**Guidance for Investigators Planning the Conduct of a Clinical Investigation at Multi-Center, External Study Sites Under a University-based IND/IDE Application**

1. **Background Information:**

The conduct of a multi-center clinical trial (i.e., a study involving one or more external study sites) under a University-based IND or IDE application is only permitted upon satisfaction of the requirements set forth in this guidance. Faculty seeking to conduct a multi-site clinical trial under a University-based IND or IDE must have an acceptable plan to meet the Sponsor’s obligation, as outlined in the federal regulations, to routinely monitor the progress and the conduct of the study at each site and to manage the reporting requirements between site investigators and the Sponsor of the IND or IDE application. As outlined in Section II of this document, trials of this nature require in-depth planning, adequate funding to support the Sponsor’s duties, as well as a formal application describing how Sponsor Responsibilities will be fulfilled. The application and required attachments must be submitted to IND and IDE Support (IIS) for preliminary review and after comments are addressed will then be provided to the Deputy Director of the Office for Research Protections (ORP) and the Director of Education and Compliance Support for Human Subjects Research (ECS-HSR) for subsequent approval**. Note that sponsors who are approved to conduct multi-center research under an FDA-accepted IND/IDE application will be required to complete a face-to-face meeting with ECS-HSR leadership prior to study implementation**.

In order to decrease risk to the University of Pittsburgh Sponsor-Investigator, external study sites should be highly encouraged to each submit their own IND or IDE application incorporating the common clinical trial protocol. By using this approach, Sponsor and Investigator responsibilities and associated regulatory compliance liabilities are assumed independently by each of the external study sites rather than globally by the University of Pittsburgh. The University of Pittsburgh study site can serve as the coordinating center for the multi-center clinical protocol.

**If it is not possible for each participating site to submit their own IND or IDE application, it is highly recommended that enrollment begin at the University of Pittsburgh site. Upon completion of the first monitoring visit without issues, then the other sites may be activated.**

1. **Requesting Approval to Include *External Study Sites* Under a University-based IND or IDE Application**

To request approval to conduct a study at an external study site, the attached application and required attachments must be completed and submitted to the IIS. Reviewers may approve an application, may ask for additional information or for changes in the monitoring plan, or may reject the request for failure to meet the requirements of this Guidance. Any request that is rejected may be appealed to the Institutional Official, whose decision shall be final.

The application will require detailed information on the following:

1. General clinical trial information
2. Description of procedures to meet Sponsor’s responsibilities
3. Institutional Review Board oversight
4. External site activation procedures
5. Detailed monitoring plan

Clinical trial monitoring provides assurance for the following:

* The clinical trial is being conducted in accordance with the current version of the clinical trial protocol and applicable regulations and policies
* The rights, safety and welfare of the research subjects are being adequately protected
* Adequate and accurate case histories are maintained and that these documents record all observations and other data pertinent to the evaluation of the investigational drug or device; are contemporaneous and original; and that information in the source documents is accurately captured on the case report form
* The investigational drug or device is being adequately controlled
* The research records are being maintained securely for the retention period specified by FDA regulations, the University of Pittsburgh, and the funding entity.

**As monitoring is critical to the overall conduct of a clinical trial, it is highly recommended to retain the services of an independent monitor such as the Center for Clinical Trials and Data Coordination (CCDC) or a Contract Research Organization (CRO). All questions related to the detailed monitoring plan within the application require response. If responses are inadequate or incomplete the IIS will require revision before forwarding for formal review and approval.**

1. A copy of the IND/IDE Sponsor’s Investigator’s Brochure or Device Description/Report of Prior investigations, which will be distributed to each of the external study sites. The document should contain the following information:
	1. A brief description of the investigational drug or investigational device; to include, for investigational drugs, the structural formula and the formulation.
	2. A summary of the safety evaluations of the investigational device in animals and, to the extent known, in humans; or a summary of the pharmacokinetics, pharmacological and toxicological effects of the investigational drug in animals and, to the extent known, in humans.
	3. A summary of information relating to the safety and effectiveness of the investigational device or investigational drug in humans obtained from prior clinical studies.
	4. A description of possible risks and side effects to be anticipated based on prior experience with the device or drug under investigation or with related devices or drugs; and of precautions or special monitoring to be done as part of the experimental evaluation or use of the investigational device or drug.
2. A copy of the Case Report Form(s) that will be utilized for the planned clinical trial and if electronic case report forms will be used, a certification that the electronic data capture system is 21 CFR Part 11 compliant.
3. If applicable, instructions for the collection, preparation, and shipping of biological specimens.
4. If a CRO will be used, the Scope of Work that will be included in the contract.
5. External study site procedures – because the collection of standard operating procedures is a Sponsor responsibility, it is not a requirement to provide IIS with external site procedures. However, IIS strongly encourages the sponsor to collect at a minimum a formalized procedure for drug accountability and confirmation that the external site will not initiate protocol changes without prior sponsor approval.
6. **Maintaining the Multi-Center Approval**

Once an application has been approved, no changes may be implemented without revising the application and submitting for review and approval by the ECS-HSR. Examples of changes that require a revision to the application include:

* Addition of sites
* Change in external site PI
* Change in any aspect of the detailed monitoring plan

External monitoring visit reports should be provided to the participating sites within 2-4 weeks of the conclusion of the visit. The site Principal Investigator is required to sign the report. To ensure Sponsor review of the report, provide proof of his/her review. The Sponsor’s wet signature, electronic signature, or e-mail confirmation is acceptable. Within 6-8 weeks of the conclusion of the visit, a copy of the signed external monitoring visit report must be provided to IIS by e-mail at IIS@pitt.edu.

Sponsors will receive a monthly reminder from IIS to submit external monitoring visit reports and responses to monitoring visit reports.

If it is discovered that monitoring of the external site(s) is not being conducted as outlined in the detailed plan, ECS-HSR may require a suspension of additional accrual until issues are resolved.

1. **Single IRB of record**

Should a single IRB of record be used, it is highly recommended that the University of Pittsburgh IRB act in that capacity. The IIS team assists Sponsors on protocol amendments requiring prospective notification to FDA; therefore, it is important that the IIS be notified about modifications submitted to the IRB. In the case an external IRB will act as the single IRB of record, arrangements will need to be made to ensure IIS is notified of protocol modifications.