***Protocol Development, Finalization, and Maintenance***

1. **PURPOSE**

To define the process for the development, finalization, and maintenance of the clinical research protocol in order to facilitate proper conduct, reporting, and external review of a clinical trial.

**(MANDATORY LANGUAGE)**

1. **SCOPE**

This Standard Operating Procedure (SOP) applies to the development, finalization, and maintenance of clinical trial protocols written by University of Michigan researchers. It does not include protocols written or managed by external sponsors, Clinical Research Organizations (CROs) or non-UM researchers serving as the Principal Investigator for a clinical trial.

**(MANDATORY LANGUAGE)**

*[Optional: Insert any additional details necessary to further define the scope of this SOP.]*

1. **POLICY**

This Standard Operating Procedure supports the Good Clinical Practices guidelines established by the International Conference on Harmonization (ICH), 4.4.1: *Before initiating a trial, the investigator/institution should have written and dated approval/favourable opinion from the IRB/IEC for the trial protocol.*

FDA Regulation ☐ N/A

*[If this SOP is not intended for FDA regulated clinical trials, check the N/A box]*

Per CFR Part 312Investigational New Drug, Sec. 312.23:

*(a) A Sponsor who intends to conduct a clinical investigation subject to this part shall submit an “Investigational New Drug Application” (IND) including, in the following order...(6) Protocols. (i) A protocol for each planned study...*

## Per CFR Part 812 Investigational New Device, Sec. 812.25:

*The investigational plan shall include, in the following order:*

*(a) Purpose. The name and intended use of the device and the objectives and duration of the investigation.*

*(b) Protocol. A written protocol describing the methodology to be used and an analysis of the protocol demonstrating that the investigation is scientifically sound...*

**Additional Regulations or Policies ☐ N/A**

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*[Optional: Insert any additional project, department, sponsor, institution, state or federal policies that apply]*

1. **DEFINITIONS**

CLINICAL TRIAL: A prospective study involving human subjects designed to answer specific questions about the effects or impact of particular biomedical or behavioral interventions; these may include drugs, treatments, surgical procedures, devices, behavioral or nutritional strategies. Clinical trials are typically conducted by investigators who have entered into an agreement with a sponsor to conduct the study. For clinical drug and device trials, investigators agree to conditions regarding the conduct of the study outlined by FDA.

INSTITUTIONAL REVIEW BOARD (IRB): An independent body constituted of medical, scientific, and non-scientific members that is responsible for ensuring the protection of the rights, safety, and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trial protocol and amendments and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects.

INVESTIGATIONAL DEVICE EXEMPTION (IDE): Approval by FDA for investigational device exemption (IDE) permits a device that otherwise would be required to comply with a performance standard or to have premarket approval to be shipped lawfully across state and international boundaries for the purpose of conducting investigations of that device. (FDA) Most devices under investigation should have an IDE.

INVESTIGATIONAL NEW DRUG (IND): A request for authorization from the Food and Drug Administration (FDA) to administer an investigational drug or biological product to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug or biological product that is not the subject of an approved New Drug Application or Biologics/Product License Application.

PRINCIPAL INVESTIGATOR (PI): The lead scientist or engineer for a particular well-defined science (or other research) project, such as a laboratory study or clinical trial.

PROTOCOL: A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents.

**(MANDATORY LANGUAGE)**

*[Optional: Insert any additional definitions for technical or special terms used within the Standard Operating Procedure that may not be familiar to the lay reader]*

**Note:** Many of the definitions above were obtained from the IRBMed Glossary. These definitions were current as of DD-Mon-YYYY- and are subject to change. Please see the [IRBMed Glossary](http://medicine.umich.edu/medschool/research/office-research/institutional-review-boards/guidance/glossary) for the most current definitions and additional guidance.

**(MANDATORY LANGUAGE)**

1. **ROLES AND RESPONSIBILITIES**

**Principal Investigator/Designee**

The Principal Investigator (PI) is responsible for overseeing the development, finalization, and maintenance of the research protocol document. The Principal Investigator shall be responsible for the following activities:

* Articulates clearly the research questions that are to be addressed in the trial
* Assesses protocol feasibility
* Provides protocol content
* Engages a multi-disciplinary team of contributors to address statistical, operational and other considerations specific to the research
* Solicits feedback from participating clinical sites (when applicable), research team members, etc. to promote effective execution of the research
* Approves the final protocol
* Ensures the final protocol is submitted to the sponsor as well as appropriate funding and regulatory agencies
* Revises the protocol as necessary
* Confirms approval is granted by the sponsor, as well as funding and regulatory agencies prior to the conduct of the research
* Initiates, reviews and approves protocol amendments
* Ensures protocol amendments are submitted to appropriate funding and regulatory agencies as needed
* Confirms approval is granted by sponsor as well as funding and regulatory agencies prior to the finalization of a protocol amendment

**(MANDATORY LANGUAGE)**

*[Optional: Insert any additional details regarding the responsibilities of the Principal Investigator/Designee]*

**Statistician(s)/Designee**

An individual filling the role of Statistician is responsiblefor contributing to the design of the clinical trial and ensuring that the protocol accurately describes the type and quantity of data, and analysis necessary to address the research questions. The Statistician or Designee shall be responsible for the following activities:

* Contributes to the research design
* Provides protocol content, and provides feedback from a statistical perspective
* Ensures the appropriate data and data collection time points are incorporated into the protocol for meaningful data analysis

**(MANDATORY LANGUAGE)**

*[Optional: Insert any additional details regarding the responsibilities of the Statistician/Designee]*

**Protocol Contributor(s)/Designee**

An individual filling the role of Protocol Contributor participates in the development of a draft protocol. The Protocol Contributor or Designee shall be responsible for the following activities:

* Supplies protocol language related to a specific area of expertise
* Reviews the draft protocol and provides timely feedback
* Contributes to and/or reviews protocol amendments as needed

**(MANDATORY LANGUAGE)**

*[Optional: Insert any additional details regarding the responsibilities of the Protocol*

*Contributor/Designee]*

**Protocol Author/Facilitator/Designee**

An individual filling the role of Protocol Author/Facilitator is responsiblefor coordinating the development and maintenance of the protocol document. The Author/Facilitator or Designee shall be responsible for the following activities:

* Selects protocol template, format, etc. based on sponsor, funding agency or departmental requirements, when applicable
* Recruits qualified protocol reviewers to provide feedback on the scientific, clinical, statistical, operational and technical merits of the draft protocol.
* Manages protocol drafts and circulates for review and feedback
* Revises protocol based on agreed upon recommendations
* Documents approval of the final, first version of the protocol
* Initiates the review and approval process to address protocol amendments
* Amends the protocol document as needed
* Maintains document version control
* Securely stores retired and current, approved versions of the protocol

**(MANDATORY LANGUAGE)**

*[Optional: Insert any additional details regarding the responsibilities of the Protocol Author/Facilitator/Designee]*

**Protocol Reviewer(s)/Designee**

An individual filling the role of Protocol Reviewer evaluates the final draft of a research protocol for its practical application in a research setting. The Reviewer or Designee shall be responsible for the following activities:

* Identifies protocol language that may be confusing or ambiguous
* Reviews the processes and procedures described in the protocol to ensure they can be successfully implemented
* Reviews protocol amendments as needed

**(MANDATORY LANGUAGE)**

*[Optional: Insert any additional details regarding the responsibilities of the Protocol Reviewer(s)/Designee]*

**Additional Roles and Responsibilities**  **☐ N/A**

*[Optional: Insert any additional role(s) and responsibilities that apply to this SOP]*

1. **PROCEDURE**

**Protocol Development**

*[Describe the process used to draft a protocol]*

**Protocol Finalization**

*[Describe the process used to review, revise, and approve a protocol]*

**Protocol Maintenance**

*[Describe the process for initiating and writing an amendment to the protocol]*

*[Describe the process used to review, revise and approve a protocol amendment]*

*[Describe the process for version control of the protocol]*

*[Describe the process for storing and accessing current, and retired versions of an approved protocol]*

**Additional Procedures** **☐ N/A**

*[Optional: Insert any additional relevant procedures. Provide enough detail to ensure the procedure is consistently carried out, without providing so much detail that violations occur due to normal or expected variations in the work.]*

1. **REFERENCES**

Food and Drug Administration (FDA):

<http://www.fda.gov/Drugs/default.htm>

FDA Code of Federal Regulations Title 21:

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=7.55>

International Conference on Harmonisation (ICH):

<http://www.ich.org/>

ICH Guideline for Good Clinical Practice:

<http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf>

**(MANDATORY LANGUAGE)**

*[Optional: Insert any additional SOP references]*

1. **APPENDICES**

**Appendix A:** Protocol Approval Form **☐ N/A**

**(MANDATORY LANGUAGE)**

*[Optional: Insert any additional SOP appendices]*