“(a) In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied:

(6) When [Where FDA] appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.” 45 CFR 46.111, 21 CFR 56.111

When appropriate, the IRB will require that the research plan makes adequate provisions for monitoring the data collected to ensure the safety of subjects or ensure negative outcomes do not occur. If required, the data oversight and monitoring plan will depend on the nature, size, risk, and complexity of the study.

**Determination of Whether Data and Safety Monitoring Plan is Required**

In the process of evaluating whether the IRB will require provisions for monitoring the data, the IRB assesses the following:

- Risk level of the study (i.e., minimal risk, more than minimal risk)
- Possibility that an intervention may have an adverse impact on the subjects and if so, description of the adverse impact (e.g., physical, psychological, social, economic, legal, emotional) including magnitude and likelihood
- Involvement of topics or areas that may cause distress to the subject and if so, foreseeability of distress
- Involvement of topics that may place subjects at risk by participating in the research (e.g., domestic abuse)
- Inclusion of deception or incomplete disclosure and if so, risk of distress to subjects
- Length of study (e.g., longitudinal, length of the intervention)
- Need to review data for current subjects’ safety and/or for the safety of future subjects
- Frequency for monitoring data, including who is conducting the monitoring (e.g., PI, external boards)
- Whether the activity is a clinical investigation; clinical investigations typically require a data and safety monitoring plan

**Development of a Data and Safety Monitoring Plan**

If it is determined that the research requires data and safety monitoring, the investigator must describe the provisions for monitoring the data to ensure the safety of subjects.
When required or appropriate, the PI will submit a Data Safety and Monitoring Plan (DSMP) with the IRB application. A sample template for such a plan is available on the Human Research Protection Program (HRPP) website.

Data oversight and monitoring plans should vary depending on the nature, size, risk (e.g., low risk, high risk intervention) and complexity of the clinical trial (e.g., single-site, multi-site). The oversight and monitoring plan may be conducted by various individuals or groups and in various ways. For example, the PI of a small Phase I or II study involving a low-risk intervention may be qualified to monitor the progress of such a study.

Alternatively, an independent Data Safety Monitoring Board (DSMB) may be the only entity qualified to monitor the progress of a Phase I or II clinical trial involving multiple sites, blinding, high-risk interventions or vulnerable populations. DSMBs are typically committees of non-conflicted experts, including scientists, physicians, statisticians, bioethicists, and others that perform ongoing monitoring of the data and safety of interventional research trials. These committees are usually external to the research team. A DSMB evaluates the research to assure it is safe and effective, recommends conclusion of the trial when significant risks have developed, determines if the trial is deemed unlikely to be concluded successfully, or may recommend expansion of treatment beyond experimental use if significant benefits have developed. At each meeting, DSMBs typically review summary reports of adverse events, analyze interim data, cumulative toxicity summaries, reports of related studies, major proposed protocol amendments, data and monitoring plans/reports, safety and efficacy outcomes, and other aspects of protocol compliance. Following each meeting of the DSMB, the investigator should be provided with written information concerning findings or concerns related to the study.

Several methods of data and safety monitoring can be employed, depending on the level of risk. The plan should state who would be responsible for monitoring subject safety, protocol compliance, and adverse event reporting. Specific monitoring parameters may include subjects screened and enrolled, dropouts, primary and secondary efficacy endpoints, and/or the informed consent process. The following entities are examples of entities that can monitor subject safety and protocol compliance:

- Principal Investigator: Appropriate for investigator-initiated, single-site, nonrandomized studies of low risk, provided PI has no conflict of interest
- External Monitor: A qualified individual not involved with the study, trained in monitoring (i.e. safety officer, designated Medical Monitor)
- Data and Safety Monitoring Committee: Appropriate for studies of high risk; the scientific review committee or IRB may appoint a data and safety ad hoc committee
- Data and Safety Monitoring Boards (DSMB): Some Phase I, Phase II, and other studies involving high-risk therapy and/or vulnerable subjects may require a DSMB; in many cases, industry sponsored/ U.S. Food and Drug
Administration (FDA) regulated studies, Phase III, and higher risk investigator-initiated studies require a DSMB

Investigators submitting applications for the National Institutes of Health (NIH) support of grants, cooperative agreements, or contracts should be aware that each specific institute may have its own policies regarding data and safety monitoring. Investigators are encouraged to visit the NIH website for the appropriate agency.

Assessment of Data and Safety Monitoring Plan
If it is determined that the research requires data and safety monitoring, as part of the IRB review process, the IRB will assess the appropriateness and adequacy of a study’s proposed data oversight and safety monitoring plan (or the justification as to why such a plan is not possible) based on the following criteria:

- Whether the proposed plan is commensurate with the nature, size, and complexity of the clinical trial as well as the degree of risk involved in the study
- Timeliness of the planned monitoring (e.g., annual monitoring for low risk studies, quarterly monitoring for high-risk studies)
- How monitoring conclusions are reported to the IRB and frequency of reporting
- Whether the individual or entity conducting the monitoring activities has the expertise to accomplish the monitoring mission; for studies requiring a monitoring group, the group should consist of clinical trial experts, biostatisticians, bioethicists, and clinicians knowledgeable about the disease and treatment under study
- The mechanisms for reporting adverse events to the IRB, FDA, and NIH, as applicable

The IRB is guided by the NIH Policy for Data and Safety Monitoring, further NIH Guidance on Data and Safety Monitoring for Phase I and Phase II Trials, and Good Clinical Practice: Consolidated Guidance.

Data and Safety Monitoring Reports
The PI must submit data and safety monitoring reports received from the monitor or reports generated by the PI (when the PI is the monitor) to the IRB at the time of continuing review. If a third party monitor’s report suggests a change in the study design, a temporary or permanent closure to accrual, or any other information of note, those reports should be forwarded to the IRB immediately.

Additional Considerations
For research studies subject to the requirements of the U.S. Department of Defense, see HRPP Manual 2-2-A, “U.S. Department of Defense.”