

This study involves moderate risk to subjects as it involves _____ (e.g. placebo controlled study, randomization, phase III clinical trials).

Oversight for the conduct of the study will be provided by the PI, _____ and the clinical research nurse, _____. They will ensure that all eligibility criteria and consent requirements are met prior to a subject's participation on study and that all study procedures and adverse event reporting occur according to the IRB approved protocol. They will follow all study participants, while on study treatment, on a real-time basis for development of adverse events and study endpoints, utilizing scheduled and as needed physical examinations and laboratory studies. They will make certain that all adverse events are recorded and reported according to HSPO (and FDA, etc) guidelines and that the IRB (FDA, etc) is notified in a timely manner of any significant safety or data concerns which arise from study review.

All data forms and study specific information will be kept in locked file cabinets and in a password protected computer database with access limited to the PI, clinical research nurse, and sponsor designees. Any presentation or publication of the data will be done in aggregate fashion without identifiers.

All adverse events will be documented on study specific case report forms and entered into a computer-based log. Anticipated adverse events for this study include the following: _____ (or are detailed in section __ of the protocol). The events will be graded according to _____ (e.g. the following scale, CTC criteria, etc.)

All deaths on study, not related to progression of underlying disease, will be reported to the IRB (FDA, sponsor, etc) immediately. All unanticipated AEs related or possibly related to the study will be reported by the PI/designee to the IRB according to HSPO policies and procedures.

Primary monitoring of the study will be performed by the study team, who will review accrual, adverse events, and dose limiting toxicities on a real-time basis. Cumulative adverse events and study toxicities will be reviewed weekly. The study team will make decisions regarding dose escalation, cessation of accrual, and whether stopping rules have been reached. If stopping rules have been reached, this will be communicated to the IRB immediately.

A DSMB (charter and members' list attached) will review the study progress at six month intervals, with study progress reports provided to the DSMB by the study team and statistician. A DSMB report will be generated by the DSMB and forwarded to the IRB and the PI. A copy of any interim DSMB reports will be included with continuing review reports submitted by the PI for IRB review.