National Institute of Neurological Disorders and Stroke

NINDS Standard Operating Procedure

NINDS SOP 9

SOP Title: CTU Protocol Development Meeting

Version: 2.0

Approval Signature: Avindra Nath -S

Digitally signed by Avindra Nath -S
Date: 2020.12.01 16:01:09 -05'00'

NINDS Clinical Director

Date of Approval: 11/24/2020

Date of Implementation: 12/01/2020

Previous Versions: 12/12/2014

Table of Contents

1. PURPOSE

This SOP describes the process for conducting a Protocol Development Meeting (PDM) between the NINDS Clinical Trials Unit (CTU) and Investigators for protocols conducted within the NINDS Intramural Research Program.

The purpose of the Protocol Development Meeting (PDM) is to:

1. Provide investigators with collaborative feedback and guidance on a planned clinical trial during the protocol development phase.
2. Reduce the volume of potential stipulations following both SRC (Scientific Review Committee) and IRB (Institutional Review Board) reviews, thereby accelerating the process toward protocol approval and study implementation.
3. Identify critical aspects of protocols early in their development which might need additional consideration (e.g., requiring external expertise, etc.).
4. Ensure quality standards and compliance with NINDS, NIH and FDA regulations.
5. Assist and educate investigators in training at NIH on methodological and regulatory aspects of clinical trials conducted at NINDS.
6. Provide editorial comments on protocol documents prior to SRC and IRB submission.

2. PROCEDURES

2.0 Target Audience

Principal Investigators (PIs) and Lead Associate Investigators (LAIs) of planned clinical trials at NINDS.

2.1 Types of Protocol Development Meetings (PDM)

2.1.1 Full PDMs

- Intended to help investigative teams develop a protocol with particular attention to institutional and regulatory requirements (policy) and operational goals.

2.1.2 Focused PDMs

- Ideal for trials where the investigative team has a specific question or wants a narrow field of review (e.g., regulatory or optimization question).

2.1.3 NSR Determination

- Required for any planned clinical trial or clinical research studies that potentially include an NSR (Non-Significant Risk)device or software.
    - An NSR determination can be obtained concurrently with SRC review but must occur prior to IRB submission.
    - NINDS will provide a Sponsor's determination letter (i.e., exempt, NSR or SR [Significant Risk]) and will make recommendations accordingly to the PI and IRB.

2.2 Identifying Protocols to be scheduled for a Protocol Development Meeting

- All planned clinical trials and clinical research studies are eligible for a PDM with the CTU.
- PDMs are required for the following types of protocols:
  - NINDS Sponsor FDA-regulated clinical trials (all potential Investigational New Drug [IND] and Investigational Device Exemption [IDE] trials).
  - Multi-center clinical trials.
  - Clinical Trials involving external sponsors or other contractual party(ies).
  - Clinical Trials involving a Fellow as PI or LAI.
- For clinical research studies other than *clinical trials* per NIH definition, a PDM may also be requested.

2.3 Timeline

The recommended time-point for a PDM to take place is after conception of the outline of the research project, before a first full protocol draft is composed.

2.4 Protocol Development Meeting

2.4.1 Meeting Format

- **In-Person**
  - Required for:
    - NINDS Sponsor FDA-regulated clinical trials (all potential IND and IDE trials)
      - Except NSR device determinations
    - Multi-center clinical trials
    - Clinical Trials involving a Fellow as PI or LAI
  - Optional for any other type of PDM

- **Discussion Guide Only**
  - Required for:
    - Clinical Trials involving external sponsors or other contractual party(ies), if an In-Person meeting was not completed.
  - Optional for:
    - Focused PDMs
    - NSR Determination
    - Full PDM, except as listed as “In-Person, Required for:”

2.4.2 Scheduling a PDM

- The investigator (PI or LAI) can schedule a PDM with CTU at any time during the protocol development phase.
- The SRC, IRB, or the Clinical Director may refer investigators to the CTU for protocol development assistance.
- Individual CTU members working with the investigators may recommend a PDM at any time during protocol development.

- The scope of a PDM can be the entire protocol or specific aspects of a protocol.
- The meeting between CTU and investigators for a new clinical trial should generally be scheduled after the research group has developed a synopsis of the trial, ideally before the first full protocol draft.
- Before a meeting is scheduled, the investigator will need to submit a brief, structured protocol synopsis (see Appendix A) and proposed protocol procedure plan (see Appendix B) to the CTU. Draft versions of the protocol and consent form may also be submitted but are not required.
- The CTU will review the proposal internally before the PDM.
- The CTU aims to schedule a meeting or return a Discussion Guide within 2 weeks after the initial PDM request.

Investigators should submit a request for a PDM via the CTU SharePoint site at:
https://share.ninds.nih.gov/sites/CTU/SitePages/Protocol%20Development%20Meeting.aspx

2.4.3 In-Person Meeting Logistics

- The CTU Director or designee will chair the PDM.
- The format of the PDM will be an open meeting. Depending on the topic, additional experts outside the CTU and the clinical research study staff might be invited to the PDM.
- The meeting duration will be no longer than 1 hour, with the following items included in the agenda:
    - **Protocol Presentation -** by the investigator (10 min). This structured presentation should contain a brief scientific background, study hypothesis, population selected, as well as study procedures including interventions, inclusion/exclusion criteria, outcome measures, and the analysis and monitoring plan.
    - **Protocol Discussion -** (40 min) will be conducted in a structured manner, with comments and questions to be discussed (but not limited to) the following topics:
        - Scientific Merit/Background and Rationale
        - Objectives
        - Design
        - Subject Eligibility Criteria
        - Disease Community Engagement
        - Statistical Analysis and Sample Size
        - Data monitoring
        - Multi-Center Studies
        - FDA regulated studies requirements
        - Principal Investigator Qualifications
        - Plan to register protocol and report outcome data in clinicaltrial.gov
        - General comments
    - **Wrap-Up** - (10 min) will be a recap of main points of the discussion with summary recommendations. The next action items will be agreed upon.

NOTE: The Discussion Guide contents will mirror the points of the Protocol Discussion as listed above

2.4.4 Meeting Follow-Up

- A review report including a summary of the main points identified during the meeting will be generated by the CTU following the meeting and shared with the investigators.
- After the PDM, investigators should proceed with the development of their protocol in consideration of Sponsor required changes, as needed, and any additional recommendations.
- Investigators may consult with individual CTU members throughout the protocol development process.
- After completion of the final protocol draft, and no later than 1 week before the SRC submission deadline, the final version of the protocol documents (e.g., protocol, informed consent form, etc.) may be resubmitted to the CTU for review. In addition to any recommendations based on the final protocol-review, CTU will offer editorial assistance with language, inconsistencies, template-adherence, etc.

3. QUALITY IMPROVEMENT

- The CTU will track each stage of the protocol's process, from first contact with the CTU to IRB approval ("core" phase of protocol development), and beyond.
- Measures of efficiency of the CTU process will be documented and include time from PI request to CTU meeting, CTU meeting to SRC, IRB, FDA submissions and approval, and time to recruiting the first subject.
- Regular feedback regarding the CTU from investigators, SRC, IRB, as well as Institute leadership will be obtained, and processes modified, if necessary.

NOTE: definitions are available on the "Glossary" page of the CTU intranet.

4. APPENDICES

- Appendix A: Protocol Synopsis Template
- Appendix B: Schedule of Visits

APPENDIX A: PROTOCOL SYNOPSIS TEMPLATE

PI _____
LAI _____

Protocol Title	
Study Objective, Clinical Phase	
Background/ Rationale	
Study Population	
Primary Outcome Measure	
Secondary and Exploratory Outcome Measures	
Study Design and Duration	
Inclusion Criteria	
Exclusion Criteria	
Screening/ Recruitment	
Concomitant Medications/ Therapies	
Intervention, Control	
Investigator(s)	
Study center(s)	
Safety Considerations and Monitoring	
Sample Size and Power	
Analysis Plan	
Key References	

APPENDIX B: SAMPLE SCHEDULE OF VISITS TEMPLATE

	VISITS								
PROCEDURES									