

Johns Hopkins University

**BUILDING A CLINICAL RESEARCH HANDBOOK:
A GUIDE FOR PRINCIPAL INVESTIGATORS IN HEALTHCARE SETTINGS**

by
NANCY YANIRA PEREZ TORRES

A capstone project submitted to the
Krieger School of Arts and Sciences
Advanced Academic Programs
Johns Hopkins University
in partial fulfillment of the Degree of
Master of Science in Research Administration

Baltimore, Maryland
December 2020

© 2020 Nancy Pérez
All Rights Reserved

Abstract

Clinical research refers to studies conducted on humans to determine the safety and effectiveness of diagnosis and treatment. In clinical research it is necessary to adhere to federal regulations to protect human subjects. Clinical research conducted at medical centers provides a higher number of medical participants. These human clinical studies must be conducted with the appropriate consent given to participate in medical research.

The purpose of this Capstone Project was to build a clinical research handbook to be used as a reference guide for physicians and principal investigators of regulations and ethical policies throughout medical research at Wilma N. Vazquez Medical Center. This handbook provides a clinical research framework following federal guidelines and legal policies for principal investigators (PI) in medical research. The handbook must use clear language and organizational structure to present clinical research design topics, which explain best practices for creating an ethical framework.

Once approved by the author's Capstone Project instructor, the clinical research handbook will be submitted for review to the institutional medical director. After approval, the clinical research handbook will be available for physicians and PIs starting in January 2021. This clinical handbook starts by discussing various ways for the clinical studies to be organized and executed, including a step-by-step approach to research documentation while managing regulatory and ethical concerns in research. As a result, the handbook is intended to provide accessible information about clinical practice standards and administrative topics to increase clinical research compliance.

Table of Content

Abstract	ii
Table of Content	iii
Figures	v
Glossary	vi
Chapter 1. Introduction	
1.1. Background.....	1
1.2. Statement of the Problem.....	2
1.3. Project Question.....	2
1.4. Project Objectives.....	2
1.5. Significance.....	3
1.6. Exclusions and Limitations.....	3
Chapter 2. Literature Review	
2.1. Overview of Literature.....	5
2.2. Details of Review.....	8
2.3. Applicability of Literature.....	8
Chapter 3. Need(s) Assessment	
3.1. Need(s) Assessment.....	10
3.2. Metrics.....	10
3.3. Sources.....	11
3.4. Committees.....	11
Chapter 4. Project Description	
4.1. Discussion of Project Elements.....	12
Chapter 5. Methodology	
5.1. Methodology Overview.....	13
5.2. Project Design and Clinical Research Handbook Discussion.....	13
Chapter 6. Project Results and Discussion	
6.1. Project Result 1.....	23
Chapter 7. Recommendations and Discussion	
7.1. Introduction.....	24
7.2. Recommendation 1.....	24
7.3. Recommendation 2.....	24
Chapter 8. Conclusion	26
Bibliography	27
Appendix 1: Chart 1. Clinical Research Flowchart	30

Appendix 2: Chart 2. Clinical Research Document Checklist.....31
Appendix 3: Chart 3. Informed Consent Elements Checklist.....32
Appendix 4: Wilma N. Vazquez Medical Center Clinical Research Handbook.....33
Biography.....76

Figures

Figure 1. Theoretical Framework Flowchart	15
Figure 2. Informed Consent Process	17
Figure 3. Clinical Research CITI Training Sheet for PIs	17
Figure 4. Regulatory Documents for PIs	19
Figure 5. Clinical Research Trial Phases	21
Figure 6. Participant Coverage Analysis	22

Glossary

Human Subject: The Food and Drug Administration defines as, an individual who is or becomes a participant in research, either as a recipient of a test article or as a control. A subject may be either a healthy human or a patient.¹

Clinical Research Coordinator (CRC): An individual that handles the administrative responsibilities of a clinical trial and acts as a liaison for the clinical site. This person may collect and review data before it is entered into a study database.

Clinical Research: The National Institute of Health defines as, a patient-oriented research conducted with human subjects for which an investigator directly interacts with human subjects. Excluded from this definition are *in vitro* studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human diseases, (b) therapeutic interventions, (c) clinical trials, or (d) development of new technologies.²

CITI Program: The Collaborative Institutional Training Initiative serves the training needs to healthcare institutions, technology and governmental agencies, while fostering integrity and professional enhancement.³

¹ Children's Hospital of Philadelphia Research Institute. FDA, Human Subject. 2020. <https://irb.research.chop.edu/who-human-subject>

² NIH, NIA Glossary of Clinical Research terms. 2020. <https://www.nia.nih.gov/research/dgcg/nia-glossary-clinical-research-terms>

³ CITI Program. 2020. <https://about.citiprogram.org/en/homepage/>

Chapter 1. Introduction

1.1. Background

Clinical research, also known as medical research, refers to research whose purpose is to shed light on human health. Medical research aims towards preventing and treating diseases.¹ Consequently, conducting clinical research in a hospital setting is a fundamental approach to enhance patient care and explore ways to treat diseases.

Wilma N. Vazquez Medical Center (WNVMC), located in Vega Baja, Puerto Rico, is a general medical and surgical facility. As a teaching hospital affiliated with San Juan Bautista School of Medicine, it must ensure compliance with state law and federal regulations. WNVMC has ninety-five board-certified medical practitioners with seventeen departmental specialties and seven subspecialties. Currently, WNVMC does not have an up-to-date research framework for conducting clinical trials. WNVMC has a need for the development of a research framework that would help faculty members learn about receiving trained certifications on scientific ethics involving the use of human subjects in research. Such training would allow faculty to develop and maintain competency in this area.

Consequently, it is important to develop a clinical research handbook that includes federal guidelines and legal policies for faculty and principal investigators (PI) at Wilma N. Vazquez Medical Center. Therefore, all those conducting research will be required to follow this handbook's guidelines to ensure the PIs are following federal regulations. The handbook would serve as the document needed to support the appropriate training and certifications programs for

¹ "Participating in Health Research Studies," Harvard Countway Library, Last modified May 27, 2020. <https://guides.library.harvard.edu/healthresearch>

board-certifies physicians and PIs in order to provide them with best practices under ethical principles.

1.2. Statement of the Problem

Wilma N. Vazquez Medical Center's problem is that it does not have a handbook that provides a framework for conducting clinical research. This leaves both the WNVMC and principal investigators at risk of not understanding the appropriate clinical research procedures. It is essential to understand the impact of developing a clinical handbook within a medical center setting. The simplified access to specific guidelines associated with medical research is of great significance. Thus, its practicality is related to the ethical implications when documenting any interaction involving patient safety.

In a multifaceted hospital, the main priority is patient safety. A PI must obey ethical guidance throughout the evidence-based medicine approach. It is feasible to develop a clinical research handbook. The clinical research handbook contains easy-to-follow flowcharts with federal guidelines and protocols. Such a handbook aims to guide medical research in a hospital setting.

1.3. Project Question

During the development of a clinical research handbook at WNVMC, enhancing a patient safety culture is essential to comprehend the hospital's high-risk nature. The primary question addressed in the project is: What information is vital for PIs during medical research? The handbook will help address PIs' concerns related to regulatory guidelines in compliance with patient safety protocols at WNVMC.

1.4. Project Objectives

This project's objective was to develop a new clinical research handbook for principal investigators at WNVMC that provides practical information about clinical research's start-up process. A clinical handbook development will supply WNVMC with a step-by-step guide of the trusted standard in research ethics and regulatory compliance. The handbook also includes the website for training courses for obtaining the applicable certifications with the CITI program. This handbook provides a checklist approach as a gold standard when introducing new regulations at WNVMC for conducting clinical research.

1.5. Significance

The development of a clinical handbook will greatly benefit WNVMC. The clinical research handbook applies new institutional protocols as part of the handbook development to help guide PIs to follow directions throughout the research process. This handbook aims to promote new scientific advancements in the medical research field while complying with federal guidelines for conducting good clinical practice. Therefore, applying a checklist approach can provide a medical research framework with the guidance of the handbook. The handbook provides valuable information about updated guidelines from various federal agencies.

Therefore, the handbook encourages the PI to comply with training programs on patient care, safety, and research-quality to foster research integrity. This clinical research handbook addresses the gap between physician-investigators' clinical understanding with new institutional guidelines for managing clinical research.

1.6. Exclusions and Limitations

This resource will guide principal investigators to achieve regulatory compliance with federal regulations. The amount of information limit to help guide the start process for PIs clinical research. Also, throughout the handbook, searching for additional information from

websites and training programs is encouraged. An exemption of the project will be animal testing regulations that will not be included in the handbook since the medical research at WNVMC only involves human subjects. The handbook is a general overview limited to ethical and legal regulatory guidelines. As such, it briefly mentions ethical concerns about data sharing and storage but will not include information about devices or IT technical support. The handbook also aims to encourage the principal investigator to keep up-to-date guidelines relevant to medical research and good clinical practice.

Chapter 2. Literature Review

2.1. Overview of Literature Review

Given the nuances of the new Clinical Research Handbook at WNVMC, a literature review about research trials involving human subjects was examined. Following bioethics principles and ensuring patients' safety is the main priority for health care providers. Also, it is crucial to inflict the least amount of harm throughout medical procedures in order to reach a beneficial outcome. This beneficial outcome is also known as non-maleficence.² Since patient safety is multidimensional, all encounters with the patient must be well-documented. Consistently, healthcare systems promote a standard of care as a skillful approach among physicians for patient safety. An IRB member will assess the clinical study before any recruitment. First, the PI will evaluate the setting; in this case, the hospital setting, which requires having a board that has oversight of risk management.³

WNVMC has a Quality Improvement and Risk Management Department that manages oversight measures for patient safety. An extensive literature review illustrated the need for supporting potential areas to improve quality management for patient safety to mitigate risk during clinical trials. The importance of having well-trained medical staff is imperative to conduct ethical research by promoting collaboration across administrative departments. Thus, medical interventions require frequent updates through emerging literature for implementing best practices.

² Lisa J. Sundean, and Jacqueline M. McGrath "Ethical Considerations in the Neonatal Intensive Care Unit" *Medscape* 2013. https://www.medscape.com/viewarticle/811079_5#:~:text=Nonmaleficence%20means%20non%2Dharming%20or,saving%20treatment%20in%20the%20NICU.

³ Maliheh Kadivar et al. "Ethical and legal aspects of patient's safety: a clinical case report" *J Med Ethics Hist Med*. 2017. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6150915/>

A way to implement best practices is to have appropriate facilitation skills for implementing care teams in a multidisciplinary setting. When conducting a dynamic care management team, effective communication and an ability to adapt to a particular situation are essential. A facilitator will prepare a team to promote training facilities and resources to fostering team effectiveness and performance. In the Agency for Healthcare Research and Quality, a Practice Facilitation Handbook was developed to manage administrative tasks on patient care and prevention by creating new workflows on how to deliver care. The illustration of workflows can help guide patient visits and will identify areas for reinforcement.⁴

Another model reviewed was from Duke University on competency, following a multidisciplinary approach when implementing collaborative efforts for working in groups. This competency model creates a checklist approach for coordinators for providing appropriate feedback from fellow coordinators. This perspective takes problem-solving experiences as a form of best practices when delivering communicative effort between team members. Meanwhile, when monitoring a research application process, each coordinator must work together to facilitate a result. Therefore, a new model was needed to facilitate communication and transparency at Duke University. The Clinical Research Office continued to improve the staff environment by promoting operational training opportunities across competency areas and not just for PIs during the development of a handbook with new administrative guidelines.⁵

A research coordinator specializes in working with the clinical PI during the design, conduct, and management of clinical research. The clinical research coordinator harmonizes administrative tasks between the PI, department, sponsor, and the institute.⁶ A coordinative effort

⁴ Carolyn Shepherd "Practice Facilitation Handbook," AHRQ, <https://www.ahrq.gov/ncepcr/tools/pf-handbook/mod19.html>

⁵ Christine Deeter et al. "Professional Development for Clinical research Professional: Implementation of a Competency-Based Assessment Model" *SRAI* 2020. <https://www.srainternational.org/blogs/srai-jra1/2020/09/29/professional-development-for-clinical-research-pro>

⁶ Washington University in St. Louis, Clinical Research Coordinator Roles and Responsibilities. 2009. <https://research.wustl.edu/about/roles-responsibilities/clinical-research-coordinator/>

must be implemented at the institutional division to report on advancement and assist with necessary protocol requirements. Therefore, a fundamental strategy for both clinical coordinators and PIs is to constantly implement best practices in clinical research.

A learning method behind best practices in clinical research is to attend seminars and obtain certifications for completing trainings related to ethical principles involving human subjects. In this manner, the Collaborative Institutional Training Initiative (CITI Program) provides training initiatives at healthcare institutions that foster integrity.⁷ Such training would offer updates related to federal guidelines. Also, CITI recommends that a subsequent training course be required every three years to maintain updated information. Furthermore, the principal investigator and the research coordinator must complete the lessons on advanced role-based training of the Human Subjects Research and Good Clinical Practice from the CITI program.

The process of research approvals and meeting all the due dates on time is challenging, especially if the PI is not well versed in the research administration area. As such, having an adequate ERA software system is critical for gathering data.⁸ As well as continually having updates about the progress of approvals. Therefore, having an institutional framework is vital, along with access to flowcharts that could ease the process by accomplishing the bigger picture.

Lastly, it is crucial for clinical research to comply with the Revised Common Rule-45 C.F.R. part 46. This Rule is designed to protect human subjects during clinical studies.⁹ Physicians-investigators and private institutions must uphold federal guidelines for collecting documents through a clinical trial to study a new drug (e.g. FDA Forms 1572).¹⁰

⁷ Clinical Research Coordinator” CITI Program 2020. <https://about.citiprogram.org/en/series/clinical-research-coordinator-crc/>

⁸ Adam C. Carter “Taking collaborative approach to pre-award grants management software selection” 2019. https://www.ncura.edu/Portals/0/Docs/Magazine/2019/MarchApril2019_NCURAMagazine.pdf

⁹ Rachel Nosowsky and Ryan Meade “Legal Issues in Clinical Research. What you need to know” *HCCA Conference* 2007. <https://community.corporatecompliance.org/>

HigherLogic/System/DownloadDocumentFile.ashx?DocumentFileKey=b97b476b-d244-4614-807d-fea51b0aea5e

¹⁰ NIH, Form FDA 1572 Statement of Investigator.2020. <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/form-fda-1572-statement-of-investigator>

2.2. Details of Review

All research personnel who are involved in clinical research at WNVMC and engage with human subjects will need to complete training in the use of human subjects in research, good clinical practice, conflict of interest, and the Health Insurance Portability and Accountability Act (HIPAA). This training will be provided through the CITI program. Also, CRC training must be completed as part of the new regulations provided by the handbook. The standards for IRB for Clinical Investigators play a significant role during reviews from state policy makers to ensure protocols to protect human subjects. In addition, in order to protect the human subjects' rights and welfare under The U.S. Food and Drug Administration (FDA) regulations, an IRB group at WNVMC will review and monitor any biomedical study involving human subjects to approve such a study further.¹¹

Furthermore, developing a systematic approach for patient safety allows for the use of a series of assessments referred to as checklist that are beneficial during the study's life cycle. When creating a good-quality review for patient care, one would measure using an assessment tool. Although, the assessment of personnel training and guidelines may vary depending on the case by case study, such efforts are practical when creating a handbook.¹²

2.3. Applicability of Literature Review

Federal research oversight primarily consists of Human Subject's Protection (HSP) for clinical trials in the United States. The HSP oversight requires compliance with Institutional Review Board (IRB) assessment and informed consent, respectively, with U.S. Food and Drug

¹¹ U.S. Food & Drug Administration "IRBs and Protection of Human Subjects in Clinical Trials" (2019), <https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/institutional-review-boards-irbs-and-protection-human-subjects-clinical-trials>

¹² Xiantao Zeng et al. "The methodological quality assessment tools for preclinical and clinical studies, systematic review and meta-analysis, and clinical practice guideline: a systematic review" PubMed (2015), 8(1):2-10

Administration (FDA) regulations.¹³ Also, the IRB regulations, also known as New Common Rule reviews, approve of human subjects' participation consistent with federal standards.¹⁴

Clinical research management and compliance is a multidimensional task, that needs coordinative efforts from various departments. A practical clinical research handbook will help guide PIs throughout clinical trials cycle with the appropriate approval of Research Ethics Hospital Authority.

¹³ Deborah Zarin and et al. "Federal Human Research Oversight of Clinical Trials in the United States" (2014), <https://jamanetwork.com/journals/jama/fullarticle/1835491>

¹⁴ Federal Register "Rules and Regulations" (2018), <https://www.govinfo.gov/content/pkg/FR-2018-01-22/pdf/2018-00997.pdf>

Chapter 3. Need(s) Assessment

3.1. Need Assessment

WNVMC established the need for a clinical research handbook as a result of new PIs wanting to conduct a biomedical research. A clinical framework will be developed and will include a clinical research handbook designed to disseminate valuable information to research coordinators involved in the study. Hence, new opportunities are being presented at WNVMC for new PIs and research coordinators to engage in a clinical investigation using an innovative approach to infectious diseases treatment. In this light, the PI must document all activities involving the patients' health progression. Thus, new PIs were asking the hospital administration for the guidelines and protocols needed to conduct studies and to publish their research findings. Consequently, WNVMC determined the necessity to develop a clinical research handbook.

3.2. Metrics

Although there was an assessment of need that determined a clinical research handbook was needed, there were no metrics used to evaluate the need for the elaboration of a clinical research handbook. However, this project gathered vital information to help build an institutional framework for conducting medical research at WNVMC. This information also promoted that continual clinical training opportunities be provided for PIs and the input of research coordinators within the new clinical research framework is crucial for developing of a clinical handbook.

Consequently, the handbook will address ethical guidelines under Health Insurance Portability and Accountability Act (HIPAA), Institutional Review Board (IRB), and the U.S. Food and Drug Administration (FDA) while utilizing the International Conference on Harmonization (ICH) guidance for Good Clinical Practice. Each of which were reviewed to meet

the needs of WNVMC. The clinical research handbook will show PIs how to aim for Attributable, Legible, Contemporaneous, Original, Accurate, and Complete Data (ALCOA-C) in order to achieve consistent results in their research studies with data integrity.¹⁵ The ALCOA-C is a checklist template for conducting clinical trials using acronyms to follow a structure to achieve coordination proficiency. The use and applicability of the ALCOA-C checklist will help guide the PIs and research coordinators with good clinical documentation for best practice on procedures and outcomes.¹⁶

3.3. Sources

The project is approved by the Hospital Administrator and the President of the Board of Directors, which participated in a detailed meeting about the project. Both individuals have extensive experience in hospital management, as well as regulatory affairs and quality assurance. The clinical research handbook was developed after a literature review process with no medical personnel consultation.

3.4. Committees

No committees were used for the duration of this Capstone Project.

¹⁵ Conduct Science ALCOA-C “ICH GCP Guidance: Gold Standard” (2020), <https://conductscience.com/portfolio/alcoa-c/>

¹⁶ Chitra, Bargaje “Good documentation practice in clinical research” *Perspectives in Clinical Research*, *Perspect Clin Res* (2011): 2(2); 59-63

Chapter 4. Project Description

4.1. Discussion of Project Elements

The main element of this project includes the development of a clinical research handbook. This handbook compiles research guidelines and federal regulations to provide an attainable outcome for new physicians and PIs conducting clinical trials. Having a vigorous guidance through the clinical research handbook may help assist PIs in the medical research within the hospital setting. Another element of the Capstone Project was to create an easy-to-follow flowchart and a checklist approach for organizing the various medical research tasks by providing vital information about training programs and courses.

Chapter 5. Methodology

5.1. Methodology Overview

The development of this clinical research handbook required a comprehensive assessment of institutional policies and federal regulations on clinical research. Once the draft of the clinical research handbook is reviewed and examined, the literature review will reinforce areas for PIs when conducting a medical research at WNVMC. The development of a clinical research handbook for WNVMC was acknowledged through a series of questions in regard to proper documentation and training programs for PIs required for clinical research guidance. An overview of the elements that require additional completion of training courses relevant to physicians and PI's researchers will be enhanced with an outline to coordinate efforts with a clinical research coordinator.

A first draft of the clinical research handbook was handed to the institutional medical director to obtain appropriate feedback for any corrections or suggestions. After the draft is revised, the medical director of WNVMC will provide final approval. Ultimately, a finalized version of the clinical research handbook will be distributed between PIs, research coordinators, and medical administrators.

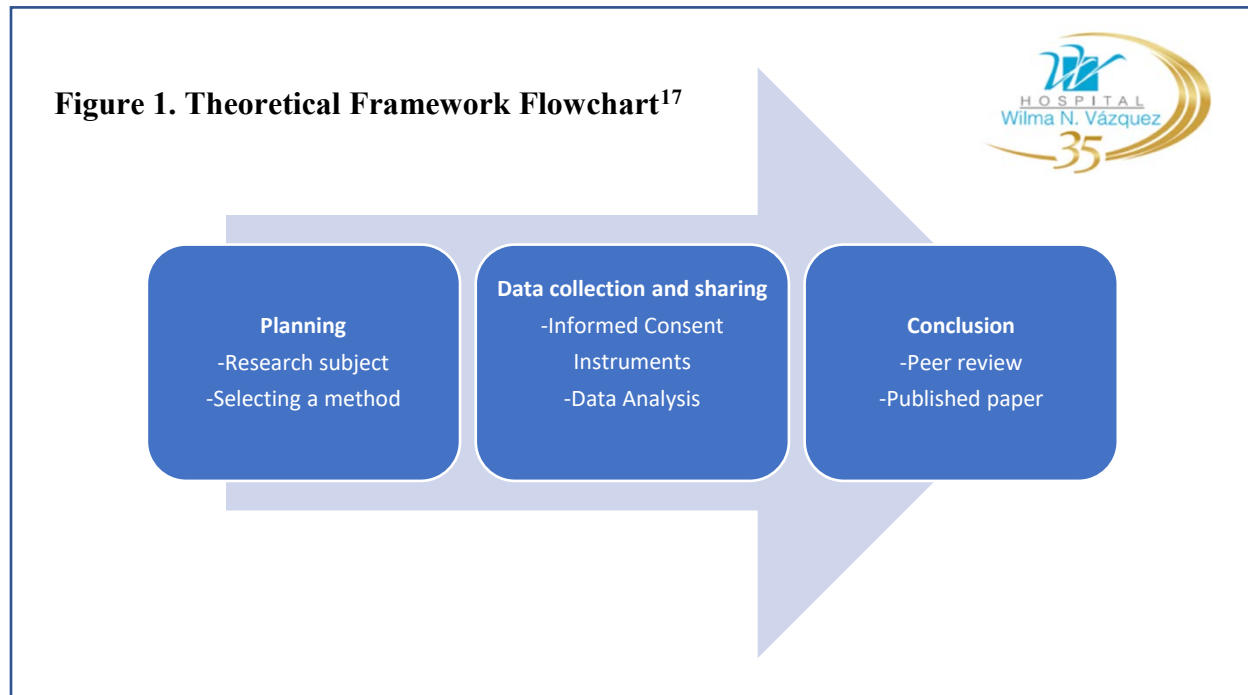
5.2. Project Design and Clinical Research Handbook Discussion

The clinical research handbook provides definitions and includes extensive reference sites of training programs that promote ethical practices when conducting clinical research with human participants. With the advancement of clinical research, access to flowcharts and checklists eases the burden to make team members comprehend the steps toward medical research.

This clinical research handbook written for PIs and CRCs illustrates using a workflow sheet and a checklist; both are tools used to assist new PIs when conducting clinical studies. The clinical research handbook divides into four chapters, easy to read with ready access to research topics. Consequently, the clinical research handbook aims towards providing PIs with a better understanding of the clinical research guidelines. As training requirements become part of the PIs responsibilities, the clinical research handbook will assist the research administrator in conducting training programs.

When designing this Capstone Project, a systemic approach was to build a clinical research handbook to facilitate a structure for PIs during medical research. As an interactive overview of the various stages of clinical research, PIs must comply with federal protocols. The clinical research coordinator will work closely with the PI to embrace institutional protocols at WNVMC to align with scientific advancements. The clinical research handbook discusses collaborative workshops for PIs to develop an organized medical research framework. This handbook has valuable information and best practices to initiate and conduct clinical research in a medical setting.

In Chapter 1, the clinical research framework supports planning and conducting clinical research in a hospital setting. Visual diagrams help illustrate planning, data collection, and conclusion study during clinical research as shown in Figure 1. A research topic embedded in a study problem further prompts the research impact in medical practice. Engaging with experienced physicians may clarify theoretical concepts to define and concise research questions through a literature review process.

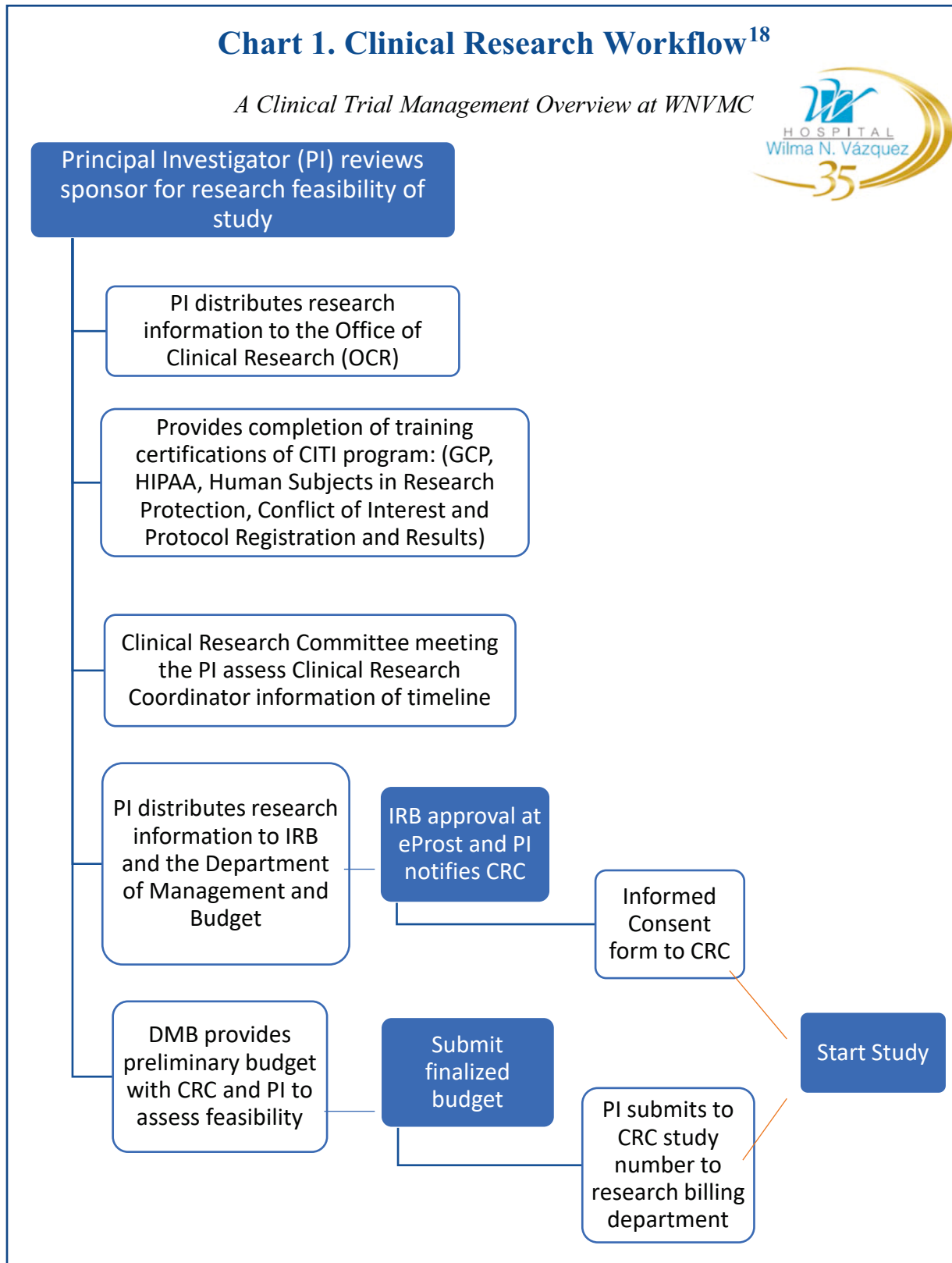


As an overview from Chapter 1 as shown in Chart 1, including a clinical research workflow as centralized access when conducting a clinical research study at WNVMC. The PI will start by reviewing the sponsor program requirements aligned with WNVMC medical research team certifications with federal regulations. The workflow's main concept is to provide a clear vision to harmonize coordinated efforts of the PI with the Office of Clinical Research with meetings with team members to harmonize ethical and legal regulations that uphold the good clinical practice for informed consent as shown in Figure 2.

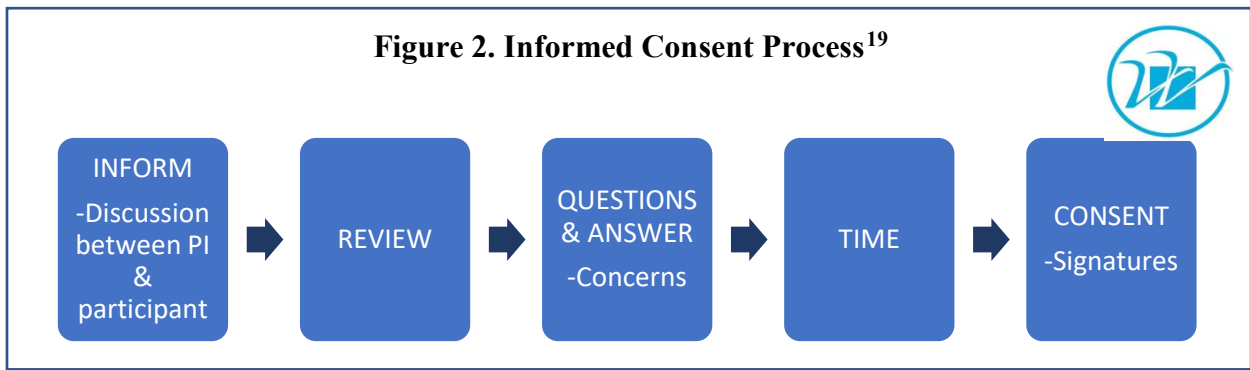
¹⁷ PhD Assistance "Why is theoretical framework important in research?" (2019), <https://www.phdassistance.com/blog/why-is-theoretical-framework-important-in-research/>

Chart 1. Clinical Research Workflow¹⁸

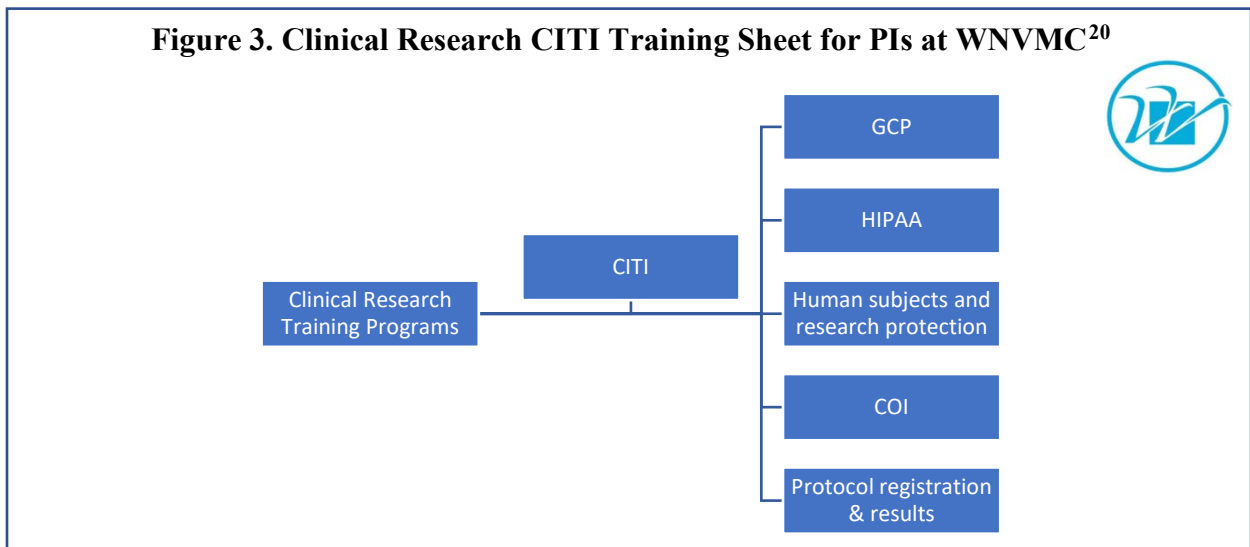
A Clinical Trial Management Overview at WNVMC



¹⁸ The Ohio State University “Clinical Trials Workflow” (2020), <https://osp.osu.edu/development/sponsors/clinical-trials-workflow/>



Chapter 2 provides an overview of the required training and certifications needed of PIs to comply with federal and institutional guidelines. When conducting training programs at WNVMC, the clinical research team must have a clear sense of direction, which is a daunting task for PIs to coordinate the various timelines and deadlines for each team member as shown in Figure 3.



The clinical research handbook will provide healthcare staff conducting training programs with a concise overview to understand what is required and accepted as good clinical practice. Chapter 2 includes a thorough overview of various elements for institutional approval

¹⁹ Ghiath Alahmad “Informed Consent Process” (2014), <https://www.slideshare.net/GHIATH-MD/informed-consent-process>

²⁰ CITI Program (2020), <https://about.citiprogram.org/en/course/good-clinical-practice-basic-fda/>

for initiating IRB submission, including certifications from the CITI program for conducting clinical research at WNVMC with a checklist for PIs, as illustrated in Chart 2.

Chart 2. Clinical Research Checklist for PIs²¹

The purpose of this checklist is to inform the research team and grantees of the necessary documentation before starting a clinical research trial at WNVMC.

Principal Investigator: _____

Department / Clinical: _____

Title: _____



Please specify the type of submission:

Initial submission Annual submission (renewal)

COMPLETED DOCUMENTS:

Principal Investigator Curriculum Vitae

Clinical licensure of PI and DEA license

IND studies: Form 1572

Intramural studies: Form 1195

Financial Disclosure Statements for Investigational New Drug studies submitted to FDA

IRB approval letter of Protocol Amendment

IRB approval letter of subject recruitment

IRB approval of Informed Consent

If applicable laboratory certifications for tests

Certificate from CITI Program on *Good Clinical Practice, HIPAA, Human Subjects in Research Protection, Conflict of Interest, and Protocol Registration and Results*

In Chapter 3, all clinical research activities must require regulatory oversight. Following federal regulations that protect human subjects' institutions have increased monitoring of

²¹ Harvard Cancer Center "Startup and Activation Checklist" (2017), Sample_Research_Start_Up_Checklist%20(1).pdf

investigational activities in hospital settings. The Office for Human Research Protections (OHRP) oversees guidelines following IRBs approval to protect participants' rights and welfare by clarifying ethical and regulatory issues in biomedical research. As part of regulatory oversight management, having financial disclosure can minimize conflict of interest. Another regulatory subject has a systematic literature review before a clinical research proposal. Throughout, the chapter will find a discussion concerning investigational new drugs with contract research organizations' support with proper PIs documentation, as shown in Figure 4.




Figure 4. Regulatory Documents for PIs²²

PIs are required to present to the CRC at the Research Department the following approvals as requisite to start with a clinical research study at WNVMC:

- Informed consent from study participants _____
- U.S. Food and Drug Administration _____
- U.S. Office for Human Research Protections _____
- Independent Ethics Committee (e.g. IRB) _____
- Financial Disclosure Form _____
- After the above checklist is completed then, _____ **Institutional approval**

Chapter 4 describes the data collection tools used for gathering sensitive data by developing a standard case report using a software database for clinical research trials. A software database supports institutions on the IT department and technology transfer before submitting licensing on behalf of the institution. An electronic database is a user-friendly

²² NIH "Regulatory Binder Checklist" (2014), Regulatory_Binder_Checklist_ver3_07-17-2015 (2)

approach to carefully review sensitive information about the IRB submission progression and participants collected data; some examples provided are the *REDCap* and *OnCore*.

Chapter 5 signifies the legal consideration of the Common Rule will further be discussed; since protecting the human subject participants is a primary concern for NIH and CDC. OHRP provides valuable information about conducting research studies with volunteers for safety monitoring at medical centers by complying with federal policy on human subjects. As shown in Chart 3 illustrates the eight essential elements required in an informed consent form (ICF) in the form of a checklist for easy to follow to mark the completed fundamentals. Every clinical study is conducted at WNVMC only after each human participant is well informed and voluntarily agrees. The ICF should include the benefits, risks, and possible outcomes of the study, including contact information of the PI, CRC, and medical facility telephone numbers.

Chart 3. 8 Basic Elements Checklist Required in an Informed Consent Form²³



Please mark the following completed elements on the informed consent form:

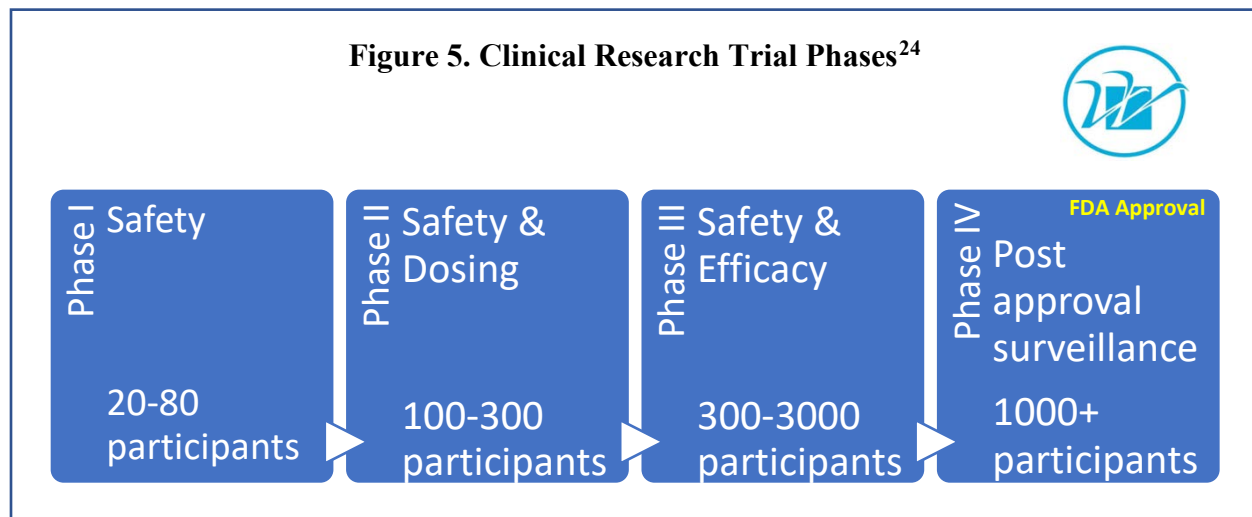
1. An invitation to participate _____
2. Risk of the study _____
3. Benefits and possible outcomes _____
4. An alternative to participation _____
5. A confidentiality statement _____
6. Stating the know about of compensation for medical treatment _____
7. Contact information of the PI, CRC, and the medical facility _____
8. Voluntary participation / withdrawal _____

²³ Jeri Barney, Michele Antisdell "Common Problems in Informed Consent" Yale University (2013), commonproblemsininformedconsent_2013_vf

A clinical research coordinator (CRC) needs to simultaneously manage more than one task simultaneously, thus requiring a great deal of coordinative effort. At the same time, the PI is primarily responsible for the clinical research trial's design and management, the CRC coordinates and facilitates daily clinical research trial activities.

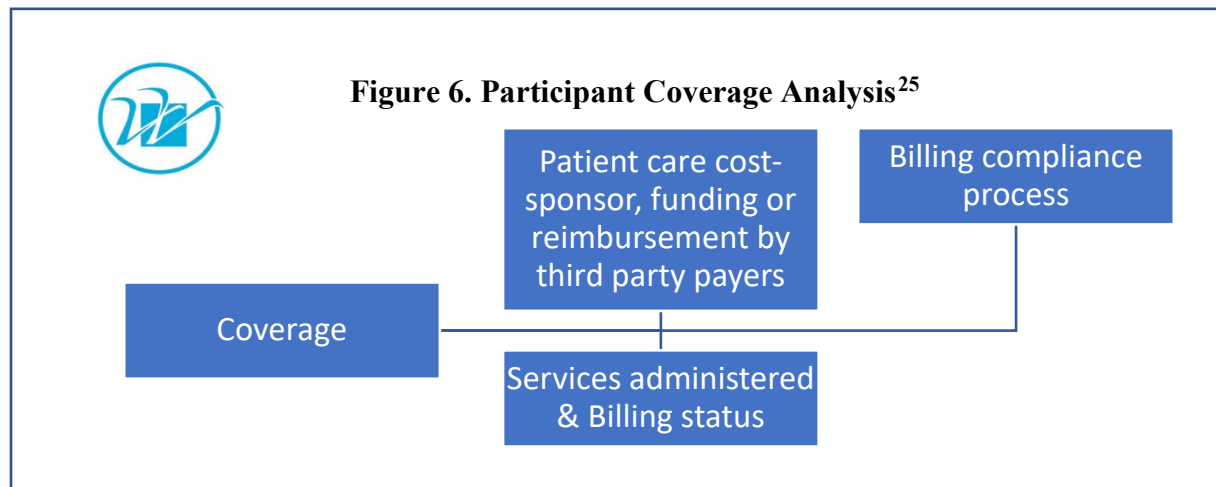
A well-advised PI is essential to incorporate all research elements and federal guidelines to align within a timeline. Therefore, a skilled PI may represent the key between the design and approval of a clinical research trial. Developing a specific framework is vital for PIs that involve human subject safety and protection with the guidance of the clinical research handbook when conducting medical research. In a hospital setting, every detail following patient safety must be checked and carefully monitored. With the implementation of a clear workflow that entails clinical research, documentation will significantly enhance patient care.

Chapter 6 describes the project and budget management plan, including the budgeting and negotiating task when handling research's finance, for example in a drug trial for FDA approval as shown in Figure 5.



²⁴ ILD Collaborative “Clinical Trial Phases” (2020), <https://www.ildcollaborative.org/resources/phase-iii-ipf-clinical-trials>

CRCs must encourage the PI to develop a participant coverage analysis before submitting a research proposal for a sponsor program, as shown in Figure 6.



As part of the Capstone Project, a clinical research document checklist was developed for revising essential protocol requirements. The clinical research checklist approach addresses in one document a guide for both the PI and the CRC when reviewing and planning on training course certifications for conducting a good clinical practice. Pairing the NIH, IRB, and FDA requirements as part of the new institutional guideline with implementing a clinical research handbook at WNVMC will ensure applicable documentation. This effort will ensure best practices before admitting official documents to federal agencies by diminishing delays and disapproval during the beginning of clinical trials.²⁶

The Capstone Project was conducted to create and implement a well-structured clinical research handbook at WNVMC. This handbook addresses PIs' research timeline concerns by promoting coordinative efforts during the initial organization and medical research design while following the IRB and FDA guidelines for approval.

²⁵ Terry Stone, Kati Cini "Clinical Trial Budgeting and Negotiation" (2018), <http://www.bumc.bu.edu/crrro/files/2018/03/RPN-Clinical-Trials-Budgeting-and-Negotiation-3-8-18.pdf>

²⁶ NIH "Tool Summary Sheet" Version 2.0 (2013).

Chapter 6. Project Results and Discussion

6.1. Project Result

The result of this project is the formation of a clinical research handbook to help establish institutional principles based on collective information on regulatory guidelines for medical research at WNVMC. Once approved by the institutional medical director, recommendations were integrated into the completed version of the clinical research handbook. The clinical research handbook will be distributed between medical departments and faculty physicians. The new clinical research handbook helps to improve patient care with up-to-date medical research guidelines.

Chapter 7. Recommendations and Discussion

7.1. Introduction

A clinical research handbook helps establish best practices while guiding administrative tasks for adequate research compliance. This clinical research handbook assists faculty physicians' and staff to further administer an excellent clinical practice through federal regulations and Institutional Review Board policies. In all studies, ethical considerations and research activities must be approved and monitored. A centralized research unit adheres to regulatory stands by implementing a clinical research handbook at the WNVMC. Recommendations ensure the proper accessibility of faculty physicians to conform to the use of the clinical research handbook protocols.

7.2. Recommendation 1: WNVMC Should Require a PI Signature as part of the Institutional Agreement for the Disclosure of the Clinical Handbook

As part of the clinical research activity in a medical setting, proper documentation is vital for a transparent interaction. A signature requirement as part of an agreed policy for a PI at the WNVMC will reflect the clinical research handbook protocols and faculty understanding. The requirement of a signature after physicians and PI's read and acknowledge the guidelines on the handbook is imperative for medical research.

7.2.1 Recommendation 2: WNVMC Should Revise and Include a Clinical Research Handbook Revision every Two Years

Another recommendation as part of this project is a clinical research handbook revision every two years to make any necessary changes with new information on federal regulations.

This handbook requires up-to-date information to further develop the clinical research framework. The handbook revision includes training programs per each member's appropriate certification renewals.

Chapter 8. Conclusion

Wilma N. Vazquez Medical Center has long been enhancing the quality and guidelines of patient care and good clinical practice. Implementing good clinical practice throughout medical research conducted at WNVMC is essential to develop a clinical research handbook by applying ethical and scientific standards for clinical research design. During medical research, the clinical research handbook application will help guide PIs to protect the patients' confidentiality and integrity of human subjects in a hospital setting. The author hopes that the clinical research handbook development serves as a valuable and practical resource for PIs and research administrators.

Bibliography

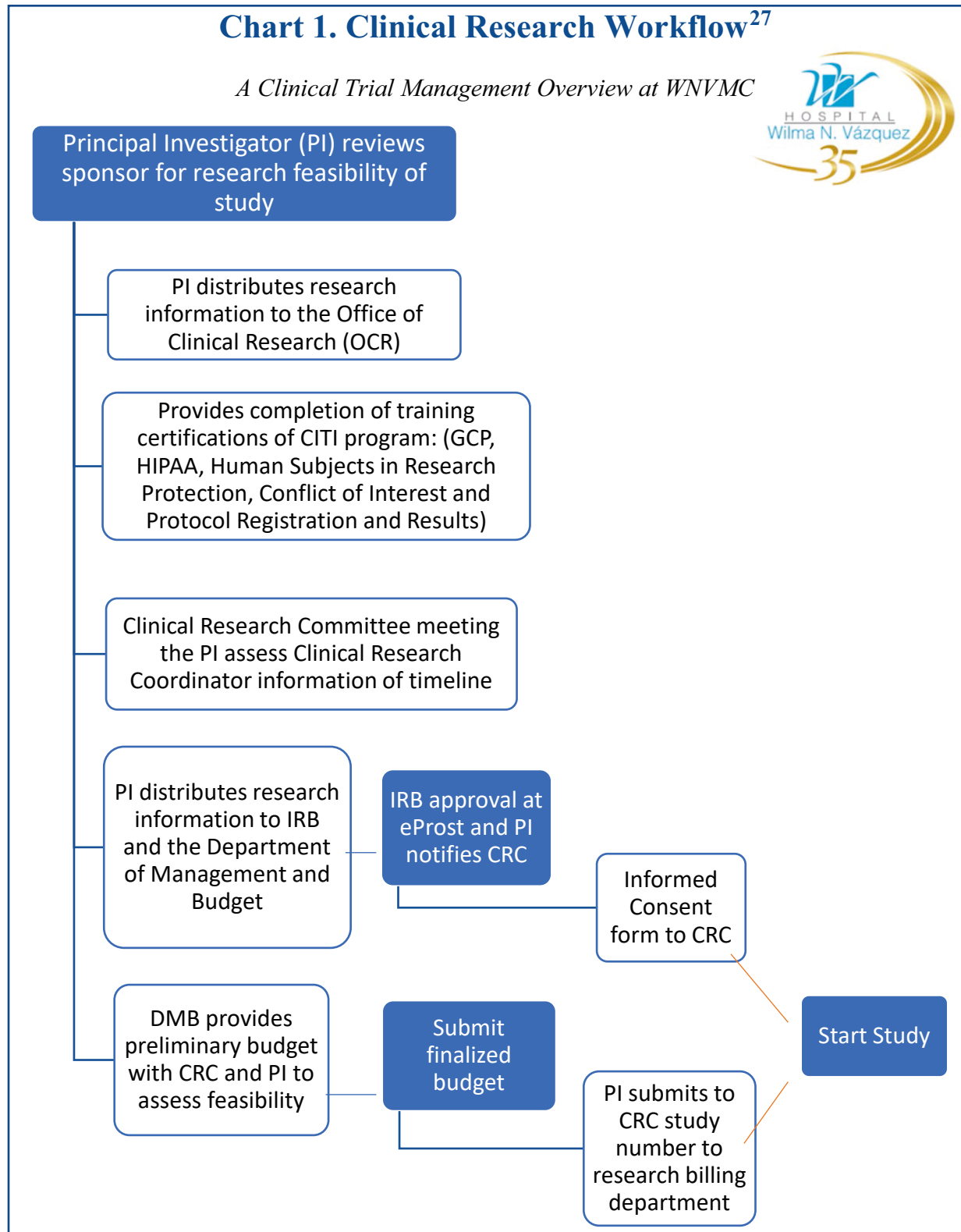
- Alahmad, Ghiath “Informed Consent Process” King Abdullah International Medical Research Center (2014), <https://www.slideshare.net/GHIATH-MD/informed-consent-process>
- Bargaje, Chitra, “Good documentation practice in clinical research” *Perspectives in Clinical Research*, *Perspect Clin Res* (2011): 2(2); 59-63
- Barney, Jeri and Antisdell Michele “Common Problems in Informed Consent” Human Research Protection Program, Yale University (2013), [commonproblemsininformedconsent_2013_vf](https://www.yale.edu/humanresearch/protected/commonproblemsininformedconsent_2013_vf)
- Carter, Adam, “Taking collaborative approach to pre-award grants management software selection” *NCURA* (2019): 51, 2, https://www.ncura.edu/Portals/0/Docs/Magazine/2019/MarchApril2019_NCURAMagazine.pdf
- CITI Program. About Research, Ethics, and Compliance Training. (2020), <https://about.citiprogram.org/en/homepage/>
- CITI Program “GCP for Clinical Trials with Investigational Drugs and Medical Devices” (2020), <https://about.citiprogram.org/en/course/good-clinical-practice-basic-fda/>
- Children’s Hospital of Philadelphia Research Institute. IRB. FDA “Human Subject” (2020), <https://irb.research.chop.edu/who-human-subject>
- Conduct Science, “ALCOA-C ICH GCP Guidance: Gold Standard” (2020). <https://conductscience.com/portfolio/alcoa-c/>
- Deeter Christine, Hannah Deborah, Reyes Camila, Mack Michelle, Soto Marissa, Freel Stephanie, Namenek Rebecca, Gaudaur Heather, Doughty Andrea and Synder Denise “Professional Development for Clinical research Professional: Implementation of a Competency-Based Assessment Model” *SRAI*, V.LI, 2. 2020. <https://www.srainternational.org/blogs/srai-jra1/2020/09/29/professional-development-for-clinical-research-pro>
- Geisinger “Research at Geisinger” Office of Clinical Research Operations (2020), <https://www.geisinger.edu/research/research-and-innovation/research-cores/office-of-clinical-research-operations>
- ILD Collaborative “Clinical Trial Phases” (2020) *A Patient-Physician Collaborative for the Understanding, Management, and Treatment of Interstitial Lung Diseases*, <https://www.ildcollaborative.org/resources/phase-iii-ipf-clinical-trials>
- Harvard Cancer Center/Dana Farber “Startup and Activation Checklist” *A Guide to Human Research Activities* (2017), [Sample_Research_Start_Up_Checklist%20\(1\).pdf](https://www.dana-farber.org/sites/default/files/2017-08/Sample_Research_Start_Up_Checklist%20(1).pdf)

- Lisa J. Sundean, and Jacqueline M. McGrath “Ethical Considerations in the Neonatal Intensive Care Unit” *Medscape* (2013), https://www.medscape.com/viewarticle/811079_5#:~:text=HigherLogic/System/DownloadDocumentFile.ashx?DocumentFileKey=b97b476b-d244-4614-807d-fea51b0aea5e
- Maliheh Kadivar, Arpi Manookian, Fariba Asghari, Nikoo Niknafs, Arash Okazi, and Asal Zarvani “Ethical and legal aspects of patient’s safety: a clinical case report” *J Med Ethics Hist Med* (2017) 10,15, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6150915/>
- NIH, “Clinical Research” *Clinical Research Coordinator and Clinical Research*, (2020), <https://www.nia.nih.gov/research/dgcn/ia-glossary-clinical-research-terms>
- NIH, *Form FDA 1572*, “Statement of Investigator” (2020), <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/form-fda-1572-statement-of-investigator>
- NIH “Essential Documents Checklist: Tool Summary Sheet” Version 2.0 (2013), retrieved from: [essential-documents-checklist-clinical-trial-interventional](https://www.fda.gov/oc/essential-documents-checklist-clinical-trial-interventional)
- NIH “Regulatory Binder Checklist” Tool Summary Sheet (2014), [Regulatory_Binder_Checklist_ver3_07-17-2015](https://www.fda.gov/oc/regulatory-binder-checklist-ver3-07-17-2015) (2)
- Nosowsky Rachel and Meade Ryan “Legal Issues in Clinical Research. What you need to know” *HCCA Conference* (2007), <https://community.corporatecompliance.org/>
- PhD Assistance “Why is theoretical framework important in research?” *Research Methodology* (2019), <https://www.phdassistance.com/blog/why-is-theoretical-framework-important-in-research/>
- Shepherd, Carolyn, Module 19. Implementing Care Teams. Agency for Healthcare Research and Quality, (2013), <https://www.ahrq.gov/ncepcr/tools/pf-handbook/mod19.html>
- Stone Terry, Cini Kati “Clinical Trial Budgeting and Negotiation” Boston Medical Center (2018), <http://www.bumc.bu.edu/crro/files/2018/03/RPN-Clinical-Trials-Budgeting-and-Negotiation-3-8-18.pdf>
- The Ohio State University, “Clinical Trials Workflow” Office of Research and Sponsored Programs (2020), <https://osp.osu.edu/development/sponsors/clinical-trials-workflow/>
- U.S. Department of Health & Human Services “Rules and Regulations” (2018), *Federal Register*, 83, No. 14, <https://www.govinfo.gov/content/pkg/FR-2018-01-22/pdf/2018-00997.pdf>
- U.S. Food & Drug Administration “IRBs and Protection of Human Subjects in Clinical Trials” (2019), <https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/institutional-review-boards-irbs-and-protection-human-subjects-clinical-trials>

Washington University in St. Louis, Clinical Research Coordinator Roles and Responsibilities. Position Role (2009), <https://research.wustl.edu/about/roles-responsibilities/clinical-research-coordinator/>

Zarin Deborah, Tse Tony, and Menikoff Jerry “Federal Human Research Oversight of Clinical Trials in the United States” *JAMA* (2014), <https://jamanetwork.com/journals/jama/fullarticle/1835491>

Appendix 1. Clinical Research Flowchart



²⁷ The Ohio State University “Clinical Trials Workflow” (2020), <https://osp.osu.edu/development/sponsors/clinical-trials-workflow/>

Appendix 2: Clinical Research Document Checklist

Chart 2. Clinical Research Checklist for PIs²⁸

The purpose of this checklist is to inform the research team and grantees of the necessary documentation before starting a clinical research trial at WNVMC.

Principal Investigator: _____

Department / Clinical: _____

Title: _____



Please specify the type of submission:

Initial submission Annual submission (renewal)

COMPLETED DOCUMENTS:

Principal Investigator Curriculum Vitae

Clinical licensure of PI and DEA license

IND studies: Form 1572

Intramural studies: Form 1195

Financial Disclosure Statements for Investigational New Drug studies submitted to FDA

IRB approval letter of Protocol Amendment

IRB approval letter of subject recruitment

IRB approval of Informed Consent

If applicable laboratory certifications for tests

Certificate from CITI Program on *Good Clinical Practice, HIPAA, Human Subjects in Research Protection, Conflict of Interest, and Protocol Registration and Results*

²⁸ Harvard Cancer Center “Startup and Activation Checklist” (2017), Sample_Research_Start_Up_Checklist%20(1).pdf

Appendix 3: Informed Consent Elements Checklist

Chart 3. 8 Basic Elements Checklist Required in an Informed Consent Form²⁹



Please mark the following completed elements on the informed consent form:

1. An invitation to participate _____
2. Risk of the study _____
3. Benefits and possible outcomes _____
4. An alternative to participation _____
5. A confidentiality statement _____
6. Stating the know about of compensation for medical treatment _____
7. Contact information of the PI, CRC, and the medical facility _____
8. Voluntary participation / withdrawal _____

²⁹ Jeri Barney, Michele Antisdel “Common Problems in Informed Consent” Yale University (2013), commonproblemsininformedconsent_2013_vf

Appendix 4: Wilma N. Vazquez Medical Center Clinical Research Handbook



CLINICAL RESEARCH HANDBOOK

A Guide for Principal Investigators to Gain Insight into Clinical
Research in Healthcare Settings

©2020 Edition
All Rights Reserved

Table of Content

Table of Content	ii
Figures	iv
List of Abbreviations	v
Introduction	1
A. Purpose of Handbook.....	1
B. Mission Statement.....	1
C. Vision Statement.....	1
D. Resources.....	1
E. Definitions.....	3
F. Roles and Responsibility.....	4
Chapter 1. Clinical Research Framework	5
1.1. Planning.....	5
1.2. Data collection.....	7
1.2.1. Informed consent guidance for PIs, IRBs and Sponsors.....	7
1.2.2. Data sharing.....	10
1.3. WNVMC Clinical Research Department.....	10
1.4. Peer-reviewed Publication.....	10
1.5. Conclusion.....	11
Chapter 2. Required Training and Certifications	12
2.1. Research Workshops.....	12
2.2. Code of Federal Regulations.....	12
2.3. CITI Program.....	13

Chapter 3. Regulatory Oversight.....	15
3.1. Research Committee.....	15
3.1.1. Research Committee Functions.....	15
3.2. Conflict of Interest.....	17
3.3. Financial Disclosure Form.....	17
3.4. Reporting to the Institutional Review Board.....	17
3.4.1. Initial Clinical Study Submission to the IRB.....	17
3.5. Systematic Literature Review.....	18
3.6. Contract Research Organization.....	19
3.7. Investigational New Drug.....	19
Chapter 4. Data Capture Tools.....	20
4.1. Standard Case Report Form Design.....	20
4.2. Software Database for Clinical Research Trials.....	21
Chapter 5. Legal Considerations.....	23
5.1. Research Contract.....	24
Chapter 6. Project and Budget Management.....	25
6.1. Project Management Plan.....	25
6.2. Budget Management Plan.....	26
6.2.1. Budgeting Negotiation and Finance.....	27
Reference.....	28
Appendix 1. Chart 1. Clinical Research Workflow	31
Appendix 2. Chart 2. Clinical Research Checklist for PIs	32
Appendix 3. Chart 3. 8 Basic Elements Checklist Required in an ICF.....	33

Appendix 4. Informed Consent Template.....34

Figures

Figure 1. **Theoretical Framework Flowchart.....6**

Figure 2. **Informed Consent Process.....8**

Figure 3. **Clinical Research CITI Training Sheet for PIs.....14**

Figure 4. **Regulatory Documents for PIs.....16**

Figure 5. **Clinical Research Trial Phases.....25**

Figure 6. **Participant Coverage Analysis.....27**

List of Abbreviations

CFR: Code of Federal Regulations

e-CFR: Electronic Code of Federal Regulations

eCRF: Electronic Case Report Form

CRA: Clinical Research Associate

CRC: Clinical Research Coordinator

CRO: Contract Research Organization

CSR: Clinical Study Report

COI: Conflict of Interest

FDA: U.S. Food and Drug Administration

HIPAA: Health Insurance Portability and Accountability Act

ICF: Informed Consent Form

ICH GCP: International Conference on Harmonization-Good Clinical Practice

IRB: Institutional Review Board

NIH: National Institute of Health

OHRP: Office for Human Research Protections

OFR: The Office of Federal Register

PI: Principal Investigator

SOP: Standard Operating Procedures

WNVMC: Wilma N. Vazquez Medical Center

Introduction

A. Purpose of Handbook

The Clinical Research Handbook is intended to serve as a guide for principal investigators (PIs) and clinical research coordinator (CRCs) in the management of medical research at Wilma N. Vazquez Medical Center (WNVMC). The purpose of the clinical research handbook is to help investigative faculty and medical staff to manage clinical research following federal regulations and institutional policies. This clinical research handbook provides an overview of the required training courses and certificates required of PIs to be used as a reference guide for conducting an ethical and legal medical research trial. Innovation comes from knowledge, and to advance in all disciplines, WNVMC will continually seek better health-related solutions involving the best clinical outcomes.

This handbook has divided into sections for an easy access to topics of interest. *Readers should be advised that variations in policies and regulations may occur and will attempt to keep the valuable information up-to-date.*

B. Mission Statement

WNVMC's commitment is to maintain the highest quality services in a safe and reliable environment while having an excellent multidisciplinary medical faculty team that offers the best care for our patients' needs.

C. Vision Statement

To inspire and contribute to every patient's healthcare and well-being by providing the best care integrating medical practice, education, and clinical research.

D. Resources

The Collaborative Institutional Training Initiative (CITI Program) attends healthcare institutions to foster integrity through advanced learning. The following modules surround compliance training programs, obtained from the website

<https://about.citiprogram.org/en/courses/>.¹

Training and Certifications

- Good Clinical Practice
- Privacy and Security Rule from Health Insurance Portability and Accountability Act (HIPAA)
- Human Subjects Protection
- Responsible Conduct of Research
- Informed Consent and Clinical Investigations: A Focus on the Process
- ClinicalTrials.gov: Protocol Registration and Results Disclosure

Institutional Review Boards (IRB)

The IRB is an independent body that is constituted of medical, scientific and nonscientific members whose obligation is to ensure the protection of rights, safety, and well-being of human subjects involved in clinical trials by providing protocols and reviewing methods used when documenting informed consent. A human subject is a patient or healthy individual who may become a participant in a research, either as a recipient of an intervention or as a control.² IRB protocols under monitor biomedical research involving human subjects. Following

¹ CITI (2020), https://about.citiprogram.org/en/courses/?fwp_search=protocol%20and%20registration

² NIH (2020). Glossary of Clinical Research Terms, <https://www.nia.nih.gov/research/dgcg/nia-glossary-clinical-research-terms>

FDA regulations, a study must request authorization of the IRB to secure the protection of rights and welfare of human participants during a clinical research.

E. Definitions (National Institute of Health Clinical Research Terms)

Clinical Research: Clinical trials are voluntary research studies conducted in people and designed to answer specific questions about the safety or effectiveness of drugs, vaccines, other therapies, or new ways of using existing treatments.

Conflict of Interest: A conflict of interest occurs when individuals involved with the conduct, reporting, oversight, or review of research, which may also have financial or other interest, from which they can benefit, depending on the results of the research.

Food and Drug Administration (FDA): An agency within the U.S. Department of Health and Human Services (DHHS) responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, nation's food supply, cosmetics, and products that emit radiation.

Good Clinical Practice: A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial participants are protected.

Informed Consent Form: A document that describes the rights of a study participant and provides details about the study, such as its purpose, duration, required procedures, and key contacts. Risks and potential benefits are explained in the informed consent document.

Intervention: A procedure or treatment such as a drug, nutritional supplement, gene transfer, vaccine, behavior or device modification that is performed for clinical research purposes.

Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule: The first comprehensive Federal protection for the privacy of personal health information. The Privacy Rule regulates the way certain health care groups, organizations, or businesses, called covered entities under the Rule, handle the individually identifiable health information known as protected health information (PHI).

F. Roles and Responsibilities

Principal Investigator (PI): The person responsible of a clinical research which prepare, conduct, analyze, and reports the results of the research trial.

Clinical Research Coordinator (CRC): An individual that handles the administrative and day-to-day tasks of a clinical research trial by acting as a liaison for clinical site. This person may collect and review the data before it is entered into a study database.

Chapter 1. Clinical Research Framework

1.1. Planning

A theoretical framework is a guidance tool that enables developing a research problem with the applicable theory. A clinical research handbook guides and assist the PI to address questions present throughout the development of a clinical research trial. Through the guidance of a clinical research framework, assist PIs when addressing questions while recognizing pertinent data limitations. A clinical research framework must clarify the design structure and analyze the ethical and legal protocols' groundwork. PIs must directly interact with human subjects through patient-oriented informed consent for the participant to provide consent for a clinical research trial.

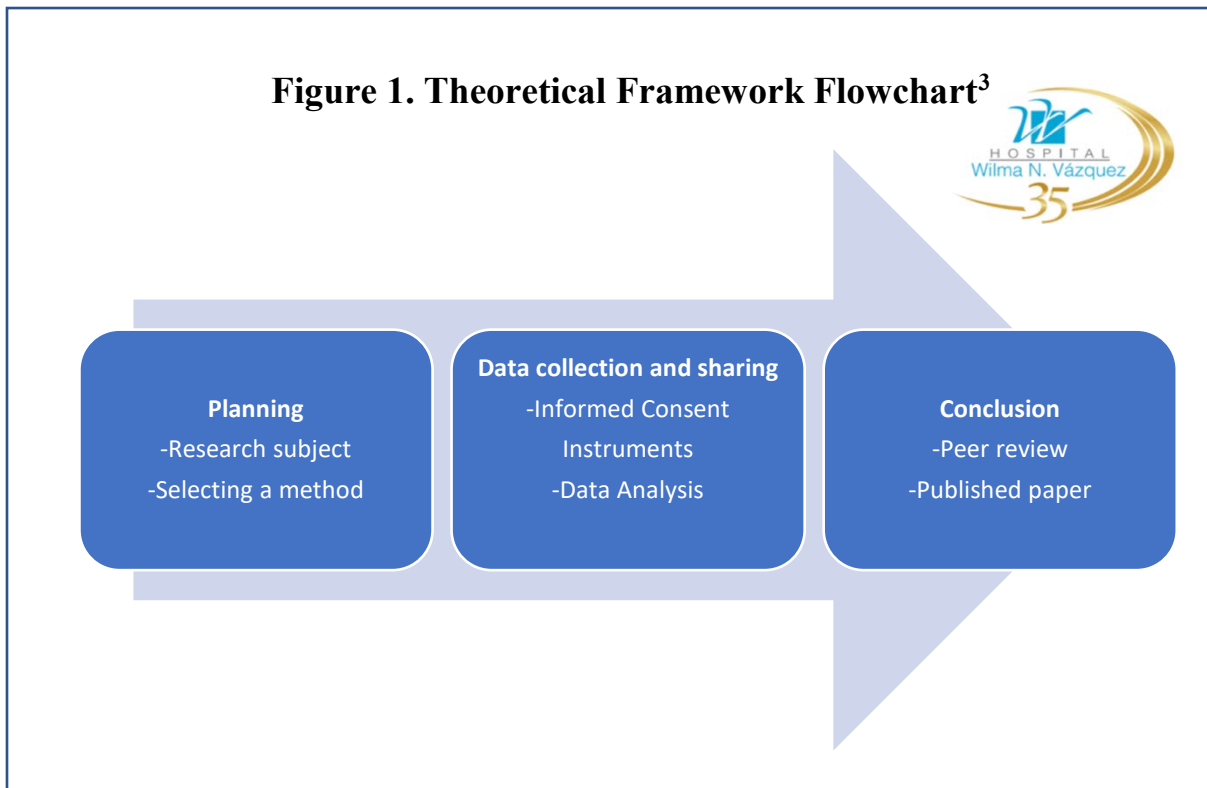
The research subject identification process will narrow the possibilities to center a research plan. At the beginning of developing a draft proposal, the PI must explore the current standard of care regarding a specific disease or treatment to align with the initial research design. As described in Figure 1. when selecting the population, participants in clinical research the PI must ensure the clinical research complies with the NIH guidelines following ethical principles, justice, beneficence, and non-maleficence. Subsequently, primarily in a healthcare setting, therapeutic effectiveness includes medical advancements, which the medical care can further research.

During clinical research development, the PI recognizes the impact on patient care while developing an eligibility criterion when narrowing the subject population. Narrowing the study's scope will help the PI plan and guide the research towards answering a particular research topic. The research topic consists of a set of ideas following related research questions, in which a CRC ensures that the PI refines the population and the study's problem.

A clinical research study will start with a fundamental question concerning a study's classification whether an investigation is qualitative or quantitative. A qualitative research discovers and describes the how and why of medical outcomes. Another type of research is a quantitative study, providing numerical statistical significance between volunteer groups. At WNVMC, most of the clinical research aims towards a primary clinical research study to gather new valuable patient-data to further draw conclusions when compared to a database.

How to narrow the scope of a clinical research?

- Analyze and gather the clinical research elements
- Conduct an in-depth overview of the literature review about the subject area
- Evaluate the PIs' training on the subject to match federal guidelines



³ PhD Assistance “Why is theoretical framework important in research?” (2019), <https://www.phdassistance.com/blog/why-is-theoretical-framework-important-in-research/>

A good clinical practice is to improve the collaborative research process between participant and physician. Good communication between physician-patient is based on trust, especially during a clinical research trial, which may help reduce the burden of clinical trial participation. The process of taking care of patients during a clinical research trial must be the main priority for PIs. During the enrollment process, having a theoretical framework for clinical trials fosters research structure while breaking down significant clinical assessment aspects for a well-informed patient. After the decision-making process, informed consent must foster the patient's autonomy during a research trial.

At WNVMC, part of the clinical research department's contribution is to monitor such activities to increase diversity among participants in a clinical study. After the proper documentation and data have been collected, PIs must comply with the data collection and storage.

1.2. Data Collection

When collecting medical research data, it is crucial to identify the type of study. Establishing a precise and reliable form of data collection will lead the approach in patient-physician effectiveness. For example, the data collection could become an observation, a comparison to other clinical that integrate medical records, patient interviews, and administrative data collection for further use.⁴

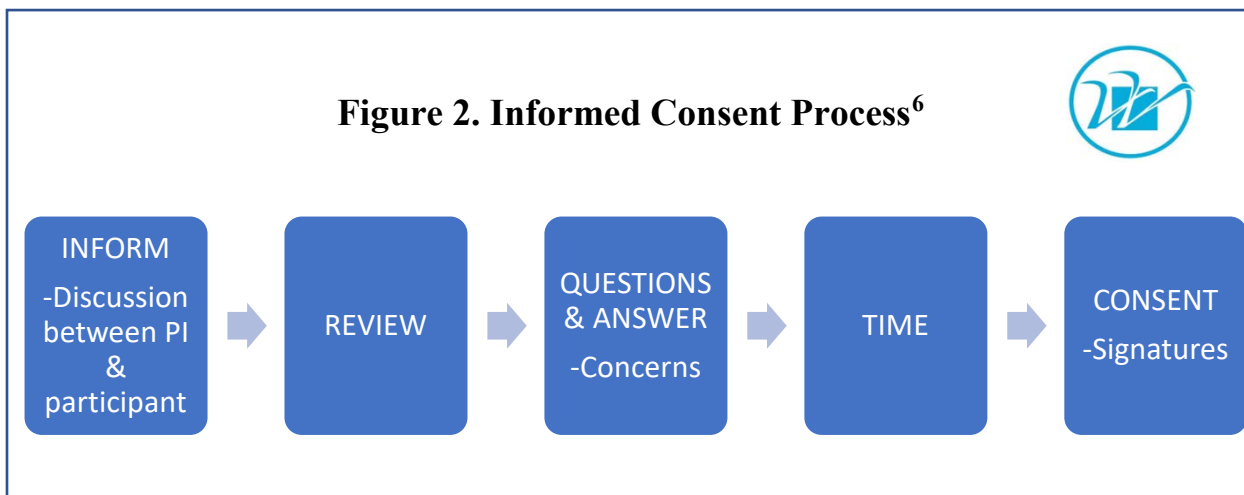
1.2.1. Informed consent guidance for PIs, IRBs and Sponsors

To enhance human subject protection the Department of Health and Human Services, Office for Human Research Protections and FDA are working together on recommendations for

⁴ Jane, Saczynski. et. al. "Commonly utilized data collection approaches in clinical research" (2013), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3827694/>

regulatory requirements for human subject research.⁵ FDA’s informed consent guidelines set forth regulations on the Protection of Human Subjects (21 CFR part 50).

Informed consent is a central element to uphold good clinical practice during clinical trials and must state a clear and precise protocol description. When starting the process of informed consent for clinical trials, the PI must explicitly state that the subject’s participation is voluntary, and the subject can withdraw at any time. Informed consent tends to be a written document such as an Informed Consent Form (ICF) and must be signed and dated by both the PI and participant. Informed consent is more than just a document. An informed consent is the process of informing the participant when enrolling in a clinical research trial.



The ICF’s purpose is to provide valuable information about clinical trials in a simple language in the process of answering questions the participant may encounter. A well-informed subject may comply with the study’s requirement because the participant comprehends the study’s significance. Additionally, the ICF may include interviews for which permission is

⁵ FDA “Informed Consent” (2014), <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/informed-consent>

⁶ Ghiath Alahmad “Informed Consent Process” (2014), <https://www.slideshare.net/GHIATH-MD/informed-consent-process>

present by the participant given pertinent information about benefits and risks while always having the option to refuse their participation.

Chart 3. 8 Basic Elements Checklist Required in an Informed Consent Form⁷



Please mark the following completed elements on the informed consent form:

- | | |
|---|-----|
| 1. An invitation to participate | ___ |
| 2. Risk of the study | ___ |
| 3. Benefits and possible outcomes | ___ |
| 4. An alternative to participation | ___ |
| 5. A confidentiality statement | ___ |
| 6. Stating the know about of compensation for medical treatment | ___ |
| 7. Contact information of the PI, CRC, and the medical facility | ___ |
| 8. Voluntary participation / withdrawal | ___ |

A well-informed participant may better adhere to a study’s protocol. PIs are obligated to share new information related to their clinical trial participation, including newly identified side effects. For informed consent to be valid, the role of effective communication between participants and researchers is vital to promote the protection of rights and safety of participants in clinical research.⁸ Please follow the example provided of the informed consent template in

⁷ Jeri Barney, Michele Antisdell “Common Problems in Informed Consent” Yale University (2013), commonproblemsininformedconsent_2013_vf

⁸ Andrew Pick et. al. “The role of effective communication in achieving informed consent for clinical trials” (2014), <https://journals.rcni.com/nursing-standard/the-role-of-effective-communication-in-achieving-informed-consent-for-clinical-trials-ns.29.10.45.e9443#:~:text=Informed%20consent%20is%20fundamental%20to,would%20like%20to%20take%20part.>

Appendix 4. All clinical trial activities involving human participants in exempt research must be reviewed and approved by WNMVC Institutional Review Board.

1.2.2. Data sharing

NIH communication concerning data sharing and facilitation encourages parties to implement policy statements as many NIH grants opportunity announcements intend. Research data is factually recorded material that is considered accepted by the scientific community that validates research findings. The data collected by a clinical researcher must remain confidential by the PI until publication in a peer-review journal, protected under law (e.g., intellectual property) and of the disclosure from unwarranted personal private information.⁹

1.3. WNVMC Clinical Research Department

WNVMC Clinical Research Department provides access to multiple services that could help in clinical trial design, would connect the PI with a grant writer and even, statistical guidance through discussing case-control and cohort studies. Research design and developing concepts are vital for the research team to visualize in forms of objectives ensuring meeting deadlines and goals. At WNVMC, the research department will monitor team metrics to improve medical staff performance and compliance with federal and institutional guidelines.

For more information, visit the WNVMC website: <http://www.wilmamed.com/>.

1.4. Peer-Reviewed Publication

A peer-review is a process used to verify, validate and collect data before publication in a medical journal. Independent researchers may assess the manuscript's originality and help the

⁹ NIH "Data Sharing Policy" (2020), https://grants.nih.gov/grants/policy/data_sharing/

editors with publication following the journal's criteria. The peer-review aims to foster integrity among scientific papers by sorting quality-control measures to identify and remove invalid papers. After approval or non-approval from the US Food and Drug Administration, such requests were conducted for drug application to ensure any medical treatment safety measures. As a result, a peer-reviewed medical journal includes an oversight process after finalizing a clinical study for an accurate and relevant publication.

1.5. Conclusion and Discussion

The importance of developing a clinical research framework is to facilitate oversight of federal research regulations. Throughout a clinical framework promotes effective communication between physician and patient while gathering crucial data; this is a challenging task. Having research that forces a patient's privacy measures throughout a study contributes to improving patient care. A clinical research framework aims to optimize planning when conducting a clinical trial at WNVMC. Ultimately, a PI would interpret the research findings in compliance with good clinical practices following a peer review process before publication.

Chapter 2. Required Training

Identifying the federal regulations and responsibilities of PIs during clinical research helps develop a clinical research framework. Various methods can certify protocol requirements, starting with the PI's recognition of the researcher responsible for dispensing and administering medical interventions to a research participant (21 CFR 312.3). PIs are accountable for initiating and conducting a clinical research study. At WNVMC, a PI is a board-certified physician who already performs clinical functions following ethical principles.

2.1. Research Workshops

Following workshops that promoted continuous education on PIs and CRC training curriculum on training programs will expand in developing skills to start up a clinical research framework at WNVMC. Organizing efforts between CITI programs with WNVMC further contributes to the well-being of clinical research, the clinical research associate (CRA) manager to create new relations during the training and conference that the National Council of University Research Administrators (NCURA) would offer. NCURA is an organization with professional research administrators and sponsored programs that offer annual meetings for networking and networking information on services that could help support the institution.

2.2. Code of Federal Regulations

The Code of Federal Regulations (CFR) is an annual edition on the codification of regulations published in the Federal Register by federal agencies. The codification structure is divided into title, part, subpart, and revision year. Each chapter subdivides depending on the

information within a CFR citation. Federal agencies are in charge of keeping up-to-date citations for refining search results.

2.3. CITI (Collaborative Institutional Training Initiative) Program

As part of the clinical checklist of elements for PIs, a series of certifications are required to conduct a clinical research at WNVMC. Completing the CITI program includes certification on:

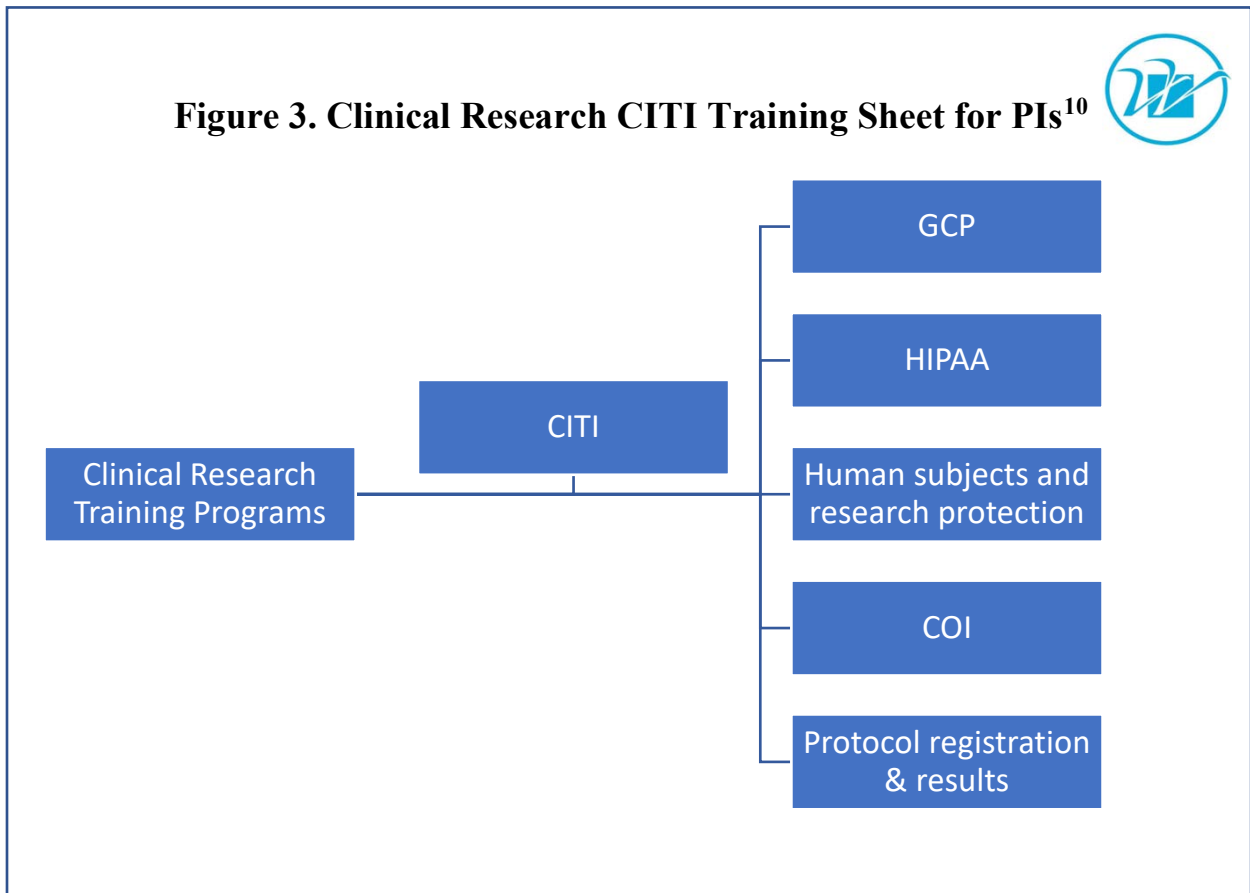
- Good Clinical Practice,
- HIPAA,
- Human subjects in research protection,
- Conflict of Interest, and
- Protocol Registration and Results

The CITI program fosters integrity between healthcare institutions and research organizations, dedicated to offering training courses on enhancing human research protections. Hospital-based training to further enrich research education by encouraging good clinical practice when disseminating research findings. Tracking the number of publications of PIs at WNVMC could determine new ways for implementing research training programs to participate in live session conferences as a group session. The hospital culture must promote values and attitudes to support federal policy compliance for providing a patient's best treatment.

Training Elements for Clinical Research

- Principal Investigator meets institutional requirements to conduct clinical research.
- Research Committee may impart policies and procedures for a multidisciplinary approach to conducting clinical research.

- Transparency when establishing a research budget per study providing financial expenses.



For more information about other featured courses, please visit the CITI website: <https://www.citiprogram.org/index.cfm?pageID=14>. This website has been at the forefront of online compliance training for over two decades. The CITI programs offer the latest federal regulations in clinical research, ethics, and healthcare institutions' compliance.¹¹ Every three years, PIs will need to renew the CITI program certification and present a printout version of completion to the CRC at WNVMC.

¹⁰ CITI Program “GCP for Clinical Trials” (2020), <https://about.citiprogram.org/en/course/good-clinical-practice-basic-fda/>

¹¹ CITI Program “Benefits for Organization” (2020), <https://about.citiprogram.org/en/advantages-for-organizations/>

Chapter 3. Regulatory Oversight

Clinical research in healthcare systems relates to clinical practices while reviewing and planning methodology and publication. Addressing ethical and legal issues is vital when disclosing various elements during a research study to ensure a well-designed project integrity following good clinical practice. In the development of clinical research, the PI tends to delegate most responsibilities. Therefore, having a well-trained PI and research administrator will further help pursue best practices through clinical research oversight. Developing a clinical research framework in a medical center includes a complex set of coordinative tasks promoting communication between PI and CRC while creating a timeline.

3.1. Research Committee

The Research Committee at WNVMC reviews institutional research proposals and activities following federal guidelines. All PIs are responsible for reviewing *Clinical Trials Workflow Appendix 1*, *Clinical Research Checklist for PIs Appendix 2*, and *Informed Consent Elements Checklist Appendix 3* to comprehend the required documents expected before presenting a request to conduct research to the Research Committee. After the Research Committee reviews all the required documents for PI, training certifications, and appropriate medical licensing for practice as shown in Figure 4., they will approve the research application submission.

The Research Committee will review the Clinical Research Handbook every two years for keeping up-to-date information on federal guidelines.

3.1.1. Research Committee Functions

The main functions of the Research Committee are:

- To make recommendations on policy matters relating to clinical research.
- To review licenses of medical researchers following institutional policy on research integrity and ethics.
- To oversee quality management activities
- To review Annual Reports relating to clinical research and make recommendations.
- To approve procedures when allocating funds for enhancing PIs training programs.
- To establish and promote communication between PIs and advisory committees on ethical policy of clinical research.

Figure 4. Regulatory Documents for PIs¹²



PIs are required to present to the CRC at the Research Department the following approvals as requisite to start with a clinical research study at WNVMC:

- Informed consent from study participants _____
- U.S. Food and Drug Administration _____
- U.S. Office for Human Research Protections _____
- Independent Ethics Committee (e.g. IRB) _____
- Financial Disclosure Form _____
- After the above checklist is completed then, _____ Institutional approval

¹² NIH “Regulatory Binder Checklist” (2014), Regulatory_Binder_Checklist_ver3_07-17-2015 (2)

3.2. Conflict of Interest

It is important to be guided through managing conflicts of interest to increase transparency between the PI and participant. A conflict of interest (COI) refers to challenging situations in which financial gains or personal considerations may compromise the integrity when conducting research. Federal regulations recommend promoting disclosure of activities and promotes the implementation of a committee that would monitor such disclosure forms.¹³

3.3. Financial Disclosure Form

PIs must address financial disclosure under the Department of Health and Human Services. The PI needs to disclose financial interests, arrangements, and payments (21 CFR § 54.4 (a)(3)), thus reporting of investigator, spouse, and dependent children.

- Any proprietary interest tests a product including, patent, trademark, copyright or licensing agreement.
- Any equity in a sponsor and the company or institution interest exceeds \$50,000 in value during the time the clinical research study was carried up to one year after completion.
- Request an application form provided by WNVMC for financial disclosure.

3.4. Reporting to the Institutional Review Board (IRB)

Under FDA guidelines, IRBs have the authority to approve or disapprove research involving human participants. On a federal level, regulation can safeguard participants' well-being depending on a complete reviewal of institutional, legal, and scientific publications.

3.4.1. Initial Clinical Study Submission to the IRB

¹³ UCSF "Conflict of Interest in Research" (2020), <https://coi.ucsf.edu/>

The initial submission of a clinical research study to the IRB that involves human subjects (does not apply to research involving fetuses or pregnant women) may undergo one of three types of review:

- a) Exempt review; such category includes surveys, interviews, educational and public observations as part of the analysis for the benefit of the public and consumer acceptance.
- b) Expedited review; such category includes clinical studies involving drugs and medical devices, collecting blood samples, biospecimens, noninvasive procedures, and research involving materials (data, documents, records, or specimens). Also, the expedited may include the following: video, digital, voice, or any image for research purposes.
- c) Full Board Review; applies for research that is greater than minimal risk and does not qualify for exempt or expedited review.¹⁴ After the PI completed identifying the above category will send the completed application and documents to the IRB inbox at irb@wnvmc.edu.

For IRB, initial submissions for exempt and expedited reviews will not have a deadline for modifications, but it is recommended to have all pertinent documents 30 days before the project expiration date following IRB protocol for early submission.

3.5. Systematic Literature Reviews

A systematic literature review overviews published papers related to the research topic. Conducting an in-depth approach to a systematic literature review before initiating in a clinical

¹⁴ BU “Initial Submission” (2020), <http://www.bu.edu/researchsupport/compliance/human-subjects/submitting-an-irb-protocol/>

research proposal will interpret recruitment methods, questionnaires, and statistical strategies that support the study's value.

3.6. Contract Research Organization

Regulatory services can facilitate a company or institution on biotechnology and medical device services on a contract agreement. A contract research organization (CRO) aims to lower costs for institutions that are developing new drugs and medicine to assure the new technology entry into drug marketplaces.

3.7. Investigational New Drug

The application process for an investigational new drug (IND) for placebo-control, dose comparison, and active-treatment control may be subject to FDA regulations (21 CFR 314.126). Before any new drug or biological effect may enter the market, the PI needs to take into account deadlines and permits. Deciding whether risking exposure subjects for a study to collect valuable information may require approval from IRB which faces challenging ethical issues (FDA-2014-D-1288).¹⁵

¹⁵ FDA "Drug Study Designs" (1998), Last revised on 2014, <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/drug-study-designs>

Chapter 4: Data Capture Tools

A case report form (CRF) design tends to be an electronic-based assisting institution when designing a good Electronic Case Report Form (eCRF). The purpose of data capture tools is to design a form that would lower the cost, be easy to follow and save time for participants and PIs. Having an eCFR would increase monitoring data quality and compliance with communication among participants and PI. An important aspect of eCRF is when handling sensitive information by providing a platform that promotes security measures. The CRF records each human participant's data and other information during the clinical research trial following institutional protocols.

Please do not confuse with the Electronic Code of Federal Regulations (e-CFR) currently updated as of November 25, 2020, following amendments produced by the National Archives and Records Administration's Office of the Federal Register (OFR) governmental office.¹⁶

4.1. Standard Case Report Form Design

A standard design is required when planning an eCRF intended to gather accurate data by facilitating source documents for a safe and efficient method essential to support data entry. The standardized case report design comprises a PI, clinical research coordinator, data manager, biostatistician, database programmer, and other data entry personnel. Also, eCFR must be user-friendly to adhere to and facilitate data analysis for PI.

For best practices using eCRF is to eliminate uncertainty when formulating questions, try using *yes* and *no* answers to remove the discrepancy. Another principle is to avoid using the free

¹⁶ e-CFR "Electronic Code of Federal Regulations" (2020), <https://www.ecfr.gov/cgi-bin/ECFR?>

text option since it requires additional forms for quantifying data. In most cases, a clinical research coordinator will support the PI by encouraging multiple-choice questions for a definite and concise answer.

During the clinical research trial management, the software captures and safely integrates research calendar, billing per visit, and helps keep track of IRB submissions.

4.2. Software Database for Clinical Research Trials

A software database supports collaboration to monitor patient data for managing protocol development during clinical research trials. For example, clinical research modules consist of patient registry and biospecimen management in a multidisciplinary approach such as *REDCap* and *OnCore* (Research Electronic Data Capture) used by academic institutions such as Johns Hopkins University, University of Maryland, and the University of Washington, among others. Both databases are secure websites that help institutions build and manage multi-site research studies and online surveys. A good clinical practice must provide a flexible data entry design to help manage daily patient count and tasks.

Clinical Research Management Software must include the following:

- Electronic case report forms to export on excel or SAS/OR software
- Monitoring data
- FDA annual reports
- Following federal protocol and interact with Clinicaltrials.gov
- Tracking patient visits and scheduling capabilities
- Budgeting and billing
- Task management

- Optimize security¹⁷

REDCap supports more than 4683 institutions as a network collaborator in 139 countries. Also, REDCap is a browser that supports researchers who manage clinical research projects as a secure research electronic database following the Health Insurance Portability and Accountability Act (HIPAA). For more information about REDCap, please visit the website and join the software at: <https://projectredcap.org/partners/join/>.

Also, OnCore is software for clinical research for patient registry and biospecimen management in academic institutions such as Yale University, University of California, and the University of Wisconsin. For more information about OnCore, please visit and join the software at <https://www.advarra.com/oncore-enterprise-research-ctms/> and request a demo.

¹⁷ Yale University “What is *OnCore*?” School of Medicine, (2020), <https://medicine.yale.edu/ycci/oncore/what/>

Chapter 5. Legal Considerations

In clinical research, the legal and ethical considerations related to an agreement form between the participant and the PI under the informed consent about confidentiality and ways to diminish any research misconduct.¹⁸ Informed consent is a form of a guidance document; although guidance documents are not laws, such documents have a legal value. Therefore, CRC's will provide additional administrative efforts responsible for coordinating and implementing procedures before the applicable statute.

PIs must comply with good clinical practice standards by providing a systematic approach to collecting and analyzing human participants' data. The core principles of defining responsibilities of PIs, informed consent process, and auditing procedures related to protecting research integrity of all participants to comprehend the clinical framework at WNVMC.

The FDA and IRB plan to coordinate with federal agencies to facilitate uniformity across policies that incorporates Common Rule. In respect to the three main core ethical principles, following *The Belmont Report*:

- Respect for persons – respecting participants autonomy for research voluntarily,
- Beneficence – to protect participants from any harm and to maximize benefits, and
- Justice – when promoting equality by mitigating against participants' vulnerability and researchers financial gain.¹⁹

According to the PIs, understanding the participants' risk of benefit versus harm will help determine whether the proposed clinical research respects ethical principles. The legal framework on FDA's oversight is statutory of clinical research study for testing effectiveness and

¹⁸ Camille Yip et. al. “Legal and ethical issues in research” (2016), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5037952/>

¹⁹ HHS “The Belmont Report” (1979), <https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/read-the-belmont-report/index.html#:~:text=Beneficence.,under%20the%20principle%20of%20beneficence.>

safety under Section 505(i). The Code of Federal Regulations (CFR) assists and ensures the responsibilities of sponsors and PIs.

During the development of clinical research at WNVMC the PI must consider overseeing the progress to ensure reported data is following institutional protocols, Good Clinical Practice, Standard Operating Procedures (SOPs), and federal regulatory requirements. SOPs (ICH E6 Good Clinical Practice and 21 CFR 50) contain a clear guide for research staff describing everyday functions to achieve a specific goal within a timeline.

5.1. Research Contract

Research contracts contain the terms and conditions under which the institution conducts clinical research. A research contract is a written document that is a legally binding agreement that oversees collaboration among institutions, including funding and research conduct.²⁰

A research contract acts on behalf of the PI and the institution to negotiate agreements while assessing and managing risks. During the consultation process the PI with the guidance of a clinical research coordinator will organize appropriate terms, including the following concepts:

- Describes requirement of each party
- Ensure protection of interest of medical researchers
- Protects WNVMC interest
- Protects collaborator requirements
- Provides advice and support for managing risk

CRCs help support contract agreements when planning clinical research while planning to draft a proposal that protects intellectual property and copyright contracts.

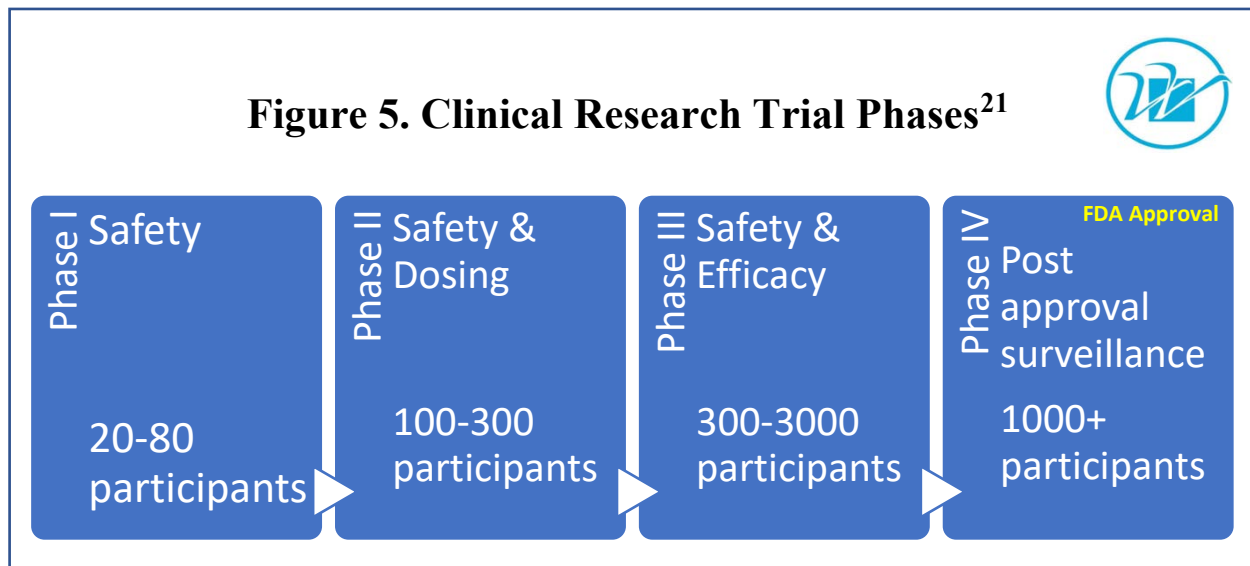
²⁰ University of Cambridge “What is a research contract?” (2020), <https://www.research-operations.admin.cam.ac.uk/research-contracts/introduction-contracts/what-research-contract#:~:text=Research%20contracts%20are%20legally%20binding,conduct%20of%20the%20research%20itself.>

Chapter 6. Project and Budget Management

6.1. Project Management Plan

A project management plan reflects aspects of time, quality, communication, resources and cost involved in clinical research activities. To prepare an effective and fitting plan during development of clinical research that helps identify and control the business activities efficiently.

If the clinical research will conduct a Phase IV study for FDA approval including a Clinical Study Report (CSR). The main purpose of presenting a project and budget management plan is to display a CSR that compiles the relationship between sustainability, research management, and regulatory requirements. A CSR is prepared upon completion of a clinical research trial, where the sponsor requires a detailed report of the medical study. Usually CSRs involved with a sponsor request a non-disclosure agreement following approval used in drug entry for FDA approval as shown in Figure 5. A clinical report simplifies and harmonizes the system for disclosing results for the FDA’s application for the decision-making process within a multi-phase integrated assessment regarding risk and benefit for new drug products.



²¹ ILD Collaborative “Clinical Trial Phases” (2020), <https://www.ildcollaborative.org/resources/phase-iii-ipf-clinical-trials>

A PI and CRC will start planning and dividing the following phases after developing a preliminary project scope. A best practice for project management is to break down the organizational structure with the project management team, **comprised of** the PI (could be more than one), grant writer, clinical research coordinator, and a software programmer once an invitation from a sponsor program is received:

- Prepare a contract negotiation
- Gather documentation following IRB guidelines for approval
- Apply for Institutional Ethical Committee application
- Read the application and approval thoroughly
- Prepare an inform consent of biospecimen and type of study for analysis
- Statistical analysis and comparison with a previous study on the subject
- Final report and delivery
- Sponsor and Internal audits
- Study close-down²²

Remember to thank participants and be engaged throughout the entire clinical research trial.

6.2. Budget Management Plan

A budget management plan help identify financial and strategic risks when developing clinical research. PIs must plan to draft a research proposal and comprehend that there is a risk and should not waste funding, time, and effort. During the team's recruitment, consider the following audits to comply with financial disclosure. At WNVMC, the PIs and clinical research staff have support salaries for which the institution provides private healthcare insurance and

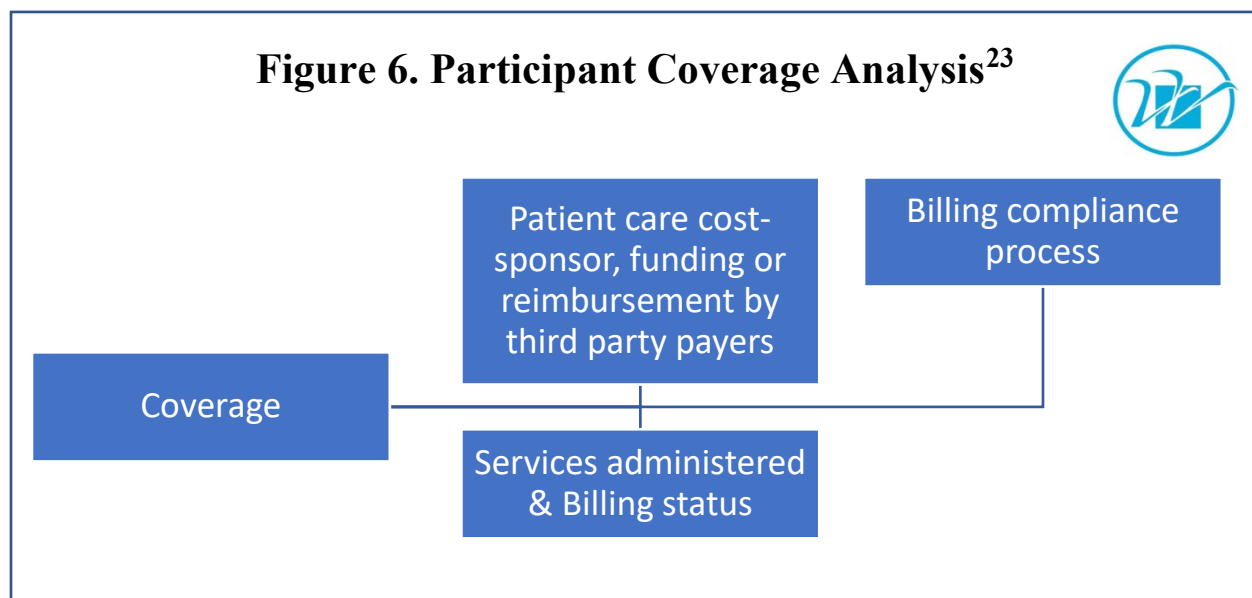
²² Doganov Boyan, Yanev Slanislav "Implementation of project management principles in clinical trial process" (2006) Project Management Institute, <https://www.pmi.org/learning/library/project-management-principles-clinical-trial-pharmaceutical-8206>

hospital donations. Salary progression related to research staff appoints an annual pay review for clinical staff as an incentive for a medical research study at WNMVC while reporting pay data analyses.

During the budget negotiation process, the PI and the CRC must create a checklist that describes the process before applying to a sponsor. The checklist must include raw material acquisition; if a drug-trial determines each phase cost by understanding the invoiced cost and per-patient treatment costs.

6.2.1. Budgeting Negotiation and Finance

In the budget negotiation and financing plan process, the PI decides whether the study is feasible following budget allocation for staff and project management, including per patient care costs, as shown in Figure 6. A major risk of not performing a coverage analysis is under billing, loss of trust by a sponsor and participants, civil fines, and increased costs associated with clinical research.



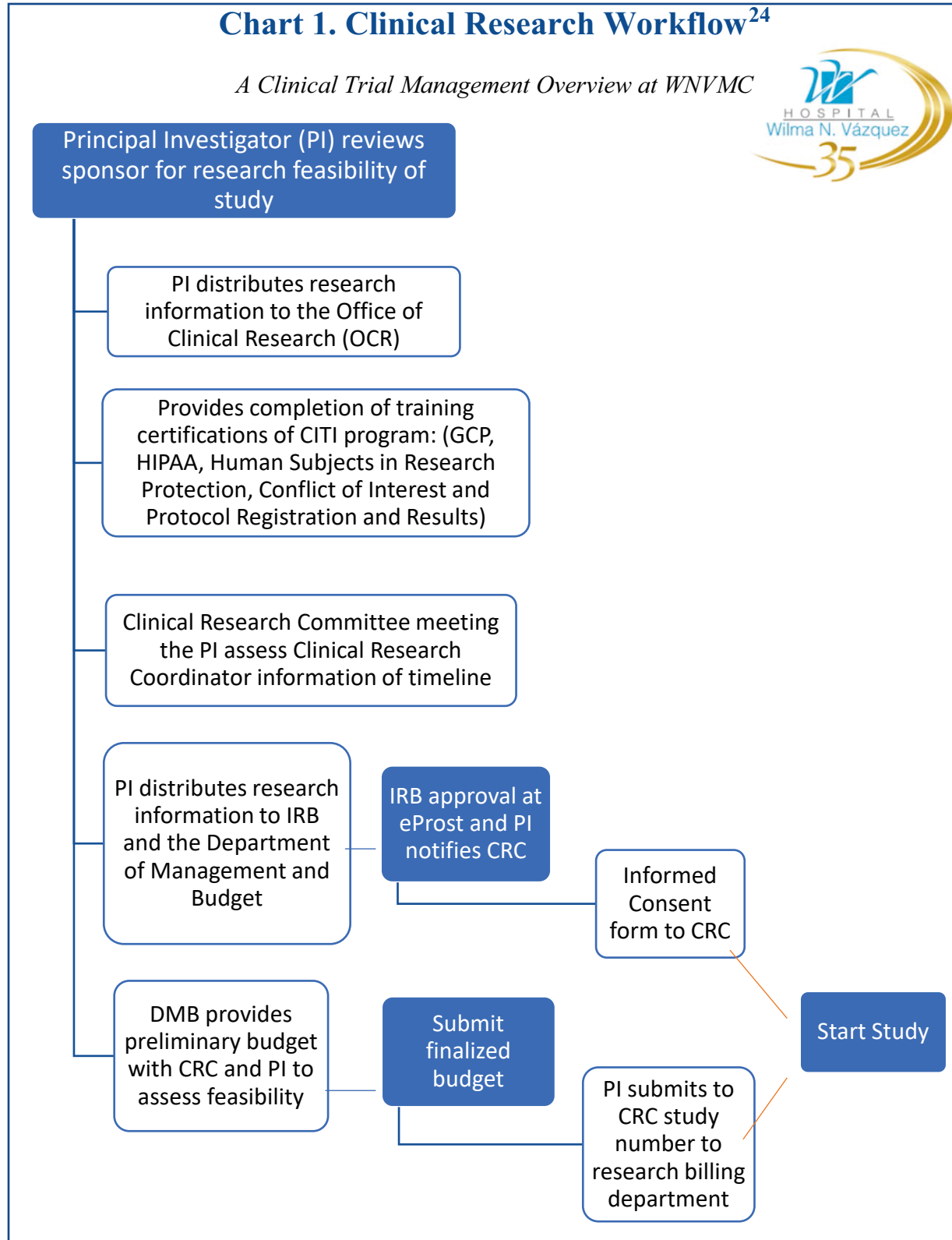
²³ Terry Stone, Kati Cini “Clinical Trial Budgeting and Negotiation” (2018), <http://www.bumc.bu.edu/crrro/files/2018/03/RPN-Clinical-Trials-Budgeting-and-Negotiation-3-8-18.pdf>

Reference

- Alahmad, Ghiath “Informed Consent Process” King Abdullah International Medical Research Center (2014), <https://www.slideshare.net/GHIATH-MD/informed-consent-process>
- Barney, Jeri and Antisdell Michele “Common Problems in Informed Consent” Human Research Protection Program, Yale University (2013), [commonproblemsininformedconsent_2013_vf](https://www.yale.edu/humanresearch/protected/commonproblemsininformedconsent_2013_vf)
- Boston University Research Support “Initial Submission” (2020), Med Campus IRB, <http://www.bu.edu/researchsupport/compliance/human-subjects/submitting-an-irb-protocol/>
- Boyan Doganov, Stanislav Yanev “Implementation of project management principles in clinical trial process” Global Congress (2006) Project Management Institute, <https://www.pmi.org/learning/library/project-management-principles-clinical-trial-pharmaceutical-8206>
- CITI Program (2020). Explore our courses, https://about.citiprogram.org/en/courses/?fwp_search=protocol%20and%20registration
- CITI Program “Benefits for Organization” *Experience & Reputation* (2020), <https://about.citiprogram.org/en/advantages-for-organizations/>
- CITI Program “GCP for Clinical Trials with Investigational Drugs and Medical Devices” (2020), <https://about.citiprogram.org/en/course/good-clinical-practice-basic-fda/>
- Columbia University (2016). Clinical Research Handbook. Version 7, retrieved from https://glori.kg/wp-content/uploads/2017/08/ClinicalResearchHandbook_EN.pdf
- e-CFR “Electronic Code of Federal Regulations” National Archives and Records Administration (2020), <https://www.ecfr.gov/cgi-bin/ECFR?>
- FDA (2020). Clinical Trials: What Patients Need to Know, <https://www.fda.gov/patients/clinical-trials-what-patients-need-know#:~:text=Clinical%20trials%20are%20voluntary%20research,does%20not%20conduct%20Clinical%20Trials.>
- FDA “Informed Consent” *Draft guidance for IRBs, Clinical Investigators, and Sponsors* (2014), <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/informed-consent>
- FDA “Drug Study Designs” (1998), *Guidance for Institutional Review Boards and Clinical Investigators*, Last revised on 2014, <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/drug-study-designs>

- Friedman LM, Furberg CD, DeMets DL. (1996) *Fundamentals of Clinical Trials* (3 ed.). Missouri: Mosby-Year Book Inc.
- HHS “The Belmont Report” *Office for Human Protections* (1979), <https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/read-the-belmont-report/index.html#:~:text=Beneficence.,under%20the%20principle%20of%20beneficence.>
- ILD Collaborative “Clinical Trial Phases” (2020) *A Patient-Physician Collaborative for the Understanding, Management, and Treatment of Interstitial Lung Diseases*, <https://www.ildcollaborative.org/resources/phase-iii-ipf-clinical-trials>
- NIH “Data Sharing Policy” Grants, Funding for Data Management and Sharing (2020), https://grants.nih.gov/grants/policy/data_sharing/
- PhD Assistance “Why is theoretical framework important in research?” *Research Methodology* (2019), <https://www.phdassistance.com/blog/why-is-theoretical-framework-important-in-research/>
- Pick Andrew, Gilbert Kayleigh, and McCaul James “The role of effective communication in achieving informed consent for clinical trials” *Nursing Standard* (2014) 29, 10, 45-48, <https://journals.rcni.com/nursing-standard/the-role-of-effective-communication-in-achieving-informed-consent-for-clinical-trials-ns.29.10.45.e9443#:~:text=Informed%20consent%20is%20fundamental%20to,would%20like%20to%20take%20part.>
- Saczynski Jane, McManus David, and Goldberg, Robert “Commonly utilized data collection approaches in clinical research” *PMC* (2013), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3827694/>
- Stone Terry, Cini Kati “Clinical Trial Budgeting and Negotiation” Boston Medical Center (2018), <http://www.bumc.bu.edu/crro/files/2018/03/RPN-Clinical-Trials-Budgeting-and-Negotiation-3-8-18.pdf>
- The Ohio State University “Clinical Trials Workflow” Office of Research and Sponsored Programs (2020), <https://osp.osu.edu/development/sponsors/clinical-trials-workflow/>
- The Ohio State University “The Ohio State University Consent to Participate in Research” Office of Responsible Research Practices (2019), <https://orrr.osu.edu/irb/investigator-guidance/exempt/>
- UCSF “Conflict of Interest in Research” *Office of Ethics and Compliance* (2020), <https://coi.ucsf.edu/>
- University of Cambridge “What is a research contract?” Research Operations Office (2020), <https://www.research-operations.admin.cam.ac.uk/research-contracts/introduction-contracts/what-research->

Appendix 1. Clinical Research Flowchart



²⁴ The Ohio State University “Clinical Trials Workflow” (2020), <https://osp.osu.edu/development/sponsors/clinical-trials-workflow/>

Appendix 2: Clinical Research Document Checklist

Chart 2. Clinical Research Checklist for PIs²⁵

The purpose of this checklist is to inform the research team and grantees of the necessary documentation before starting a clinical research trial at WNVMC.

Principal Investigator: _____

Department / Clinical: _____

Title: _____



Please specify the type of submission:

Initial submission Annual submission (renewal)

COMPLETED DOCUMENTS:

Principal Investigator Curriculum Vitae

Clinical licensure of PI and DEA license

IND studies: Form 1572

Intramural studies: Form 1195

Financial Disclosure Statements for Investigational New Drug studies submitted to FDA

IRB approval letter of Protocol Amendment

IRB approval letter of subject recruitment

IRB approval of Informed Consent

If applicable laboratory certifications for tests

Certificate from CITI Program on: *Good Clinical Practice, HIPAA, Human Subjects in Research Protection, Conflict of Interest, and Protocol Registration and Results*

²⁵ Harvard Cancer Center "Startup and Activation Checklist" (2017), Sample_Research_Start_Up_Checklist%20(1).pdf

Appendix 3: Informed Consent Elements Checklist

**Chart 3. 8 Basic Elements Checklist Required in an
Informed Consent Form²⁶**



Please mark the following completed elements on the informed consent form:

1. An invitation to participate _____
2. Risk of the study _____
3. Benefits and possible outcomes _____
4. An alternative to participation _____
5. A confidentiality statement _____
6. Stating the know about of compensation for medical treatment _____
7. Contact information of the PI, CRC, and the medical facility _____
8. Voluntary participation / withdrawal _____

²⁶ Jeri Barney, Michele Antisdell "Common Problems in Informed Consent" Yale University (2013), commonproblemsininformedconsent_2013_vf

Appendix 4: Informed Consent Template²⁷

Please delete instructions in italicized in blue font and replace with applicable language.

CONSENT
EXEMPT

Protocol Number:
Approval Date:



Wilma N. Vazquez Medical Center Consent to Participate in a Clinical Research Trial

Study Title:

Researcher:

Sponsor:

This is a consent form for clinical research participation. It contains important information about this clinical research study and what to expect if you decide to participate.

Your participation is voluntary.

Please consider and read the following information carefully. Feel free to ask any questions before making your decision whether or not to participate. If you decide to participate, you will be asked to sign this form and will receive a copy of the form.

Purpose:

Procedures/Tasks:

Duration:

You may leave the study at any time. If you decide to stop participating in the study, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. Your decision will not affect your future relationship with Wilma N. Vazquez Medical Center.

²⁷ The Ohio State University "The Ohio State University Consent to Participate in Research" (2019), <https://orpp.osu.edu/irb/investigator-guidance/exempt/>

Risks and Benefits:

Confidentiality:

Efforts will be made to keep your study-related information confidential. However, there may be circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law. Also, your records may be reviewed by the following groups (as applicable to the research):

- Office for Human Research Protections or other federal, state, or international regulatory agencies;
- Office of Responsible Research Practices;
- The sponsor, if any, or agency (including the Food and Drug Administration for FDA-regulated research) supporting the study.

Future Research: (Include one of the statements below if de-identified information will be used or shared for future research and delete the other)

*Your de-identified information may be used or shared with other researchers.

Incentives:

By law, payments to participants are considered taxable income. *(Please remove the following statement if participants will not receive compensation.)*

Participant Rights:

You may refuse to participate in this study without loss of benefits to which you are otherwise entitled.

If you choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. By signing this form, you do not give up any personal legal rights you may have as a participant in this study.

This study has been determined *Exempt from IRB review*.

Contacts and Questions:

For questions, concerns, or complaints about the study you may contact

_____:
For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who part of the research team is not, you may contact the WNVMC Clinical Research Department at 787-858-1580 ext. 3194.

Signing the consent form

I have read (or someone has read to me) this form, and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study.

I am not giving up any legal rights by signing this form. I will be given a copy of this form.

Printed name of participant

Signature of participant

Date and time

Principal Investigator

I have explained the research to the participant or his/her representative before requesting the signature(s) above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

Printed name of person obtaining consent

Signature of person obtaining consent

Date and time

Biography

Nancy Yanira Pérez Torres received a B.A. degree in Psychology from the University of Puerto Rico and earned her M.D. from the Iberoamericana University in the Dominican Republic. Nancy also obtained her Master of Science in Research Administration from Johns Hopkins University to support clinical research compliance in legal and regulatory issues. The author's research interest is to ensure the patients' rights and safety during clinical trials following federal guidelines. The author is currently working in the Department of Pulmonary and Critical Care at Wilma N. Vazquez Medical Center in Puerto Rico.