

## **RURAL HEALTH CARE RESEARCH CENTER**

### **PROCEDURES FOR DATA AND SAFETY MONITORING**

#### **Overview**

All clinical investigations conducted in the Rural Health Care Research Center (RHCRC) will follow the procedures for data and safety monitoring described below. The plan, tailored for each protocol, will be included in all applications for pilot funding and included in approved methods for each pilot projected funded by the RHCRC.

#### **Definitions**

Data and Safety Monitoring: The process of ensuring the safety of participants, the validity of data, and the appropriate termination of studies for which significant benefits or risks have been uncovered or when it appears that the trial cannot be concluded successfully.

- Data and Safety Monitoring Plan (DSMP): The Data and Safety Monitoring Plans (DSMP) assure that each clinical investigation has a system for appropriate oversight and monitoring of its conduct. This oversight ensures the safety of the participants and the validity and integrity of the data. The plan for monitoring includes adverse event reporting, safety monitoring and safety data to be collected. This is required for all investigations involving human subjects conducted in the RHCRC.
- Data and Safety Monitoring Board (DSMB): – A Data and Safety Monitoring Board is a committee of scientists, nurses, statisticians, ethicists or other experts relevant to the clinical investigation(s) it monitors that collects and analyzes data during the course of a clinical investigation to identify adverse effects and other trends (e.g. an indication that one treatment is significantly better than another, particularly when one arm of the trial involves a placebo control) that would warrant modification or termination of the investigation or notification of subjects about new information that might affect their willingness to continue in the trial. Studies that are large, involve multiple sites, focus on vulnerable populations, have interventions that are especially risky or may involve significant morbidity or mortality in the served population or are of long duration may require a DSMB.
- An adverse event is any undesirable sign, symptom or medical or psychological condition occurring in a participant, even if the event is not considered to be related to the investigation. Medical condition/diseases present before starting the investigational drug/intervention will be considered adverse events only if they worsen after the participant starts the clinical investigation. An adverse event is also any undesirable and unintended effect of research occurring in human subjects as a result of the collection of identifiable private information under the research. Adverse events also include any problems associated with the use of an investigational device that adversely affects the rights, safety or welfare of subjects.
- A serious adverse event will be considered any undesirable sign, symptom, or medical condition which is fatal, life-threatening, requires or prolongs inpatient hospitalization, results in persistent or significant disability/incapacity, constitutes a congenital anomaly or birth defect, is medically significant and which the investigator regards as serious based on appropriate medical/nursing judgment. An important medical/nursing event is any AE that may not result in death, be life-threatening, or require hospitalization but may be

considered an SAE when, based upon appropriate medical/nursing judgment, it may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed in the definitions of SAEs. Any serious psychological and emotional distress resulting from study participation (suggesting need for professional counseling or intervention) also can be considered a SAE.

- . An unanticipated problem is any event or experience that meets ALL 3 criteria below:
- Is unexpected in terms of nature, severity or frequency given the research procedures that are described in the protocol-related documents AND in the characteristics of the subject population being studied.
- Related or possibly related to participation in research. This means that there is a reasonable possibility that the incident may have been caused by the procedures involved in the research study.
- The incident suggests that the research placed the subject or others at greater risk of harm than was previously known or recognized OR results in actual harm to the subject or others.
  
- A protocol violation is defined as any change, deviation, or departure from the study design or procedures of a research project that is NOT approved by the IRB- prior to its initiation or implementation, OR a deviation from standard operating procedures, Good Clinical Practices (GCPs), or federal, state or local regulations. Protocol violations may or may not be under the control of the study team or UVa staff. These protocol violations may be major or minor violations. A major violation is a protocol violation that meets the following criteria:
  - Represent a serious or continuing failure on the part of the study team to comply with the protocol, standard operating procedures, GCPS, federal, state or local regulations.
  - Impacts subject safety or substantially alter risks to subjects. It may or may NOT result in actual harm (clinical, emotional, social, financial, etc).
  - Significantly damages the completeness, accuracy and reliability of the data collected for the study.
  - Is under control of the investigator/study team/ UVa staff
  
- A minor protocol violation (also called a protocol deviation) is a protocol violation that meets the following criteria:
  - Does NOT represent a serious failure on the part of the study team to comply with the protocol, standard operating procedures, GCPs, federal, state or local regulations.
  - Does NOT represent a continuing failure on the part of the study team to comply with the protocol, standard operating procedures, GCPs, federal, state or local regulations.
  - Does NOT impact subject safety or substantially alter potential risks to subjects(Note risk can be clinical, emotional, social, financial, etc)
  - Does NOT result in actual harm
  - Does NOT significantly damage the completeness, accuracy and reliability of the data collected for the study.
  - May or may not be under the control of the investigator/study team/ UVA staff.

## Developing the Data and Safety Monitoring Plan

The DSMP includes an estimation of risk and plans to reduce risk and procedures for identifying adverse events, unanticipated problems, and protocol violations.

1) The investigator first must identify the risks associated with participation in their clinical investigation and plans to minimize risk as is generally required in protocols submitted to the Institutional Review Board (IRB).

- The risks described in the protocol should be consistent with those in the consent form.
- Risks should be separated by source of risk with the most serious risk listed first.
- The expected frequency of occurrence should be estimated for each risk listed.
- For each risk, indicate the planned action to a) reduce the likelihood of occurrence of the risk, and b) manage the risk once it has occurred.

## IRB Reporting Requirements

The IRB has specific reporting requirements for adverse events, unanticipated problems and major protocol violations. These include:

- Adverse Events: Any internal (protocols under the purview of the UVAIRB), serious, unexpected adverse events must be reported using the IRB Online program within 7 days of the time the study team receives knowledge of the event.
- ALL unanticipated problems must be reported to the IRB-HSR. The unanticipated problem may be reported as an unanticipated problem, an adverse event, a protocol violation or enrollment exception depending on the circumstances of the problem.
- All major protocol violations must be reported to the IRB-HSR immediately upon discovering them, and no later than seven (7) calendar days from the time the study team receives knowledge of the event.

Links that provide more information about IRB reporting requirements include:

[http://www.virginia.edu/vprgs/irb/hsr\\_adverseevent.html](http://www.virginia.edu/vprgs/irb/hsr_adverseevent.html)

[http://www.virginia.edu/vprgs/irb/HSR\\_docs/Unanticipated\\_Problems-Definitions\\_and\\_Reporting\\_Guidelines.doc](http://www.virginia.edu/vprgs/irb/HSR_docs/Unanticipated_Problems-Definitions_and_Reporting_Guidelines.doc)

[http://www.virginia.edu/vprgs/irb/HSR\\_docs/Forms/Protocol\\_Violations\\_%20Enrollment\\_Exceptions\\_Instructions.doc](http://www.virginia.edu/vprgs/irb/HSR_docs/Forms/Protocol_Violations_%20Enrollment_Exceptions_Instructions.doc)

[http://www.irb.virginia.edu/HicDocs/SOP/4-1\\_r21\\_ae\\_or\\_unanticipated\\_problem\\_reporting.pdf](http://www.irb.virginia.edu/HicDocs/SOP/4-1_r21_ae_or_unanticipated_problem_reporting.pdf)

## RHCRC Oversight

The RHCRC retains responsibility for the safe conduct of research investigations. To comply with RHCRC oversight requirements all investigators will:

- Include the DSMP with each application for pilot funding from RHCRC.
- If funding is approved, obtain approval of the DSMP from the Methods director before funds are released.

- Inform the Methods director each time a report is filed with the IRB. In an email or letter describe the event, the outcome, and any changes that are needed in your protocol because of the event's occurrence. Please submit within 7 days of making the report to the IRB.
- Provide a quarterly report of all events, problems and protocol events to the Methods director, coincident with the Investigator's Council meeting.