Multi-Site Research PI Responsibilities

**Multi-center:** Refers to inclusion of at least one site external to MU.

**Overall PI:** The Overall Principal Investigator has the ultimate responsibility for the conduct of the research to ensure subject safety and data integrity.

**Site PI:** The Site Principal Investigators will be listed as co-investigators in the protocol.

**Lead Site:** This is the site of the Overall PI

1. **Overall Principal Investigator (Overall PI)**

   - Act as single liaison with outside regulatory agencies, with MU internal review and oversight committees, and with participating sites, although this may be delegated as appropriate and necessary (e.g. when she/he is out of town).
   - Coordination of the approval of the initial protocol as well as its subsequent amendments. It is the responsibility of the Overall PI to ensure that the sites are using the correct version of the protocol.
   - Identify a study contact.
   - Select qualified sites for participation. The Overall PI must obtain the IRB approval and inform the study sponsor, if applicable, which non-MU institutions will be involved in the study.
   - Ensure all participating site investigators and study staff are trained on the MU SOPs, the conduct of the protocol, study procedures, SAE reporting, and data collection.
   - Monitor progress and oversee the overall conduct of the study at all participating sites.
   - Responsible for the analysis, reporting, integrity and accuracy of data.
   - Inter-institutional agreement / contract, if applicable: This may be required in situations, (1) where financial arrangements are made, or (2) where no other agreements, such as network affiliate agreements, exist between the institutions. The agreement must be reviewed and approved by MU Business Services.
COORDINATION

Protocol

There will be one protocol document and each participating site will utilize that document. The site of the Overall PI is designated as the overall coordinating center (Lead Site) for the study.

Protocol must include:

1) Protocol Front Sheet, and Title page, with name of each participating institution and the site PI.

2) Outline of procedure for study recruitment

3) Outline of data submission schedule and process

4) Section describing how SAEs and Deviations/Violations/Exceptions will be reported from each participating site to the overall Lead Site and to regulatory agencies, if applicable

5) Section describing on-site auditing/monitoring plan for each participating site.

Informed Consent

The Lead Site study team develops the model research consent document that must include a statement that data will be shared with the sponsor or its agents (which may include an outside CRO, medical monitor, Lead Site, DSMB/DSMC and Lead Site’s study team. The consent form must state that data shared with the Lead Site may include subject identifiers (name, date of birth, medical record number), if applicable. The Overall PI or designee is responsible for obtaining copies of each site’s IRB approved consent forms.

Regulatory paperwork

Study initiation: The Overall PI must obtain documentation of IRB approval from each participating site prior to the first subject registration at that site. The Regulatory Binder for the study is kept at the Lead Site. It should be noted that the non-lead sites maintain a non-lead regulatory binder for their reference in managing the trial; however we do not keep duplicate regulatory binders at the sites. The Overall PI or designee at the Lead Site will manage all regulatory documents. The Overall PI is responsible for obtaining the regulatory documents from each participating site during the conduct of the study.

Site Communication

There must be documentation of regular communication with all participating sites. Participation includes all appropriate research staff, including investigators, research nurses and study coordinators. Communication may be by convened meetings, teleconferences or email distributions with the participating sites to update and inform about progress of the research.
Documentation of the study communication regarding protocol/research subject related issues must be filed in the Lead Site regulatory binder.

**SAE Reporting**

All participating sites report SAEs directly to the IRB of record and to the Overall PI. The Overall PI or designee will submit SAEs to the IRB if they meet the IRB SAE reporting requirements. SAEs from non-MU participating sites are reported to the IRB of record and to the Lead investigator.

Reporting unexpected problems involving research (violations/deviations/exceptions):

All participating sites report violations/deviations/exceptions directly to the IRB of record and to the Overall PI. The Overall PI or designee will submit violations/deviations/exceptions to the MUIRB.

**Coordinating Center Protocol**

Provide a full description of the study outlining how the principal investigator will assume responsibility for overall conduct of the study and all aspects of human subject protections across all sites in order to successfully implement the study. This coordinating center protocol may serve as the Operations Manual for the study. The coordinating center protocol should contain the following information:

1) A description of the study including aims, background and significance.
2) A listing of all sites where subjects will be enrolled and/or data/samples will be collected.
   a. Include the number of subjects to be enrolled at each site
   b. Include the names, responsibilities and qualifications of the individual designated as being responsible for the conduct of the research study at each site
   c. If the research will be conducted within or associated with an institutional setting, describe the size and complexity of the non-local institution that will be engaged in the conduct of the research study.
   d. If the research study is funded by a federal agency (e.g., NIH) specify the Federal Wide Assurance number assigned to the site by the Office of Human Research Protection (OHRP) for each non-local site.
   e. Specify the local IRB or other human subject protections entity responsible for the review and approval of research conducted for each non-local site. Include the approval letters from each site.
3) An outline of the organizational structure indicating any committees responsible for administrative duties, subject/data/site monitoring, facilitation of communications, data analysis, etc.
4) Anticipated timeline for start-up of the study, completion of subject enrollment, data analysis and follow-up of subjects.
5) Description and planned frequency of start-up meetings and education or training sessions required of staff at all sites prior to enrollment of any subjects.
6) Description of subject recruitment outlining the inclusion and exclusion criteria.
7) Sample protocol and informed consent documents to be distributed to each collaborating institution for review and approval by their IRB/ethics committee.

8) Copies of clear, concise, case report forms and all documents to be used at all sites for recording of study data needed on subjects including eligibility, demographic and other baseline data, sequential clinical assessments, study drug dosing information, side effects and outcome measures. Provide detailed instructions for completing each item on each form (if needed), any variables that might be encountered and the frequency of collecting the data.

9) Specify how and where the data will be analyzed and who is responsible for the analyses.

10) Describe where and how the data will be stored and for how long. Indicate how the subjects’ confidentiality is protected during the transmission of data to other sites.

11) Definitions and study parameters used in the study; e.g., laboratory values, scores on standard tests, etc.

12) If records or files are to be transmitted via the internet or shipped to another site, describe how the subjects’ confidentiality will be protected.

13) Describe the risks of the study and how adverse events will be managed and how and when they are reported to the coordinating center. Include a copy of the adverse event report forms to be used for reporting adverse event to the coordinating center.

14) Describe the central data and safety monitoring plan that will oversee conduct of the study at all sites. In addition to the information outlined in Appendix L of the IRB Reference Manual, include the following:
   a. The frequency of site monitoring visits, who will conduct them and what will occur at each visit.
   b. Schedule of required telephone contacts/conference calls with collaborating site investigators, if applicable.
   c. Forms or documents to record site visit activities or telephone conferences.
   d. Describe the anticipated potential benefits to study participation.

Additional responsibilities of the Coordinating Center:

1) Submit sample protocol and consent form(s) to all sites in order for them to seek their IRB/ethics committee review approval.

2) **If the study is federally funded**, ensure that all collaborating sites obtain an OHRP Assurance. Submit the Assurance letter, IRB approval letter and IRB-approved consents from each site. Each site’s Assurance letter and the initial IRB approval letter and consent must be submitted to the CIRB (as an expedited modification to the approved Coordinating Center Protocol) when available.

3) **If the study is not federally funded**, provide a letter (on the facility’s letterhead stationery) from the appropriate administrator of each facility. This letter should contain the following information: agreement for this study to be conducted; assurance that it is appropriate to conduct this study on the population involved; assurance of adequate facility capabilities to perform the research as approved by the IRB; and, if applicable, assurance that facility personnel involved in study procedures and data collection have appropriate expertise and will follow IRB guidelines.

4) Ensure that collaborating sites do not enroll subjects until the CIRB has reviewed and given approval to include the additional site.
5) Maintain records of IRB and approval of all protocol and consent forms for all collaborating sites throughout the duration of the study. The principal investigator at the MU site need not submit IRB of the renewal for each site to the CIRB. However, the principal investigator is responsible for ensuring that all modifications and renewals are reviewed and approved appropriately; i.e., modifications are approved prior to their implementation and protocols and consent forms are renewed in a timely manner with no lapse in the renewal.

6) Ensure that any substantive modification(s) to the protocol and/or sample informed consent documents related to risks or alternative treatments by any collaborating site is appropriately justified.

7) Ensure that informed consent is obtained from each subject in compliance with OHRP regulations.

Data Coordinating Center Protocol

A full description of the study outlining how the principal investigator will assume responsibility for collection, storage, management and (if applicable) analysis of data collected on subjects from all sites involved in a multi-site research study. This data coordinating center protocol should contain the following:

1) A brief description of the study including aims, background and significance.

2) A listing of all sites where subjects will be enrolled and/or data will be collected.
   a. Include the number of subjects to be enrolled at each site.
   b. Include the names, responsibilities and qualifications of the individual designated as being responsible for the conduct of the research study at each site. If the investigator responsible for collection or transmission of data is not the principal investigator, provide the name and qualifications of this individual.
   c. If the research study is funded by a federal agency (e.g., NIH) specify the Federal Wide Assurance number assigned to the site by the Office of Human Research Protection (OHRP) for each non-local site.
   d. Specify the local IRB or other human subject protections entity responsible for the review and approval of research conducted for each non-local site. Include the approval letters and the approved consent document from each site.

3) A description of subject recruitment outlining the inclusion and exclusion criteria.

4) Copies of all data collection instruments/forms to be used by investigators at all sites. Provide detailed instructions for completing each item on each form (if needed), any variables that might be encountered, the frequency of collecting the data and how often data are to be sent to the data coordinating center.

5) A description of the responsibilities of the data coordinating center principal investigator with regard to training of staff to ensure accurate, consistent instrument training and data management across all sites. Include specific details of any special equipment needed (e.g., scanners, computers, software) for data transfer.

6) A description of the data to be sent to the data coordinating center, how it will be sent, and how it will be identified to protect the confidentiality of the subjects and respective data. Indicate the specific department/office that will receive the data. Indicate that the investigators at the data coordinating center will review all data for completeness and
indicate who is responsible for obtain missing data or correcting errors and how this will be managed.

7) Details of how long the data will be stored, where it will be stored, who has overall control of the storage area, whether or not the data will be shared with other investigators not listed on the current study, and what will happen to the data should the subject withdraw from the study.

8) If the data coordinating center is also responsible for data analysis, include details of the analysis to be conducted and who will be doing the analysis.

9) A description of the risks of a breach of confidentiality.

10) Details of the local data and safety monitoring plan that will oversee conduct of the study at this site. Include a description of the data and safety monitoring plan that will oversee data collection and data transfer at all sites.

For more information, please access the IRB policy:
http://research.missouri.edu/policies/files/irb_off_site_research.pdf