What is the Data Monitoring Committee (DMC)? What types of studies does the DMC monitor?

The DMC is responsible for safety review and study progress monitoring for all NU Investigator-Initiated Trials (IITs) and for any trial that adheres to the Lurie Cancer Center Data and Safety Monitoring Plan (DSMP). The DMC meets semi-monthly (2\textsuperscript{nd} and 4\textsuperscript{th} Wednesday of each month) and provides the following:

- Ongoing safety reviews of all NU IITs requiring moderate and high intensity monitoring; semi-annual safety reviews for those studies determined to require minimal intensity monitoring
- Accrual reviews of all clinical trials.
- Reviews of all serious adverse events (SAEs) that occur on NU IITs.
- Reviews of all dose-limiting toxicities (DLTs) for Phase I dose-escalation studies.
- Reviews of all FDA annual reports (prior to submission to the FDA) for those studies where the NU PI holds the Investigational New Drug Application (IND) or Investigational Device Exemption (IDE).
- Reviews of protocol deviations.
- Approval of data prior to any publication.

My study has been assigned a “high intensity level of monitoring”. What does this mean? What do the different monitoring levels involve?

When a new protocol is reviewed and approved by the Scientific Review Committee (SRC), it will be assigned a level of risk and a corresponding level of monitoring. This level of monitoring determines how the DMC will monitor each study.

- **No Greater than Minimal Risk** – “Minimal Risk” means that the probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or during the performance of routine physical and psychological examinations or tests and where confidentiality is adequately protected. This category includes protocols that pose “no greater than minimal risk” according to federal regulations. Requires Low Intensity Monitoring. An example of this type of trial is a computer or internet-based strategy aimed at increasing awareness of cancer issues. The PI is not required to submit CRFs/eCRFs to the Quality Assurance Monitor (QAM) for regular review. Subject enrollment logs must be submitted at least annually to the CRO.

- **Minimal Risk** – There is a probability of the occurrence of a low-severity event that is reversible and/or there is a low probability of serious harm. Requires Minimal Intensity Monitoring. An example of this type of trial is a dietary intervention or exercise study aimed at symptom management. The PI is not required to submit CRFs/eCRFs for regular QAM review. Subject enrollment logs and adverse events must be submitted to the CRO semi-annually. DMC monitors study progress semi-annually through review of Minimal Intensity Monitoring Reports (MIMRs), which includes such information as accrual, reported adverse events, and compliance issues.

- **Moderate Risk** – There is a probability of a moderate-severity event occurring but there is adequate safety monitoring in the trial to identify events promptly and to minimize their effects. Requires
Moderate Intensity Monitoring. An example of this type of trial is a topical agent used to control a drug rash. The PI is required to prospectively register subjects and submit adverse event CRFs/eCRFs to the QAMs in real time. The PI is not required to submit other CRFs/eCRFs for regular QAM review. The PI is required to follow all NU IRB regulations related to the prompt reporting of adverse events. DMC monitors study progress semi-annually through review of Data Safety Monitoring Reports (DSMRs), which includes such information as accrual, reported adverse events, and compliance issues. In addition to this review, accrual is reviewed more frequently and is reported at each DMC meeting (semi-monthly).

- **High Risk** - There is a high probability of the occurrence of a serious adverse event and/or study monitoring and reporting requirements of the trial are such that events or event trends may not be immediately recognized. Phase I-III therapeutic drug or device trials by default are assigned to this group. Requires High Intensity Monitoring. An example of this type of trial is a chemotherapy trial aimed at treating cancer. The PI is required to prospectively register all study subjects through the QAMs and all data will be submitted to and monitored by the QAMs, per the data submission schedule outlined in the protocol. The PI is required to follow all NU IRB regulations related to the prompt reporting of adverse events. In addition, the PI must submit all SAEs to the QAMs in real time, as defined by each protocol. These events are reviewed at the next scheduled DMC meeting. Safety reviews for these studies are done in real time and are ongoing. For phase I studies, safety data are presented in total after each cohort is complete. Outcome data are presented at least quarterly. For phase II and III studies, safety and outcome data are reviewed in total at least quarterly, and may occur more frequently if issues arise. DSMRs are completed semi-annually. The DMC conducts a comprehensive review of study progress semi-annually through review of DSMRs, which includes such information as accrual, reported adverse events, and compliance issues. In addition to this review, accrual is reviewed more frequently and is reported at each DMC meeting (semi-monthly).

**Over the course of the study, how is a PI expected to interact with the DMC?**

The PI is expected to submit SAEs, data, and protocol deviations as there are defined by each protocol. The PI is expected to promptly respond to any DMC communications regarding SAEs, data, deviations, or accrual issues. The PI is expected to review, sign, and respond to semi-annual progress reports for each study monitored by the DMC.

If a PI intends to publish an abstract or manuscript for a study, the data must be approved by the DMC prior to its use in a publication. PIs must request DMC approval of data via the QAM a minimum of four weeks prior to a publication deadline.