PROTOCOL INSTRUCTIONS

The objective of the PCRC protocol instructions and template is to assist you in creating a comprehensive study protocol that describes the study rationale, study objective(s), design, methodology, statistical considerations, organization and ethical considerations.

As you read through this protocol, please respond to all text in blue. Required PCRC language is in black.

A study protocol should follow the format described below.

Title	
Protocol Number	*Protocol number will be formulated by PCRC Operations*
Sponsor	
Principal Investigator	
Lead Statistician	
Coordinating Centers	
Protocol Version Release Date	

Protocol Synopsis (one page)

High-level one-page document including the following:

Study Title

Specify the full title of the study.

Study Design

If you are using an intervention, please outline the intervention using the PICOT framework (see below). Comment on the feasibility of implementing the intervention across a wide range of geographically dispersed settings. *If you will not use an intervention, describe the study design and outcome variables.*

PICOT:
P: Population (i.e. target group for the intervention)
I: Intervention (e.g. for an observational study, identify the exposure)
C: Comparison (e.g. usual care, attention control, etc.)
O: Outcome (e.g. primary and secondary)
T: Timeframe (i.e. duration of follow-up)

Significance

Briefly describe the need, relevance and priority for the study.

Study calendar

Create a study calendar showing milestones – detail of when which measures will be collected (e.g. enrollment begins, enrollment ends, analysis, manuscripts, etc.). A schematic diagram is recommended; see Appendix sample 3.

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1 Background and Rationale (one page)

Provide the scientific or scholarly background and rationale for the research based on existing literature and justification for undertaking the study. **Please note:** When the study involves a drug or other potentially unsafe intervention, a description of the biological rationale and known safety studies should be included. Discussion should include relationship with PCEOL research objectives.

2 Aims and Objectives

Describe primary and secondary aims/objectives using neutral wording (e.g. to compare the effect of treatment A versus B on outcome X), or hypotheses (e.g. the predicted effect of the intervention on the trial outcomes). All primary and secondary aims/objectives should be included. List relevant hypotheses (under each aim/objective) if applicable.

3 Study Design

Describe the study design and indicate how the design will achieve the goal(s) of the study. Please describe study groups/arms, if applicable, and for more complex study deigns, include a table/diagram/flow chart.

3.1 Study population

Indicate from where the study population will be drawn, including when, where, and how potential participants will be recruited.

3.1.1 Eligibility criteria

Outline inclusion and exclusion criteria for participants. This can include demographic information; type of severity of health condition; comorbidities; previous or current treatment; diagnostic procedures; pregnancy; or relevant considerations. Please include your intention to enroll all participants regardless of sex or race and to analyze the results of your study by sex and/or racial differences if appropriate.

3.1.2 Enrollment Details

Particular attention to how recruitment will take place with a vulnerable population, including, but not limited to, cognitively impaired persons at the end of life, etc. should be outlined.

3.2 Study measures and outcomes

Describe and explain the rationale for the choice of outcomes: primary, secondary and other outcomes as applicable. Please incorporate PCRC data elements and measures. For those that are ***not*** part of the PCRC data dictionary, provide rationale for including them.

3.2.1 Study events description

Describe study events (schema/diagram) and identify total participant length of time.

3.2.2 Exposure/Outcome measures and instruments

Describe plans for assessment and collection of exposure variables (when applicable), including outcome, baseline, and other study data, and including any related processes to promote data quality.

3.2.3 Data management

Outline plans for data entry, coding, and storage, including any related processes to promote data quality (e.g. double data entry). Please detail all data security details in Section 5.3.

3.3 Interventions (when applicable)

Describe intervention(s) for each group in detail, including how and when they will be administered. Also define who will be masked after assignment to interventions and how this will be ensured. If masked, outline circumstances under which unmasking is permissible, and the procedure for revealing a study participant's allocated intervention during the study.

3.3.1 Drug Administration (if applicable)

If the study involves drug administration, each drug product should be listed. Subsections to include: formulation, packaging, labeling, preparation, administration, storage, dosage and accountability procedures.

3.3.2 Randomization (if applicable)

Describe randomization procedures, if applicable. If a control group is used, include a rationale for the choice of control (e.g. placebo, no treatment, active drug).

4 Statistical and Data Handling

4.1 Statistical considerations

Describe the statistical methods for analyzing primary and secondary outcomes.

4.1.1 Sample size

Provide an estimated number of participants needed to achieve study objective(s) and how it was determined, including clinical and statistical assumptions supporting any sample size calculations.

4.2 Management of data

4.2.1 Source documents [Site data management]

Source documents are the original records of participant information. The ICH-GCP guidelines define source documents as "original documents, data, and records." Source documents may include study specific Data Collection Tools (DCTs). DCTs are instruments/tools used to collect/document the requested data at each of the sites involved in the project. The DCTs contain those variables listed in this protocol. Examples of source documents include: all medical and laboratory records, X-rays, subject diaries, pharmacy records, etc. Examples of DCTs include subject diaries, research files, surveys and specific research worksheets used to document key research data elements. Consent forms (if applicable) and an enrollment log is kept at the sites to know which participants are being followed and to ensure accurate enrollment and comply with local IRB regulations. Source documents/DCTs remain on site and are not submitted/transferred to the central coordinating center.

4.2.2 Data capture [Central data management]

The site personnel enters the data for this study into the PCRC Electronic Data Capture (eDC) system. The system to be used for this study is _____. The IT platform for each study is mutually decided the PI and PCRC Informatics/Data Management team. This occurs during protocol development. Once decided, details of that IT platform will be inserted into the protocol.

4.2.3 Record retention

- Any study records (including DCTs, etc.) will be retained in the site's research record for 10 years after the study is completed in accordance with Good Clinical Practice guidelines. At that time the research information will be destroyed by each site's research document destruction rules/regulations.
- Any research information already included in medical records will be kept indefinitely.
- The de-identified data that is collected and entered will remain in the central database indefinitely. All future data analysis is performed on de-identified data in the PCRC central database.

4.2.4 Data sharing

The PCRC fully supports the Final NIH Statement on Sharing Research Data and will provide assistance to all investigators and personnel for compliance. Consistent with OMB Circular A-110 and subsequent NIH Grants Policy Statements, the PCRC will provide access to all de-identified data collected as part of PCRC-supported

investigations, insofar as access is consistent with IRB/CHR rules, local, state, and Federal laws and regulations, and the HIPAA Privacy Rule.

5 Ethics and Dissemination

5.1 Ethics and regulatory compliance

Describe plans for seeking research ethics committee/institutional review board (REC/IRB) approval.

5.2 Confidentiality

Detail how personal information about potential and enrolled study participants and loved ones, (if applicable) will be collected, shared, and maintained in order to protect confidentiality before, during, and after the study

5.3 Data security

Describe research data security plans including location of data, who will have access to the final dataset and outline plans for investigator(s) and sponsor(s) to communication study results, plans to protect PHI, server and data transfer security, etc.

6 Safety Considerations

6.1 Risks

Outline the risks, discomforts or inconveniences to the participants considering physical, social, psychological, economic and legal impacts. Whenever possible, cite relevant published research or data. Describe how risks above will be minimized (e.g. monitoring, trained personnel who can respond to emergencies, or coding of data to ensure confidentiality). And provide definitions of Adverse Events (AE) and outline procedures for collecting, assessing, reporting and managing AEs.

6.2 Benefits

Describe the possible benefits study participants may experience (e.g., benefits to society of the knowledge gained). If there is no direct benefit, that should be stated. **Please note**: compensation is not a benefit.

6.3 Monitoring

ALL clinical trials supported by NINR should have some form of monitoring based on a data and safety-monitoring (DSM) plan. The level of monitoring should commensurate with the 1) size and complexity of the trial; 2) level of risk to the study participants and 3) phase of the trial.

NOTE: a DSMB plan is required for Phase III clinical trials involving interventions that entail potential risks to participants (multi-site). All DSM plans are subject to IRB review and approval.

DSM plans should address the following essential elements:

A. Monitoring entity or who will monitor the study—e.g., PI, independent safety monitor, data and safety monitoring board (DSMB) or study monitoring committee (SMC). The roles and responsibilities of everyone on the team involved in monitoring to include entity responsible for submitting necessary reports to NINR.
B. Procedures for 1) monitoring study safety to include monitoring schedule, auditing selected cases for compliance with IRB requirements, conformance with informed consent requirements, verification of source documents, and investigator compliance; 2) minimizing research-associated risk, and 3) protecting the confidentiality of participant data.
C. Procedures for identifying, reviewing, and reporting *adverse events* and *unanticipated problems* to the IRB, NINR, and FDA (if applicable). If applicable, the type and number of events that would halt accrual and would generate a review of eligibility, monitoring, assessments, intervention, and how the resumption of accrual would occur. For further information, see: *NIH Guidance on Reporting Adverse Events to Institutional Review Boards for NIH-Supported Multicenter Clinical Trials (http://grants1.nih.gov/grants/guide/notice-files/not99-107.html)
   * OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events (http://www.hhs.gov/ohrp/policy/advevntguid.html)
D. For multi-site studies, procedures to ensure compliance with the monitoring plan and reporting requirements across study sites.
E. An assessment of external factors or relevant information (i.e., developments in the literature, results of related studies) that may have an impact of the safety of participants or on the ethics for the research study.
F. The advanced plans for interim and/or futility analysis.

References

Include all relevant references.

Appendices

See samples of suggested appendices on following pages.

Sample Appendix 1: Study Glossary

Provide a study glossary of common terms and expressions used in your protocol, similar to the example below.

Term	Definition
AE	Adverse event
AHRQ	Agency for Healthcare Research and Quality
AKPS	Australia-modified Karnofsky Performance Status Scale
AT	As Treated
CI	Confidence interval
CK	Creatine kinase
CRC	Clinical research coordinator
CRF	Case report form
CTCC	Clinical Trials Coordinating Center
DSMB	Data Safety Monitoring Board
ESAS	Edmonton Symptom Assessment System
HIPAA	Health Insurance Portability and Accountability Act of 1996
ICH	International Conference on Harmonization
IRB	Institutional Review Board
ITT	Intent To Treat
KPI	Key performance indicator
KPS	Karnofsky Performance Status
LAR	Legally Authorized Representative
LFT	Liver function test
MI	Myocardial infarction
MQOLQ	McGill Quality of Life Questionnaire
NIH	National Institutes of Health
PCRC	Palliative Care Research Cooperative
PI	Principal Investigator
QOL	Quality of life
RCT	Randomized controlled trial
SAE	Serious adverse event
SOP	Standard operating procedure
SPMSQ	Short Portable Mental Status Questionnaire
SSDI	Social Security Death Index

Sample Appendix 2: Study Calendar

Create a study calendar, similar to the example below, to ensure that key milestones are met in a timely manner.

	STUDY PERIOD							
	Screening / Enrollment	Allocation	Post-allocation					Close-out
TIMEPOINT	< 30 days	Day 0	Day 7	Day 14	Day 21	xxx	xxx	xxx
ENROLLMENT								
Eligibility screening	x							
Informed consent	x							
(List other procedures)	x							
(List other procedures)								
(List other procedures)								
(List other procedures)								
Allocation		x						
INTERVENTIONS								
(Intervention A)								
(Intervention B)								
(List other study groups / interventions								
ASSESSMENTS								
(List baseline variables)	x							
(List outcome variables)								
(List outcome variables)								
(List other data variables)								
(List other data variables)								