

APPENDIX P

COORDINATING CENTER GUIDANCE

In a multicenter study, an individual or several individuals are generally responsible for the coordination of all phases of the collaborative research study. This may be limited to the review and oversight of adverse events or data; or may encompass all aspects of administrative, clinical and technical expertise and leadership in the design and coordination of the multi-site collaborative study.

The following information is being offered as guidance for developing a protocol to address the investigator's role and responsibility as the overseer of a coordinating center. There are several different types of coordinating centers as stated above and this document provides detailed information which must be addressed when applicable depending on the type of coordinating center being proposed.

Definitions

Coordinating Center: A **coordinating center** is defined as a site that provides the administrative, clinical and technical expertise and leadership in the design and coordination of the multi-site collaborative research for a multi-center trial. The principal investigator will be responsible for all site monitoring and for the coordination of subject recruitment, screening, enrollment and retention, data and safety monitoring, data collection and analysis, adherence to the protocol-directed procedures and guidelines, and the prompt review, reporting and resolution of adverse events.

Data Coordinating Center: A **data coordinating center** is defined as a site that is responsible for the collection and storage of data collected from all sites involved in a multi-site trial.

Note: If the University of Pittsburgh/UPMC investigator will also be enrolling subjects, it is strongly recommended that the Coordinating Center Protocol be submitted as a separate protocol from the clinical research protocol to be used at the local site.

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. Description of all study drugs, doses, dosing schedule, route of administration and any study endpoints for change the dose or stopping the drug(s). Include the FDA approval status of all drugs and IND number, if applicable.
 9. Description of study devices. Include the FDA approval status and IDE, if applicable.
 10. 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.
 11. Specify how and where the data will be analyzed and who is responsible for the analyses. 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.
 12. Definitions and study parameters used in the study; e.g., laboratory values, scores on standard tests, etc.

13. If tissue or blood samples will be collected, describe how and when they are to be collected, where the analysis will be performed, and how samples will be delivered to the respective laboratories.
 - a. If samples are to be mailed to another site other than where collected, describe who is responsible for delivery of biological sample collection kits to each site. Indicate how the samples will be labeled to protect the confidentiality of subjects.
 - b. Describe how and when lab reports are to be sent to site investigators.
 - c. Describe management of abnormal screening lab results.
 - d. Describe management of abnormal test results during follow-up and throughout the study.
14. If drugs or devices are to be used, describe how they will be delivered to each site and how the dispensing/distribution will be monitored. Include all product inventory or accountability forms.
15. If records or files are to be transmitted via the internet or shipped to another site, describe how the subjects' confidentiality will be protected.
16. 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.
17. 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.
 - e. Include IND number, IDE number and/or Investigator's Brochure, if applicable. For an investigator-initiated study, provide the IND or IDE application.

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 UPitt IRB (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 UPitt IRB has reviewed and given approval to include the additional site.
5. Maintain records of IRB/ethics committee review and approval of all protocol and consent forms for all collaborating sites throughout the duration of the study. The principal investigator at the Pittsburgh site need not submit IRB/ ethics review of the renewal for each site to the UPitt IRB. 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 trial. 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. Please see Appendix L of the IRB Reference Manual for information required.