



# **Investigator's Guide: Research Overview and Protocol Development**

Palmetto Health  
Research Compliance

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This overview is designed to give some quick answers to questions that investigators frequently have. For more detailed information on protocol development, please consult the appendices in this guide and the links and references for other research topics which are not emphasized here. The Palmetto Health Research website contains a wealth of information that the investigator will find to be important and helpful. This information can be accessed by going to <http://www.palmettohealth.org/>, clicking on “Education, Residency Programs & Research” and then choosing “Research Division.” The “Compliance” page contains this guide and research division policies.

### *Compliance with Federal Regulations*

The ethics of human subject research and federal regulations have evolved over the past 50 years. Compliance with the requirements of the federal regulations, even for non-federally sponsored/regulated research, protects the rights and welfare of subjects. Palmetto Health (PH) requires compliance with federal regulations for all human subject research regardless of source of support.

### *Proposal Development*

The research question(s) is fundamental and may arise out of the literature search or be modified by the search. Depending upon the state of knowledge in the field of interest and experience of the investigator, the first step in addressing the research question(s) may be a pilot study. Rather than comparing the effects of treatments, a pilot study may have feasibility goals or may aim to provide parameter estimates (e.g., means, standard deviations) to be used in a sample size calculation for a larger, more definitive study.

The investigator then must decide on the design to be used to answer the research question(s). Clinical research designs take two primary forms. One is an experimental approach (i.e., clinical trials) in which a factor of interest is introduced and its effect on the subjects is observed at a later point in time. The other is an observational (epidemiological) approach in which the interest is in establishing associations with other factors.

Because the allocation of treatment in experimental research is under the control of the investigator (through the protocol), there are issues that must be addressed in the study document (e.g., stopping rules) that are not required in observational studies. For both clinical trials and observational research there are some frequent issues that result in approval delays including failure to justify the sample size, as well as a vague or missing statistical section which describes the proposed analysis. In addition, care must be taken to ensure that the inclusion criteria, design and analysis are all consistent with the stated study purpose. Appendices A and B give observational and experimental study protocol formats respectively. Appendix C lists the resources that Palmetto Health makes available to investigators to assist in all phases of their research. You can find in Appendix D a list of abbreviations used in this document.

Protocol development assistance is available at Palmetto Health. To arrange for this assistance, see Appendix C. Sometimes the investigator has an idea that needs refinement. At other times the investigator is ready to actually develop the protocol and should bring to the initial session the research question(s), literature review (background section) with references and a list of variables needed to address the research question(s). For comparison studies, some idea of an

expected or minimally important effect size will also be needed. Often more than one session is required to complete the protocol.

Statistical analysis assistance is also available at Palmetto Health. If this assistance will be needed, it is strongly recommended that protocol development assistance also be obtained through our office. The investigator should bring to the initial session an approved protocol for which the analysis is being carried out and the data itself. Data should be in a format suitable for analysis. Examples would include Microsoft Excel spreadsheet, Microsoft Access database, or text file. PDF files should not be the format delivered for analysis. Deadlines, graphics, tables and analyses not specified in the protocol will be negotiated at the initial visit or as soon thereafter as possible. Typically the analysis report will consist of edited statistical software output, including univariate summaries, tables, and summaries of regression models. This is usually in the form of a text file. The report will include interpretations of statistical models, and where deemed necessary, of tables. Graphics will be supplied in a file format requested by the investigator. A paragraph describing the statistical methods used will be included.

#### *Human Subjects Protection Training*

Investigators and Key Study Personnel are required to complete training on ethical principles and regulations pertaining to research with human subjects. *Key Study Personnel* include any person who is actively involved with human subjects through one or more of the following categories: 1) The informed consent process, 2) Performs study related interventions on human subjects, or has 3) Access to study subjects' identifiable private health information for research purposes. Research personnel must affiliate with Palmetto Health and complete required training modules through the Collaborative Institutional Training Initiative (CITI) prior to conducting research with human subjects. Research personnel should log onto the CITI website at [www.citiprogram.org](http://www.citiprogram.org). Every two years research personnel are required renew their training by completing designated refresher modules from the CITI. Refer to [Education for Investigators and Research Staff PGR](#) for complete details.

#### *Electronic Institutional Review Board (eIRB) Submission System*

Investigators seeking Palmetto Health Institutional Review Board (IRB) review of their proposals must submit through eIRB. Prior to submitting an IRB application, you must register at [eirb.healthsciencessc.org](http://eirb.healthsciencessc.org). The registration form can be completed in a few minutes, and will be validated by Palmetto Health IRB Administration. Once you are able to login, you will be given the option to create an IRB application by selecting "Create New Study".

#### *Scientific Review*

All proposed human subject research must receive scientific review prior to IRB review. The exceptions for obtaining scientific review through Palmetto Health's Scientific Review Committee (SRC) include those studies that have obtained previous peer review including industry-sponsored studies and those studies that qualify as exempt from the requirements of 45 CFR 46.101(b) and as not human subjects research. Principal investigators of proposals that have had scientific review elsewhere should submit a copy of the review report in eIRB. Scientific review is an assessment of the scientific merit of the research design. IRB review shall not begin until the protocol has secured SRC review. The goal of the SRC is to respond to protocol submissions in eIRB requiring SRC review to the investigator within 10 calendar days

by e-mail with an approval letter or a list of required protocol changes. If protocol changes are required, a revised protocol must be submitted to the SRC by way of the eIRB system, and the review process will begin again.

### *Institutional Review Board*

Generally, investigative projects at Palmetto Health fall into one of the following categories:

1. Not Human Subjects Research - “Human Subject” is defined as "a living individual about whom an investigator (whether professional or student) conducting research obtains: 1) data through intervention or interaction with the individual; or 2) identifiable private information." “Research” is defined as "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.” The usual situations where a project at PH may not be human subjects research include some quality improvement activities and other studies where the investigator is given a de-identified dataset by an individual having access to the data but who is not part of the study team. In this scenario the investigator will not have viewed individual identifiers. The investigator may submit the proposal through eIRB and obtain a determination indicating that the project is not human subjects research.
2. Exempt research in our setting usually involves the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects. At PH the determination that a study is exempt is made by submitting the proposal through eIRB.
3. Expedited research involves projects where perhaps the data is prospectively collected or contains individual identifiers but is still minimal risk (the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests).
4. If the proposal does not qualify for one of the above review mechanisms, it will be considered requiring full board review.

The IRB responds to protocol submissions in eIRB after SRC approval (if required) to the investigator by e-mail with an approval letter or a list of required changes. This IRB response is within 30 days of receipt of a complete application in the case of full board reviews and 14 days otherwise.

### *Palmetto Health Administrative Research Review (PHARR) Process*

The Palmetto Health Administrative Research Review (PHARR) process provides a standard method for research compliance issues to be assessed. Items to be reviewed include conflict of interests, scientific validity of projects performed by the Scientific Review Committee, research/subaward contracts, financial feasibility, etc. Investigators must complete the PHARR form and upload it with the specified attachments into the eIRB system at the time of the initial study submission. The IRB and PHARR review will run simultaneously. As of January 1, 2013, all research studies are required to be submitted through the PHARR process. For further information regarding available training, policies/procedures, and forms, go to [www.palmettohealth.org/ResearchCompliance](http://www.palmettohealth.org/ResearchCompliance).

### *Manuscript Preparation*

Palmetto Health strongly encourages the dissemination of research findings through publications and presentations. To assist with this process an internal review process prior to publication/presentation has been established. The review process is not an evaluation of scientific merit, but instead serves as a check system to ensure that all facility and privacy policies are upheld.

Once a manuscript, abstract or presentation has been drafted for submission send a copy of the material, along with the following information, to Research Compliance at [Research-Assist@PalmettoHealth.org](mailto:Research-Assist@PalmettoHealth.org)

Please include:

- Proposed journal/book/society/etc to which the material is being submitted
- Publication / presentation title
- List of authors
- Date of anticipated publication / presentation

The review process will occur within a timely manner and the results will be communicated through e-mail. This communication will either issue a request for changes prior to submission of the material to outside sources OR will issue an approval to proceed with submission.

As a general rule:

- All research actives must have received applicable institutional approvals (such as IRB approval) prior to study implementation.
- All publications and presentations of Palmetto Health supported research must acknowledge Palmetto Health in the following manner:

For Palmetto Health funded research, the following acknowledgement (or similar acknowledgement) must be included in the publication /presentation: “This material is based upon work supported by Palmetto Health.” The specific department providing the funds may be recognized as well.

If Palmetto Health provides no direct research funding, but the research involved the use of Palmetto Health resources, e.g. facilities or patients, then an acknowledgement similar to the following should be included within the publication/presentation: “This material is the result of work supported with resources and the use of facilities at Palmetto Health.”

- If necessary, the investigator should ensure that any clinical trial research activity is appropriately registered through ClinicalTrials.gov.
- All identifiable protected health information should be removed.
- Funding acknowledgements must be present for all studies funded in whole or in part by federal money or other private sponsors.
- For multicenter projects sponsored by an outside entity, the investigator should comply with all agreed upon standards regarding publication of results.

- All Palmetto Health employees should acknowledge their Palmetto Health employment with the publication/presentation.

A complete copy of the “Publication/Presentation of Research Results” policy as well as the “Authorship for Research Publications/Presentations” policy is available online at Research Compliance website located under Policies and PGRs. The policies can be accessed directly at:

<http://www.palmettohealth.org/documents/Research%20Administration/Policy-PresentationofResearchResults.pdf>

<http://www.palmettohealth.org/documents/Research%20Administration/PGR-Authorship.pdf>

#### *Other Resources*

Organizations which sponsor meetings where posters and oral presentations are given describe their guidelines on their websites and these are often quite helpful. For example, see the American College of Physicians link below:

[http://www.acponline.org/residents\\_fellows/competitions/abstract/prepare//](http://www.acponline.org/residents_fellows/competitions/abstract/prepare//)

## APPENDIX A

### Outline for Writing an Observational Study Proposal

**TITLE PAGE:** complete formal project title, principal investigator, co-investigators, corresponding addresses

#### **1. ABSTRACT**

#### **2. BACKGROUND/JUSTIFICATION FOR STUDY**

- Current Status of Research in the area being investigated
- Data in the literature with references
- Reasons for conducting the project in light of current knowledge

#### **3. RESEARCH AIMS**

- Clear statement of the clinical/scientific question
- Main objective
- Secondary objective(s) (optional)

#### **4. STUDY POPULATION**

- Number of subjects
- Inclusion/Exclusion criteria

#### **5. STUDY DESIGN**

- E.g., cross-sectional, case-control, cohort (retrospective or prospective)

#### **6. STUDY PROCEDURES**

- What is done, who does it, when
- Duration of the entire study and the duration of participation for each included subject

#### **7. VARIABLES MEASURED AND MEASUREMENT METHODS**

- Identify how the variables relate to the research objectives
- Variable type (e.g., continuous) and expected typical values
- Data management, including software and security

#### **8. STATISTICAL ANALYSIS**

- Justification of sample size estimate
- Statistical tests used for each analysis and the rationale for the analysis

#### **9. STUDY BUDGET**

#### **10. BIBLIOGRAPHIC REFERENCES**

#### **APPENDICES**

- Questionnaires, surveys, assessment tools, consent form, diaries/journals, quality of life, and/or data collection forms.

*Note: If statistical design support or analysis is needed after first draft, please see Appendix C of this handbook.*

## **APPENDIX B**

### **Outline for Writing a Clinical Research Protocol**

**TITLE PAGE: complete formal project title, principal investigator, co-investigators, corresponding addresses, and name of sponsor**

#### **1. ABSTRACT**

- Objectives: Materials, methods and evaluation criteria
- Research Plan
- Methodology
- Expected results and possible implications

#### **2. RATIONALE**

- Protocol Summary
- Statement of the Problem
- Hypothesis or Key Questions
- Specific Objectives of the Program
- Significance of this Research
- Current Status of Research in the area being investigated
- Data in the literature with references
- Reasons for conducting the project in light of current knowledge

#### **3. OBJECTIVES**

- Main objective
- Hypothesis or hypotheses to be tested
- Secondary objective(s) (optional)

#### **4. TECHNICAL DATA ON MATERIAL OR DRUGS TO BE TESTED (optional)**

- Investigator's brochure for drugs, devices or materials, which have not received FDA approval.

#### **5. EXPERIMENTAL DESIGN**

- Volunteers (healthy subjects and/or patients), number of subjects, source of recruitment.
- Inclusion criteria (clinical, biological, demographic)
- Exclusion criteria
- Concerning past history, concomitant diseases
- Concerning the study product
- Experimental protocol
- Type of trial (controlled or uncontrolled; open, blind, double-blind; cross-sectional or longitudinal)

- Study design (optional)
- Treatment(s) tested (formulation, dosage, times per day, duration)
- Reference treatment or placebo
- Randomization method
- Study procedures (clinical and biological procedures with the time schedule): what is done, who does it, when
- Criteria for discontinuing the study for a participating subject
- Associated treatments: (always anticipate)

## **6. VARIABLES MEASURED AND MEASUREMENT METHODS**

- Biological variables
- Parameters measured
- Place where analyses are performed
- Method(s) used
- Person in charge of the analyses
- Clinical variables
- Parameters measured
- Place where analyses are performed
- Method(s) used
- Person in charge of the analyses

## **7. NUMBER OF SUBJECTS INCLUDED**

The sample size, or the number of subjects included, depends on the *alpha* and *beta* risks accepted, on the degree of difference between the evaluation criterion to be demonstrated between the groups, and on the variance of this criterion in the control group.

## **8. SAMPLE LABELING, PRESERVATION AND TRANSPORTATION**

## **9. ANALYSIS METHODS AND PARAMETERS MEASURED**

- Strategy for statistical analysis (which parameter should be compared and correlated with which other parameter)
- Statistical tests used for each analysis and the rationale for the analysis.
- Place where data analysis is performed and software used.
- Person in charge of the statistical analysis.

## **10. ADVERSE EVENTS**

- Modalities for detecting and recording an adverse event
- Severe adverse events must be reported to the IRB and Sponsor
- Names and telephone numbers of persons to be contacted in the event of a serious adverse event

## **11. ADDITIONAL ASPECTS**

- Subject Compliance to Treatment (assessment method) (as applicable)
- Observation Diary/Journal (who keeps the diary; who comments)
- Surveys, Questionnaire or Other Assessment Tools

- Drug routing via the Hospital Pharmacy (if applicable)
- How Written Informed Consent will be obtained
- Authorized Persons to obtain Informed Consent
- How Protocol Amendments will be processed
- Sponsor Contact Information
- Study Monitoring/Quality Assurance
- How is Patient Anonymity Guaranteed?
- Maintenance of Records and Archives
- Stipends which may be provided for participating Study Volunteers

## **12. STUDY DURATION**

Indicate the planned duration of the entire study and the planned duration of participation for each included subject .

## **13. LOCATION OF PROGRAM ACTIVITIES**

Indicate all locations and sites participating in the study.

## **14. PUBLICATION(S)**

Indicate the form of the publication (official report, scientific article) and who will write the final report of the study in accordance with legal requirements. Give the names of the authors of the final report and if possible the order of authorship.

## **15. BIBLIOGRAPHIC REFERENCES**

## **16. APPENDICES**

Include as needed such as:

- Questionnaires
- Surveys
- Assessment tools
- Diaries
- Journals
- Quality of life
- Data collection forms
- Informed Consent - The form must be written in easily understood non-technical terms (lay language). The information and consent form may be given as a single document; the volunteer is to initial each page and sign the document at the end. The original consent form is placed in the patient's medical record. Copies of the signed consent document are given to the volunteer and kept with your study records. Consult with the IRB to obtain an appropriate informed consent template.
- Clinical Trial Agreement
- Study Budget/Financial Resources

All of the sections indicated above in these guidelines may not be pertinent for all projects and other pertinent sections necessary for specific trials have not been mentioned. However, we hope that these guidelines will be helpful for investigators.

The protocol need not be lengthy but the above components should be included; if not applicable, so note. All questionnaires and surveys should be included as appendices.

You may also wish to visit the web site that contains the National Institutes of Health Guidelines for Writing Research Protocols. To reach the web site, paste the following into your browser:

<https://ccrod.cancer.gov/confluence/download/attachments/74481885/M972+-+Guidelines+for+Writing+Research+Protocols.pdf?version=1&modificationDate=1325017227970>

## APPENDIX C

### **Resources for Investigators**

#### Research Design and Statistical Consultation

Investigators seeking assistance in developing a research protocol should contact Martin Durkin, MD for design support with their study. Dr. Durkin can help the investigator with the protocol prior to submission in eIRB. Data analysis assistance is also available.

Initial contact should be to:

Martin Durkin, MD, MPH

SRC Vice Chair

Senior Researcher/Biostatistician

Palmetto Health

803.434.6963

E-mail: [martin.durkin@palmettohealth.org](mailto:martin.durkin@palmettohealth.org)

#### IRB Submission:

Once the protocol has been developed under the guidance of these professionals, Investigators should submit their protocol to Palmetto Health for review through the eIRB. The submission should include the Protocol with all Appendices including any Data Collection Tools and Surveys/Questionnaires.

Questions regarding IRB should be directed to:

Mary Prather

IRB Administration

Research Manager

803.434.6983; Fax: 803.434.6754

E-mail: [mary.prather@palmettohealth.org](mailto:mary.prather@palmettohealth.org)

#### Palmetto Health Administrative Research Review:

The Palmetto Health Administrative Research Review (PHARR) process ensures Palmetto Health's compliance with research regulations and best practices. The PHARR process includes the scientific review of protocols by Palmetto Health's Scientific Review Committee (SRC).

Questions regarding the PHARR process should be directed to:

Rebecca Marigliano, PhD

Director, Research

Research Division

803.434.4898; Fax: 803.434.6754

E-mail: [rebecca.marigliano@palmettohealth.org](mailto:rebecca.marigliano@palmettohealth.org)

Regulatory and Study Coordination:

Investigators may choose to contract with the Palmetto Health Clinical Trials Department (CTD) if assistance with data collection, study coordination, budget, and/or regulatory assistance is needed.

To learn more about how the CTD may be able to assist you please contact:

Adreane Burgess, RN, BSN, CCRP

Manager, Clinical Trials

Clinical Trials Department

Phone: 803-434-7311; Fax: 803.434.3949

Email: [adreane.burgess@PalmettoHealth.org](mailto:adreane.burgess@PalmettoHealth.org)

## **APPENDIX D**

### **Index of Abbreviations**

CFR	Code of Federal Regulations
CITI	Collaborative Institutional Training Initiative
eIRB	Electronic Institutional Review Board
FDA	U.S. Food and Drug Administration
IRB	Institutional Review Board
OHSR	Office of Human Subjects Research
PH	Palmetto Health
SRC	Scientific Review Committee