1. **Executive Summary**

The University of Pittsburgh is committed to supporting collaborative research among investigators conducting Food and Drug Administration (FDA) regulated research. This guidance document outlines the requirements, expectations, and considerations in planning the conduct of an FDA-regulated clinical trial at external sites. Sections include:

* Application Requirements
* Consideration of Number of Participating Sites
* International External Sites
* Maintaining the Multi-Center Application

To request permission to conduct a multicenter trial, a formal application is required.

1. **Applicability**

This guidance applies when:

* The Investigational New Drug (IND) or Investigational Device Exemption (IDE) application related to the study is sponsored by a University of Pittsburgh faculty member; and
* The FDA-regulated clinical trial is conducted at multiple sites (with one or more sites external to the University of Pittsburgh or UPMC campuses).
1. **Application Requirements**

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. Sponsors seeking to conduct a multi-center clinical trial under a University-based IND or IDE must have an acceptable plan to meet their 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. 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.

To conduct a study at an external study site, the [Application to Conduct a Multicenter Trial](https://www.ecshsr.pitt.edu/sites/default/files/2_multicenter_application_final_v.1.4_11.25.20.docx) must be completed and required materials submitted to IND and IDE Support (IIS). All questions related to the detailed monitoring plan within the application require a response. If responses are inadequate or incomplete revisions may be required before forwarding for formal review. The Assistant Vice Chancellor of the Office for Research Protections (ORP) and the Director of Education and Compliance Support for Human Subjects Research (ECS-HSR) may accept an application, may ask for additional information, or request changes to the plan. For studies where the Sponsor and reviewers are unable to develop and reach consensus on the acceptability of the plan, the matter will be referred to the Dean’s office of their school for adjudication.

The application will require detailed information on the following:

* General clinical trial information
* Description of procedures to meet Sponsor’s responsibilities
* Institutional Review Board oversight
* External site activation procedures
* Detailed monitoring plan

Note: As monitoring is critical to the overall conduct of a clinical trial, it is highly recommended to retain the services of a qualified independent monitor such as a consultant or Contract Research Organization (CRO). In support of this recommendation, the University has entered into Contracted Suppliers Agreements with multiple organizations as an option for retaining research services. Please refer to this website for contact information <https://www.ecshsr.pitt.edu/multicenter-guidance>.

* If a CRO or other outside organization will be used, please provide the Scope of Work that will be included in the contract.
* A copy of the IND/IDE Sponsor’s Investigator’s Brochure (IB) or Device Description/Report of Prior investigation. As the Sponsor of a multi-center clinical trial, per FDA regulations, an (IB) or Device Description/Report of Prior investigations is required to be provided to all participating Investigators.
* A copy of the paper Case Report Form(s) that will be utilized for the planned clinical trial. Alternatively, if an electronic data capture (EDC) system other than the validated instance of REDCap is being used, electronic versions of the CRFs need to be provided. Note that any other EDC system must be validated for 21 CFR Part 11 compliance and approved by the Health Science’s Information Technology (HSIT) group.
* If applicable, instructions for the collection, preparation, and shipping of biological specimens.
1. **Consideration of Number of Participating Sites**

Appropriate resources are needed to conduct multi-center clinical trials. Only those applications that demonstrate a robust plan with dedicated infrastructure for site monitoring for compliance, communications, and data and safety oversight will be considered.

The IND/IDE Sponsor should take into consideration the level of support that can be provided by the ECS-HSR when planning the conduct of the multi-center clinical trial so that alternative arrangements can be made to ensure compliance with federal regulations.

Refer to the table below.

|  |  |
| --- | --- |
|  | **Services Provided by the ECS-HSR** |
| **Number of External Sites** | **Review and Submission of FDA Materials1** | **Monitoring of the University of Pittsburgh Site**  | **Monitoring of the External Sites** | **Review of External Monitoring Visit Reports by Compliance Activity Reviews Subcommittee (CARS)** | **Provide Education and Guidance on FDA Regulations and GCP** |
| 1-5 (Small) | Yes  | Yes | No | Yes | Yes |
| 6-15 (Medium) 2 | TBD3 | TBD3 | No | TBD3  | Yes |
| Greater than 15 (Large)2 | No4  | No4 | No | No4 | Yes |
| 1. Commercial INDs cannot be submitted to the FDA by IIS.
2. The multicenter application must still be completed and submitted for review and acceptance.
3. Determined upon discussion between the Sponsor and ECS-HSR.
4. Unless an exception is granted.
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1. **International External Sites**

International sites are not permitted to be included as participating sites under a University-based IND or IDE. International sites must identify a qualified Sponsor-Investigator and submit their own application, including the multicenter clinical protocol, to their appropriate regulatory agency.

1. **Maintaining the Multi-Center Application**

To maintain compliance with FDA regulations, any changes to the application must be submitted to and prospectively reviewed prior to implementation. These include but are not limited to:

* Addition of sites
* Change in PI at any site
* Significant changes in the detailed monitoring plan, (e.g., change in CRO).

For those trials where external monitoring reports are required to be reviewed by the CARS, external visit reports should be provided to the participating sites within 2-4 weeks of the conclusion of the visit. The site Principal Investigator and the Sponsor are required to sign the report (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.

Concerns reviewed at the CARS meetings may be discussed with the IRB and communicated to the Sponsor, as needed.

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