Data and Safety Monitoring Plan

Data and Safety Monitoring Plan

SOP #: ADCR-12	**Next Review Date: 09/2014**
Version #: 1.0	**Review Interval Period: Annual**
Approved Version #: 1.0 Date: 09/2013	**Policy Reference:**

Data and Safety Monitoring Plan

Data and safety monitoring plans (DSMPs) are an essential component to any clinical research study. They ensure that the rights and safety of research participants are protected and that the reported trial data are accurate, complete, and verifiable from source documents.

One protocol may have more than one data and safety monitoring plan including a description of the principal investigator's (PI) and research team's plan, the research organization's plan, or the sponsor's plan. Some studies may require a formal data monitoring committee (DMC), also known as data and safety monitoring board or committee (DSMB or DSMC, respectively).

DSMPs should be based on the study's expected risks associated with the research, the population being studied, the size (e.g., larger enough to require multiple sites versus a single site), nature and complexity of the protocol, and population being studied. The plan should be included in the protocol to allow an institutional review board (IRB) and other regulators to assess the plan's feasibility and appropriate rigor based on the risk level.

1 Principal Investigator/Research Team

All protocols should include a DSMP which describes how the investigator plans to oversee research subject safety and ensure data integrity. The PI and his/her research staff are part of the monitoring plan but may not be the only ones conducting monitoring activities for any given protocol.

The following language is to be used in all protocols that are enrolling subjects:

The clinical research team will meet on a regular basis {insert frequency} when patients are being actively treated on the trial to discuss each patient. Decisions about dose level enrollment and dose escalation if applicable will be made based on the toxicity data from prior patients.

All data will be collected in a timely manner and reviewed by the principal investigator or a lead associate investigator. Adverse events will be reported as required above. Any safety concerns, new information that might affect either the ethical and or scientific conduct of the trial, or protocol deviations will be immediately reported to the IRB using iRIS (if applicable) and to the Sponsor.

The principal investigator will review adverse event and response data on each patient to ensure safety and data accuracy. The principal investigator will personally conduct or supervise the investigation and provide appropriate delegation of responsibilities to other members of the research staff.

2 Sponsor Monitoring Plan

Sponsor monitoring plan would only be needed if the study involved an IND/IDE. Per the regulations, the FDA requires all sponsors of FDA-regulated research to have a monitoring plan in place to assess the progress of the clinical investigation. This includes both Industry-sponsored research and NIH-sponsored research where an NIH Investigator or IC is the sponsor.

The following language is to be used for CCR or Investigator-held IND studies:

This trial will be monitored by personnel employed by Harris Technical Services on contract to the NCI, NIH. Monitors are qualified by training and experience to monitor the progress of clinical trials. Personnel monitoring this study will not be affiliated in any way with the trial conduct.

At least 25% of enrolled patients will be randomly selected and monitored at least biannually or as needed, based on accrual rate. The patients selected will have 100% source document verification done. Additional monitoring activities will include: adherence to protocol specified study eligibility, treatment plans, data collection for safety and efficacy, reporting and time frames of adverse events to the NCI IRB and FDA, and informed consent requirements. Written reports will be generated in response to the monitoring activities and submitted to the Principal investigator and Clinical Director or Deputy Clinical Director, CCR, NCI.

NOTE: Please contact Caryn Steakley at steaklec@mail.nih.gov if your protocol requires a sponsor monitoring plan (i.e., a NCI investigator holds the IND or IDE).

3 Safety Monitoring Committee (SMC)

Protocols that WILL REQUIRE a SMC include:

- All NCI CCR multi-institutional treatment protocols for which the NCI CCR is the coordinating site, unless the study has already a designated Data and Safety Monitoring Board (DSMB) or equivalent. These studies will be monitored across the sites for unusual, significant toxicities that are related to the investigational agents being used. The SMC will not monitor a CTEP-sponsored protocol of this type if this is the only SMC qualifying criterion for the protocol.
- All protocols using gene transfer or gene therapy methodology. Monitoring of these protocols will focus on unusual toxicities specific to gene therapy.

- All protocols that the CCR believes require special attention due to high public interest or public perception of risk or potential conflict of interest. These include studies where the PI or an AI holds a patent on any agent being used in the protocol. For these protocols, the review will focus on unusual, significant toxicities that are related to the investigational agents being used, as well as on the potential perception of a conflict of interest regarding issues such as the continuing study relevance vs. investigator benefit.
- All protocols that are deemed to pose potentially very high risk to patients.
- Protocols can be referred to the SMC by the Clinical Director, the Branch Chief of the branch in which the protocol originates, or the IRB Chair.

Timing of protocol review by the SMC:

- Protocols referred to the SMC will be reviewed initially as soon as possible after their annual NCI-IRB continuing review date. Subsequently, each protocol will be reviewed as close to annually as the quarterly meeting schedule permits or more frequently as may be required by the SMC.
- For initial and subsequent reviews, protocols will not be reviewed if there is no accrual within the review period.

The following language is to be used in protocols that require a SMC:

This protocol will require oversight from the Safety Monitoring Committee (SMC). Initial review will occur as soon as possible after the annual NCI-IRB continuing review date. Subsequently, each protocol will be reviewed as close to annually as the quarterly meeting schedule permits or more frequently as may be required by the SMC. For initial and subsequent reviews, protocols will not be reviewed if there is no accrual within the review period. Written outcome letters will be generated in response to the monitoring activities and submitted to the Principal investigator and Clinical Director or Deputy Clinical Director, CCR, NCI.

NOTE: Please contact Susan McMullen at mcmulles@mail.nih.gov or 301-402-5931 if your protocol requires SMC review or if you have any questions about the above criteria.

4 Data Safety Monitoring Board (DSMB)

A DSMB is an impartial group established to oversee a clinical trial and review the results to determine if they are acceptable. Members of a DSMB must be multidisciplinary and include members with relevant clinical and statistical expertise. The DSMB should meet at least annually or more often depending on the activity and nature of the clinical trial being monitored.

Protocols that WILL REQUIRE a DSMB include:

- Protocols that generate blinded, randomized data;
- Phase III single institution trials (NCI only) presenting more than minimal risk;
- Phase III multi-institutional protocols coordinated by the CCR presenting more than minimal risk without an outside DSMB.

Protocols that MAY REQUIRE a DSMB include:

- Protocols that the NCI IRB believes require special scrutiny because of high public interest, public perception of risk, or the inclusion of vulnerable populations.

The following language is to be used in protocols that require a DSMB:

This protocol requires monitoring by the NCI CCR Data Safety Monitoring Board (DSMB) as described in Section X.X. [insert appropriate statistical considerations section/subsection number here]. Interim outcome results will not be revealed to the investigators of the trial; results will be presented to the investigators prior to final accrual to the trial only if the DSMB recommends early termination of the trial. (NOTE: the study statistician is responsible for providing the description of how the monitoring will take place, including endpoints to be monitored and the frequency or timing of monitoring.)