1.0 POLICY

1.1 Background

1.1.1 Congressional and public concern about patient safety in research has increased the demand for investigators to establish plans for ongoing, real time data and safety monitoring in studies involving human subjects. The method and amount of monitoring required depend on the degree of risk involved to the participants, the use of vulnerable populations, the design and complexity of the research, and the research sponsor. In general minimal risk studies do not require establishment of a data safety monitoring plan (DSMP) or Data Safety Monitoring Board (DSMB).

1.1.2 All studies of more than minimal risk and clinical research, clinical investigations, and clinical trials funded by the National Institutes of Health (NIH) or regulated by the Food and Drug Administration (FDA) must undergo IRB review and approval of data and safety monitoring plans. Some private sponsors require this as well.

1.1.2.1 NIH POLICY FOR DATA AND SAFETY MONITORING, Release Date June 10, 1998 requires each Institute and Center (IC) have a system for the appropriate oversight and monitoring of the conduct of clinical trials to ensure the safety of participants and the validity and integrity of the data for all NIH-supported clinical trials. The establishment of data safety monitoring boards (DSMBs) is required for multi-site clinical trials involving interventions that entail potential risk to the participants. The data and safety monitoring functions and oversight of such activities are distinct from the requirement for study review and approval by an Institutional Review Board (IRB). The plan should be tailored to the nature, size, and complexity of the research, the expected risks, and the type of subject population being studied.

1.1.2.2 DEPARTMENT OF DEFENSE REGULATIONS AND REQUIREMENTS: The DoD requires that IRBs consider the appointment of a research monitor for research of greater than minimal risk and, if appropriate, for research involving research of no more than minimal risk. The independent research monitor is to be appointed by name and has the authority to stop a research study in progress, to remove individuals from the study, and to take any other steps needed to protect the safety and well-being of participants until the IRB can assess the situation.

1.1.2.3 The need for data and safety monitoring is not limited to medical studies. Socio-behavioral studies too may also pose greater than minimal risks to participants and threats to the integrity and validity of data.
1.1.2.4 The use of students to screen participants and collect data also poses the need for data and safety monitoring to identify risks to participants and maintain study integrity.

1.1.2.5 Multisite studies may increase the risks to both participants and data integrity.

1.1.3 A Data Safety Monitoring Plan (DSMP) is a description of how participants and accumulating data will be monitored to ensure safety of human subjects and human research data, the validity of data, and the appropriate termination of studies. The investigator develops the plan, oversees its implementation, and reports problems to the IRB.

1.1.4 A Data Safety Monitoring Board (DSMB) is an independent body composed of clinical research experts and community representatives that reviews data while a clinical trial or study of greater than minimal risk is in progress to ensure that participants are not exposed to undue risk. A DSMB may recommend that a trial be stopped if there are safety concerns or if the trial objectives have been achieved.

1.2 Policy Statement.

1.2.1 The UA IRB requires (a) all research studies posing greater than minimal risks of harm to human subjects (including investigator-initiated studies), (b) all clinical research or clinical investigations funded by the National Institutes of Health (NIH), the Department of Defense, or regulated by the Food and Drug Administration (FDA), (c) all studies whose sponsors require it, and (d) some studies involving vulnerable subjects to incorporate a written data and safety monitoring plan [DSMP] for the safety of the participants as part of the research protocol.

1.2.2 The minimum elements to be included in a data safety monitoring plan (DSMP) are:

1.2.2.1 A description of how risks are minimized

1.2.2.2 A description of how risks are reasonable in relation to anticipated benefits

1.2.2.3 Identification of an internal or external data safety monitor.

1.2.2.3.1 For investigator-initiated, single site, nonrandomized studies of relatively low risk, an internal monitor may be appropriate. This may be the investigator, a research coordinator, or a research assistant with the necessary training, or a person external to the study as long as the person has no conflict of interest with the study.

1.2.2.3.2 For sponsored studies, multisite studies, randomized studies of significant risk, an external monitor is appropriate. This must be an individual not involved with the study who is also trained in monitoring (i.e. safety officer, designated medical Monitor).
1.2.2.4 A description of what will be monitored to assure progress and safety, which may include some or all of the following components:

1.2.2.4.1 A plan for safety review at predetermined intervals relevant to the complexity and risk of the research

1.2.2.4.2 Assessments of data quality, timeliness, and participant recruitment, accrual, and retention relevant to the complexity of the study

1.2.2.4.3 Procedures for detecting and reporting unanticipated problems involving risks to participants or others, and other events or information as listed in POLICY: Reportable Events: Protocol Deviations, Unanticipated Events, and Adverse Events Involving Risks to Participants or Others and GUIDANCE: Reportable Events.

1.2.2.4.4 Identification of who will be monitoring and collecting the unanticipated problems (e.g., the investigator, research coordinator, research assistant. If the latter, the assistant must have the necessary skills or training.)

1.2.2.4.5 Specification of who, besides the IRB, will be notified of events and information that require prompt reporting (e.g., NIH, FDA, PI, etc.)

1.2.2.4.6 A reporting plan indicating the timing of reports in accordance with the GUIDANCE: Reportable Events.

1.2.2.4.7 A plan for reporting of adverse events at continuing review

1.2.2.4.8 A description of the plan to assure data accuracy and protocol compliance.

1.2.3 Depending upon the nature and complexity of the study, and/or the severity of the harm anticipated to occur during the research study, the establishment of an external and independent Data Safety Monitoring Board [DSMB] may be required to monitor the progress and safety of research participants. This is especially likely for some Phase I or II clinical trials and other studies involving high-risk therapy and/or vulnerable subjects. In many cases Industry Sponsored/FDA Regulated Studies, Phase III, and higher risk investigator-initiated studies require a DSMB.

1.2.4 The required elements for a DSMB include:

1.2.4.1 The credentials of board members which must be appropriate to the protocol and support the expertise of members for their roles;

1.2.4.2 A schedule or specification of frequency of meetings;

1.2.4.3 A specified reporting format;

1.2.4.4 Designation of individuals to receive reports of unanticipated problems, adverse events, or participant or research team complaints.
1.2.4.5 A stated frequency of report submissions (no less than annually or on an IRB-specified schedule)

1.2.4.6 Specification of criteria for stopping the study, either for harm or for making benefits available to the general population

1.2.4.7 Data reflecting/regarding actual harm to research participants compared to anticipated harm to research participants

1.2.4.8 Data reflecting/regarding actual benefits to research participants compared to anticipated benefits to research participants

1.2.4.9 Causality of unexpected harm, if identified.

1.2.5 The IRB will determine during the initial review, continuing review or reviews for study modification whether a research plan includes adequate provisions to monitor collected data in providing for the safety of subjects.

1.2.6 The IRB has the authority to appoint an internal or external study monitor or a data safety monitoring board if it deems it necessary.

1.2.7 The IRB has the authority to seek consultation about data safety monitoring plans, boards, or reports if it deems it necessary.

1.3 Objective.

1.3.1 Implementation of this policy will ensure the safety of human participants and adherence to federal or private sponsor requirements through monitoring data collected to provide for participant safety, preserve the integrity and credibility of studies, and identification of how unanticipated or adverse events will be characterized and reported.

1.4 Responsibility.

1.4.1 The Vice President for Research is ultimately responsible for this policy. Enabling parties include principal investigators, study personnel, and the IRBs.

2.0 PROCEDURE

2.1 Initial Review of Applications with a DSMP or DSMB

2.1.1 The Investigator will complete an appropriate DSMP for inclusion during initial submission of the research protocol. See GUIDANCE: Developing a Data and Safety Monitoring Plan (DSMP) or a Data Safety and Monitoring Board (DSM).

2.1.2 The Research Compliance Specialist forwards the plan to the IRB for full board review and determination of the adequacy of the DSMP and membership, structure, and functioning of the DSMB.
2.1.3 Issues that the IRB chair/primary reviewer, and IRB will consider in evaluating the adequacy of a DSMP to protect participants and provide timely review of useful information include:

2.1.3.1 Reporting mechanisms;

2.1.3.2 The frequency of the monitoring, such as points in time or after a specific number of participants are enrolled;

2.1.3.3 The entity that will conduct the monitoring, such as a data monitoring committee, a DSMB, medical monitor, investigator, or independent physician;

2.1.3.4 The qualifications of people conducting the monitoring and their freedom from conflicts of interest;

2.1.3.5 The specific data to be monitored;

2.1.3.6 Actions to be taken upon specific events or end points;

2.1.3.7 Communication procedures from the data monitor to the IRB and all study sites the IRB.

2.1.4 Upon final determination of the adequacy of the DSMP the IRB Chair will provide written notification to the investigator regarding the outcome of the review, including:

2.1.4.1 Upon Disapproval: Listing of failures

2.1.4.2 Upon Approval: The frequency of reporting required.

2.1.4.2.1 Minimum reporting frequencies for DSMPs will be a yearly report submitted at the time of continuing review and at study closure.

2.1.4.2.2 Minimum reporting frequency for DSMBs will be 30 days or less after the DSMB meets and issues a report.

2.1.4.2.3 Minimum reporting frequency for Industry Trials will be a yearly report submitted at the time of the continuing review

2.1.4.2.4 For Sponsor/Investigator Trials, quarterly reports will be sent to the IRB and the Office of Research Compliance. The ORC will apply its standard procedure for determining that the monitoring is being conducted according to the plan and will issue a report to the IRB.

2.2 Continuing Review

2.2.1 The Investigator will include a monitoring report as requested on the FORM: IRB Renewal Application or as required by the IRB or DSMB reports when appropriate.

2.2.2 The IRB Chair, designee or IRB will review the reports issued, the monitoring plan, safety reports and reported deviations and note:
2.2.2.1 Any changes in the monitoring plan or frequency of monitoring that may be required to enhance data integrity and participant well-being and preserve the risk/benefit ratio,

2.2.2.2 Adherence to the monitoring plan and schedule,

2.2.2.3 Appropriate application of actions such as stop rules or endpoints,

2.2.2.4 Procedure for analysis and interpretation of the data appear correct.

2.2.3 The IRB will notify the Investigator of its review and any requested changes.

2.2.4 Investigator compliance with IRB requests will be monitored by the Research Compliance Specialist and the Research Compliance Manager (if study is recommended for or selected for routine post-approval monitoring or if circumstances arise that lead to monitoring for cause.

3.0 REFERENCES

3.1 45 CFR §46.111(a)(6)

3.2 21 CFR §56.111(a) (6), 21 CFR §312.56, 21 CFR §312.60.


3.4 DoD: SECNAVINST 3900.39D, para.6c

4.0 RELATED SECTIONS

4.1 POLICY: Reportable Events: Protocol Deviations, Unanticipated Events, and Adverse Events Involving Risks to Participants or Others

4.2 GUIDANCE: Developing a Data and Safety Monitoring Plan (DSMP) or a Data Safety and Monitoring Board (DSM)

4.3 GUIDANCE: IRB Application Guide

4.4 FORM: IRB Renewal Application

4.5 GUIDANCE: General Responsibilities of Investigators

4.6 GUIDANCE: Reportable Events

4.7 POLICY: Routine Post-Approval Monitoring of Protocols

4.8 POLICY: Monitoring of Previously Approved Research for Cause: Suspension and Termination
4.9 GUIDANCE: Department of Defense Regulations for Human Subjects Research