Randhawa, Pawanpreet, Assisting the Implementation of a Centralized IRB in Multiple Categories of Research at Medical City of Fort Worth. Master of Science (Clinical Research Management), April, 2017, 110 pp., 2 figures, 27 appendices, reference list, 17 titles.

Introduction: As a collection of ethical principles and guidelines regarding biomedical research on humans, the Common Rule has remained largely unchanged since its inception while the clinical research landscape has grown dramatically in size and complexity. Now with the Common Rule being modernized, one of the proposed changes being executed is the requirement of a centralized Institutional Review Board (IRB) for multi-site research studies. This transition of a research site operating under a local IRB to a centralized IRB is expected to greatly improve collaborative studies. **Objective**: The main goal of this practicum project is to assist in the implementation of a centralized IRB for multi-site research at Medical City of Fort Worth in order to comply with the changes to the Common Rule. **Methods/Results**: To achieve the goal of this practicum project, the operational rules and regulatory processes at Medical City of Fort Worth were updated. This included revising the institutional IRB and FWA, adverse event and serious adverse event reporting, and audit policies, establishing a local database for active studies, converting study-related materials to an e-records system, and revising the institutional exemption status policy. **Conclusion**: These activities led to the completion of the transition of Medical City of Fort Worth from a local IRB to a centralized IRB. Additionally, documentation of the process yielded a procedural guide for other institutions undergoing the same transition.

ASSISTING THE IMPLEMENTATION OF A CENTRALIZED IRB IN MULTIPLE CATEGORIES OF RESEARCH AT MEDICAL CITY OF FORT WORTH

PRACTICUM REPORT

Presented to the Graduate Council of the

Graduate School of Biomedical Sciences

University of North Texas

Health Science Center at Fort Worth

in Partial Fulfillment of the Requirements

For the Degree of

MASTER OF SCIENCE IN CLINICAL RESEARCH MANAGEMENT

By

Pawanpreet "Bobby" Randhawa, B.S.

Fort Worth, Texas

April 2017

ACKNOWLEDGMENTS

I would first like to recognize the research team at Medical City of Fort Worth for providing me with an outstanding internship experience over the past six months. A great deal of thanks to Dr. Rubina Muzina for her incredible mentorship and support. She invested countless hours in helping me gain practical knowledge in the field of clinical research, for which I am grateful. A special thank you to Bhagawathy Sarma and Brenda Tapia for your continued assistance and support throughout my internship experience.

I would like to greatly thank Dr. Patricia Gwirtz. She has been extremely patient and supportive throughout my practicum project, let alone my time at UNTHSC. I am beyond grateful for her investment in me and my future. I would also like to extend my thanks to Dr. Caroline Rickards and Dr. Stephen Mathew, my committee members, for their assistance and input during the thesis process. Their guidance was indispensable to the overall success of my project.

Finally, I am thankful for my friends and family for their continuous support and encouragement

TABLE OF CONTENTS

FIGURE LIST/APPENDIX LIST

Page

Page

LIST OF ABBREVIATIONS

- **AE** – Adverse Event
- **CFR** – Code of Federal Regulations
- **CITI** – Collaborative Institutional Training Initiative
- **FDA** – Food & Drug Administration
- **FWA** – Federalwide Assurance
- **GCP** – Good Clinical Practices
- **HHS** – Department of Health & Human Services
- **ICF** – Informed Consent Form
- **ICH** –International Conference for Harmonization of Technical Requirements for Pharmaceuticals for Human Use
- **IRBO** – IRB Organization
- **IRB** – Institutional Review Board
- **NIH** – National Institutes of Health
- **NPRM** – Notice of Proposed Rulemaking
- **OHRP** – Office for Human Research Protections
- **PI** – Principal Investigator
- **SAE** – Serious Adverse Event
- **SOP** – Standards Operating Procedure
- **WCG** – WIRB-Copernicus Group
- **WIRB** – Western Institutional Review Board

CHAPTER I

Introduction

As a collection of ethical principles and guidelines regarding biomedical research on humans, the Common Rule has been pivotal in human subject protection. In the time since its inception by numerous federal departments and agencies in 1991, the set of federal regulations and policies serving as the source for these ethical rules has remained largely unchanged. Conversely, within that same time frame, "the clinical research landscape has vastly changed, with dramatic increases in complexity, collaboration, and cost" [1]. In order to adapt to the current research environment, a number of federal agencies and departments, such as the National Institutes of Health (NIH) and the Food and Drug Administration (FDA), have proposed changes to the current policies and regulations from which the Common Rule is derived. One of the primary elements requiring modernization is the use of multiple Institutional Review Boards (IRBs) for multi-site research. Currently, a majority of institutions participating in human research rely on local IRBs to evaluate research protocols and monitor trial operations. For collaborative studies, this system has led to a decrease in quality and efficiency for several reasons, such as increased time for complete review and approval through multiple, independent IRBs. As the number of multi-site human research trials continue to expand, there is a need to establish an efficient system which can ensure protection of human subjects within today's complex clinical research environment. Thus, with the upcoming revisions to the Common Rule, institutions have been encouraged to implement a centralized IRB. By transitioning to a central IRB, institutions could greatly improve collaborative studies in numerous ways, such as "reducing costs, ensuring consistency across all sites, and assist[ing] with study start-up and drug

approvals progressing more quickly" [2][3]. In addition, transitioning to a central IRB would benefit institutions and investigative sites by allowing a refocus of resources, reduction in investigator and research staff burden, and increased productivity in other areas of importance, such as adverse event management.

With several areas in clinical research requiring an update in order to ensure human subject protection within the current landscape, the numerous federal agencies that have adopted the Common Rule, such as the department of Health and Human Services (HHS), have issued national changes to the guidelines and regulations constituting this federal policy. Examples of these changes include enhancing security and privacy safeguards, requiring the use of central IRBs, strengthening and streamlining informed consent, and expanding the rule of oversight to include privately funded studies.

The primary objective of this practicum project is to update the standard of operational rules and local regulatory processes at Medical City of Fort Worth in light of the national changes to the Common Rule and the institution's transition to a central IRB. This practicum project is designed to assist and examine the process of transitioning an institution involved in multi-site human research from a local IRB to a centralized IRB. In order to accomplish this, local operational rules and regulatory processes will be revised and updated to comply with new policies and national changes. In addition, this study will seek to contribute to the development of efficient centralized IRB implementation methods.

CHAPTER II

Background

In 1979, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research published the Belmont Report. Centered around the concepts of justice, beneficence, and respect for persons, "this report would set forth the basic ethical principles for research involving human subjects" [4]. In 1981, the HHS and FDA revised existing federal regulations governing human subjects research to make those regulations compatible with the contents of the Belmont Report. This implementation of the Belmont Report led to the publication of The Federal Policy for the Protection of Human Subjects by HHS as part 46 of Title 45 of the Code of Federal Regulations (CFR)[5]. In 1991, this policy was adopted by eighteen federal agencies and departments, which led to its labeling as "The Common Rule". This system for protecting human research subjects "outlines the basic provisions for IRBs, informed consent, and Assurances of Compliance" [6]. Furthermore, the Common Rule provides additional protections for certain vulnerable research subjects, including pregnant women, fetuses, prisoners, and children.

While the Common Rule has governed the ethical conduct of research concerning humans for the last 25 years, these regulations have become outdated as the clinical research environment has vastly changed during the same time span. During the intervening years since the inception of the Common Rule, there has "been substantial growth in the amount of clinical research generally, the number of multicenter trials, and the size and complexity of late-stage trials" [6].

In response to the transitioning landscape within human research, the HHS and fifteen other federal departments and agencies have announced revisions to update and modernize the

federal policies and regulations from which the Common Rule is derived. The primary goals of this Notice of Proposed Rulemaking (NPRM) was to "enhance respect and safeguards for research participants and to increase research efficiency by reducing unnecessary burdens and calibrating oversight to the level of risk"[1]. The key changes brought forth by this update to the Common Rule include: requiring consent for research involving biospecimens, granting broad participant consenting requirements for future use of data and biospecimens, bolstering privacy and security safeguards in order to combat unauthorized use of data, requiring reliance on a single IRB for multi-site studies, and broadening oversight to include privately funded studies.[1]

Over 30 years ago, the Common Rule mandated IRBs to serve as local committees to review and provide oversight regarding the ethical aspects of research involving human subjects. Since the time of the Common Rule's inception, however, the expansion and development of the clinical research landscape has led to its policies becoming burdensome for sponsors and clinical investigators seeking IRB review for multi-site trials, as well as for IRBs performing the reviews. Amongst the numerous obstacles faced in these situations, the most prevalent are redundant review, extensive delays, and increased costs[8]. In response to these burdens faced by local IRBs in multi-site trials, as well as the national changes brought forth by the modification of the Common Rule, numerous federal agencies, including the FDA and the NIH, have issued proposals and policies that encourage the transition of multi-site research to utilize a single or centralized IRB.

Currently, two primary forms of IRB review and approval prevail amongst most institutions: local or centralized. Local IRBs are constituted by a committee within the institution which has the responsibility of overseeing the research performed within the single investigative

site. Central IRBs, in contrast, are a single committee responsible for reviewing and approving research for multiple investigative sites.

With the environment of human research having become more complex, expensive, and collaborative, the implementation of a central IRB can overcome the inefficiencies of local review and improve the quality and efficiency of multi-center trials[5]. One of the benefits of centralized IRBs is that they can resolve unnecessary delays[9]. "Local review can significantly delay research projects as protocols and other documents must be reviewed and approved by numerous IRBs before multi-site studies can be initiated. Sometimes the IRBs may disagree about changes to the research, which may require some back and forth before the project can be approved. Delays due to local review of multisite research can range from several weeks to several months" [9]. A centralized IRB would eliminate delays, such as redundant review, by allowing more frequent review by a consistent group of reviewers. Another benefit from the implementation of a centralized IRB is the reduction of costs. For investigative sites utilizing local review for multi-site research, some examples of costly expenses which arise include IRB submission preparation, "responding to IRB stipulations and queries, and submitting amendments, adverse events reports, and protocol violations, as well as expenses related to IRB review, such as support staff and administration" [9]. By utilizing a centralized IRB, an institution can relegate these responsibilities and costs to the single IRB. A third advantage of centralized IRBs is their ability to reduce the burden on investigators and research staff.[9] With the decrease in responsibility and duties for the staff, investigators can refocus resources and redeploy staff for activities directly related to human subject protection, such as recruitment and informed consent. Additionally, the staff may also divert their time and effort towards improving oversight on other studies, adverse event management, further training and educating staff, and quality

assurance. Finally, a fourth advantage of utilizing a centralized IRB is its bolstering of consistent human participant protection[9]. With the presence of numerous local IRBs, there is a prevalence of variability in local review of multi-site research. This variability from local review introduces three types of ethical concerns. "First, contradictory IRB requirements can lead to cost increases, frustration and delays, as investigators negotiate with different IRBs while shepherding their projects through the approval process. Second, variation in IRB practices suggests that IRBs are interpreting research regulations differently, and they cannot all be correct… Third, if IRBs reach different decisions concerning the same research proposal, then human participants may not receive equal protection." [9]. These ethical concerns and the number of other concerns posed by local IRBs can be resolved by a centralized IRB.

Despite the benefits brought about by the implementation of a centralized IRB, there is a reluctance by many institutions to shift to a single IRB for a number of reasons. One argument against central IRBs is their lack of local cultural context[9]. Through their consistent exposure and interaction with the local population, institutions can argue that local IRBs are more qualified and effective at undertaking the responsibility of reviewing various aspects of human research, such as consent forms, advertisements, recruitment strategies, and survey documents, because of their better grasp of the factors which are important to the community[9]. This advantage is thought to enhance the consent process, recruitment, and the protection of human participants. Another argument against centralized review is its reduced ability to address community needs and concerns. "Local IRBs, through the academic institutions that house them, reflect those institutions' complex relationships with their communities" [22]. Therefore, local IRBs are thought to be more accountable and accessible due to their integration within the community and regular interaction with community members[9]. A third concern about central

review is its less effective communication with investigators[9]. Due to the lack of the IRB being present within the institution, investigators would have to rely on long-distance communication, such as email or telephone, which causes a loss of comfort for investigators and possible delays. Finally, the fourth argument against central IRBs is institutional "liability for patient harm if there are problems in a clinical trial"[2]. This concern rises from the fact that a local site can still be sued for negligence or fraud, despite relying on a central IRB.

While these concerns about the implementation of central review are warranted, they are easily resolved by the collaboration of a central IRB with the local institution. By communicating with a committee of representatives from the institution, central IRBs would be able to gain insight of the local context within a certain community or population. This would allow the IRB to enhance informed consent and subject recruitment. Furthermore, collaboration with a local institution would allow information from the community to be relayed to the central IRB. In addition, the local institution can assume the duties of solving on-site issues and assume the responsibility of collaborating with PIs [23]. Utilizing effective communication between a local committee and the central IRB will allow a decrease in burden for investigators and research staff. Finally, despite a local institution relegating many of its responsibilities to a central IRB, the institution can maintain local oversight of research, thus minimizing liability risks for the local institutions.[2]

CHAPTER III

Significance of Practicum

Implementation of a centralized IRB could vastly improve the review and monitoring of multi-site human research through reducing delays, decreasing expenses, lessening investigator burden, and promoting consistency in human participant protection. With a number of federal agencies and departments proposing changes to those partaking in multi-site research to shift to a centralized IRB, each institution is responsible for transitioning their day-to-day operations to comply with these new policies. The goal of this practicum is to assist Medical City of Fort Worth in the transition from a local IRB to a centralized IRB. Accomplishing this goal should improve the efficiency and quality of research conducted at the site by reducing delays, saving money and other resources, decreasing the burden on research staff, and promoting consistency amongst sites participating in the study.

Because few institutions have undergone the change to a centralized IRB, there is little instruction on how to move forward with this process. As a result, this transition can create additional costs and burdens to the IRB process due to uncertainty in roles, responsibilities, and processes, such as consent approval. By documenting Medical City of Fort Worth's process of implementing a centralized IRB and the institution's organization of material for central IRB utilization, this practicum can provide other institutions with guidance and direction on how to facilitate the implementation of a single, centralized IRB efficiently.

CHAPTER IV

Methods/Results/Discussion

The transition of an institution from a local IRB to a centralized IRB and implementing the changes which accompany this transition requires numerous procedures. Figure 1 summarizes the process of transitioning from a local IRB to a centralized IRB. Once this transition has been completed, the institution must organize study material and update numerous policies and procedures in order to comply with the central IRB. Figure 2 summarizes the procedures done to organize study material and update site policies and procedures.

This practicum project was conducted at Medical City of Fort Worth. The research studies at Medical City of Fort Worth are all clinical trials focused on cardiovascular and neuroscience research. Currently, there are eleven research studies being conducted at the site which are under the involvement of four different PIs. The number of subjects within these studies range from fifteen to forty subjects depending on the study.

Figure 1: IRB Transition Process Summary

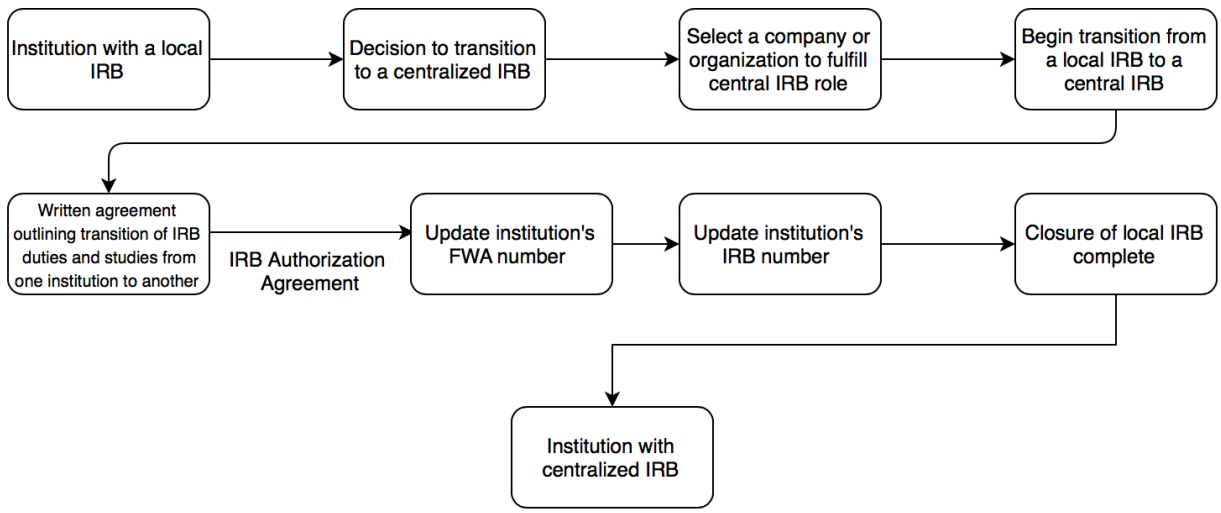
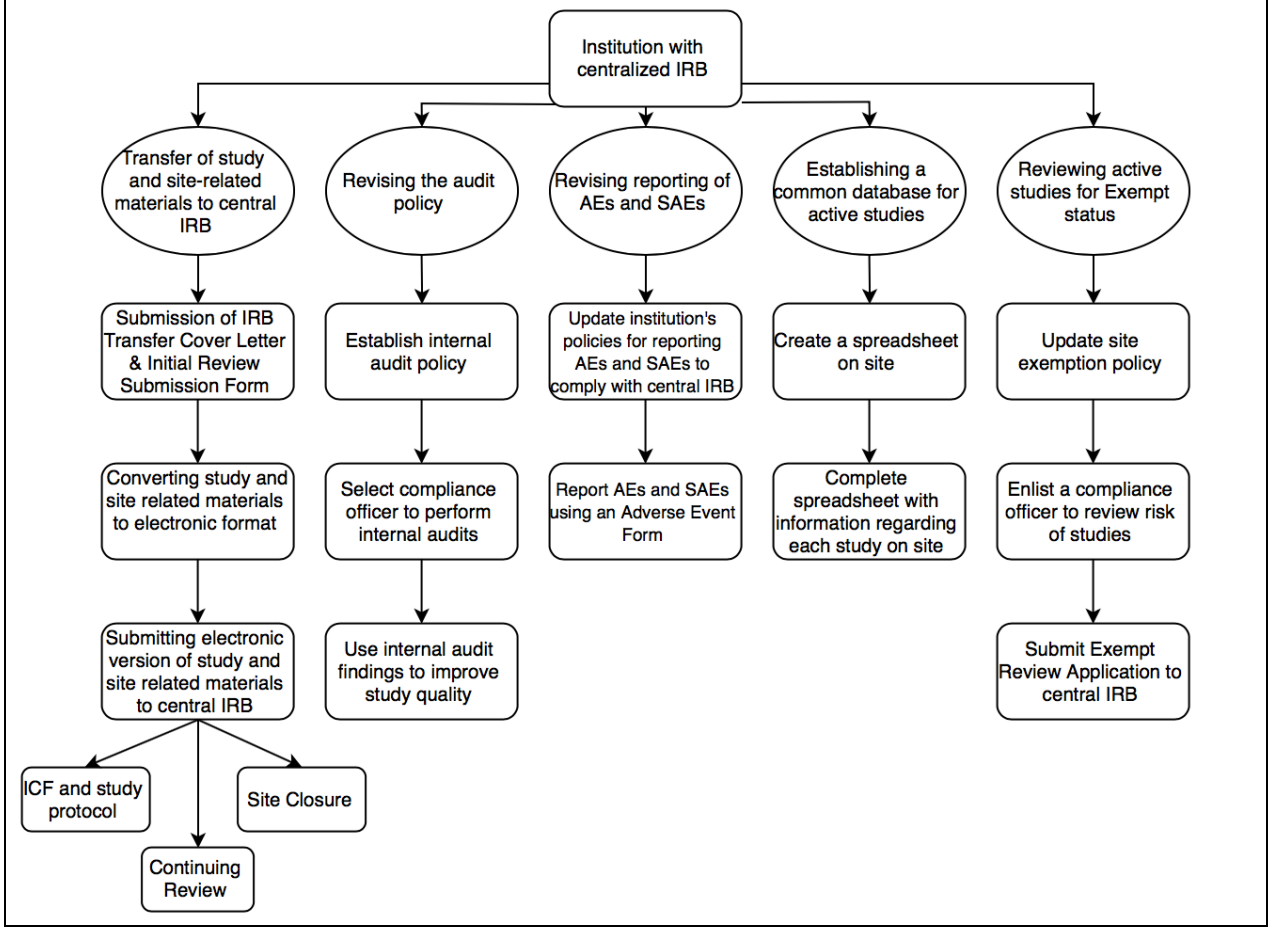


Figure 2: Central IRB Implementation Summary



Revising operational research activities under new oversight of a central IRB (transferring IRBs)

For any human research activities performed at an institution, regardless of whether the research is subject to the U.S. Federal Policy for the protection of Human Subjects (or Common Rule), the institution is governed by a statement of principles which states its responsibilities for protecting the rights and welfare of human subjects of research conducted at or sponsored by the institution [10]. This Federalwide Assurance (FWA) for the Protection of Human Subjects applies to any institution that engages in human subject research conducted or supported by U.S. federal departments or agencies that have adopted the Common Rule, such as the Department of Health & Human Services (HHS). The FWA is the principal mechanism for compliance oversight by the Office of Human Research Protections (OHRP). Additionally, each institution with an FWA is issued a unique FWA number.

Whenever an institution relies upon an IRB operated by another institution or organization for review of research to which the FWA applies, both institution must ensure that this arrangement is documented by a written agreement between the institution and the other institution or organization operating the IRB that outlines their relationship and includes a commitment that the IRB will adhere to the requirements of the institution's FWA [10]. In order for one institution to adhere to the FWA of another, both institutions are required to utilize an IRB Authorization Agreement provided by the OHRP or the parties involved may develop their own agreement based on the OHRP recommendations[11]. This process encompasses the studies both IRBs agreed to collaborate on and works to transfer these active studies to the new IRBs, prior to the closure of the current IRB.

As Medical City of Fort Worth's research department is transitioning to centralized IRB oversight, the IRB Authorization Agreements were completed and signed by our institution and

the central IRB that the institution chose, Western Institutional Review Board (WIRB), to frame the responsibilities of both the central or partner IRB being used for the specific study, as well as Medical City of Fort Worth, to ensure compliance with the IRB's determinations and with the terms of its OHRP-approved FWA. A template of the IRB Authorization Agreement utilized by Medical City of Fort Worth's research office is displayed in Appendix 1.

Following the transfer of active studies to the new IRB, the next phase in completing the full transition to a partner/sister IRB is closure of the local IRB. This two-step process begins with updating or renewing the current FWA of the institution. Prior to this step, however, the institution must connect and transfer its active studies to the sister/partner IRB. As a result, the institution's FWA remains active and the site may continue research throughout the transition process. Appendix 2 through Appendix 6 illustrate the procedure for updating an institutions FWA number, which are as follows[12]:

1. Go to the site: http://ohrp.cit.nih.gov/efile/FwaRenew.aspx
2. Click on "I Need an Electronic Submission Number"
3. Fill out the necessary fields and click "Submit"
4. A submission number will be delivered momentarily through email
5. Once the submission number is received, repeat step 1
6. Click on "I Have an Electronic Submission Number"
7. Fill out the "Submission Number" and "Password" fields and click "Submit"
8. Your institution's FWA number will be presented to be updated/renewed

Following the above steps will result in submission for renewal of the institution's FWA, a process which institutions must complete every five years to maintain an active FWA.

Additionally, this process must occur within 90 days of beginning the IRB transition process. "Failure to renew or update a site's FWA may result in the restriction, suspension, or termination of OHRP's approval of the institution's FWA" [10].

Once the renewal of an institution's FWA is submitted, the next step in the closure of the local IRB is to update the site's IRB number. Performing this step strictly following the renewal or update of an institute's assurance is critical in the closure of the local IRB. Failure to renew the institution's FWA prior to updating the IRB number would invalidate the FWA number for the site, resulting in the institutions inability to continue performing research. Appendixs 7 through 12 illustrate the procedure for updating an institutions IRB number, which are as follows[13]:

1. Go to the site: http://ohrp.cit.nih.gov/efile/IrbRnwStart.aspx
2. Click on "I Need an Electronic Submission Number"
3. Fill out the necessary fields and click "Submit"
4. A submission number will be delivered momentarily through email
5. Once the submission number is received, repeat step 1
6. Click on "I Have an Electronic Submission Number"
7. Fill out the "Submission Number" and "Password" fields and click "Submit"
8. Your institution's registration records should be presented so you can update/renew the registration
9. Follow the steps for updating the IRB organization's (IRBO) IRB registration information

Following the steps above will result in submission for the update of an institution's IRB number. Once this step has been completed, as well as after the submission of FWA renewal, an

institution may view the documents submitted to the OHRP over the last 60 days. This responsibility falls upon the research staff at the institution, whom frequently checks the updates on the OHRP website. It is through this process that an institution can confirm the submission of FWA and/or IRB updates and renewals, as well as the status on the submissions. Appendix 13 illustrates an example of this step, with labels regarding which action was submitted, for Medical City of Fort Worth.

It is the responsibility of the research staff to regularly check upon the status of both the FWA and IRB update or renewal. Once the local IRB has been deactivated, confirmation may be viewed online by searching for the institution on the OHRP website[14]. Appendix 14 illustrates confirmation of the submission for deactivation of the local IRB for Medical City of Fort Worth.

Upon approval of this update of IRB, the organization or corporation serving as the partner/sister IRB will have the responsibility of overseeing all current and future studies at the institution. Despite having the new IRB established, however, institutions are capable of utilizing other IRBs outside of that which has been established for oversight. This situation is common in cases where a sponsor already has an active IRB to oversee the study, such as a corporate or academic institution. In such scenarios, the sponsor facilitating research operations provides numerous benefits for the institution, such as prior approval of study protocol and protocol amendments by the sponsor, approved patient letters, doctor-to-doctor letters, and informed consent forms (ICF), and no submission fees or expenses for the research site. Furthermore, the institution has the authority to check with the IRB and upon request receive any Good Clinical Practice (GCP) materials related to study approval, renewal, or any deviation/violation on the part of the investigator for that particular study. These advantages for utilizing the IRB affiliated with the sponsor streamline and speed up the clinical operations processed. In summary, while

the partner/sister IRB is responsible for regulatory oversight within the institution, each study can be tailored to the sponsor's choice. Additionally, in situations where the sponsor has no preference in IRB, the central IRB will overtake the IRB responsibilities for the study.

Converting site study-related materials to an e-records system in order to be in compliance with centralized IRB requirements (informed consent form, submission of routine documents, initial and continuing review, and final closure)

Following the transition of a site from a local IRB to a central IRB, it is necessary for all study-related materials for IRB-approved studies to be transferred to the central IRB. Prior to any study material being transferred to a central IRB, however, the site must complete an IRB Transfer Cover Letter/Checklist and Initial Review Submission Form for each study the site is transitioning. Accomplishing this task is necessary prior to submitting any study related materials because it provides the central IRB with the necessary information regarding the study and site. The function of the IRB Transfer Cover letter/Checklist is to provide an overview of the study being transferred to the central IRB, whereas the Initial Review Submission Form provides a more comprehensive analysis of the study. Along with these two forms, the site is required to provide the central IRB with a copy of the complete current protocol, a copy of the currently approved consent form, and any documents the submitter has been instructed to provide based on the checklist. Appendix 16 and Appendix 17 illustrate the IRB Transfer Cover Letter/Checklist and Initial Review Submission Form utilized by Medical City of Fort Worth, respectively.

This process of IRB transfer is accelerated if the central IRB has already approved IRB transfer of the same study for a different site. For studies which have been previously registered at the same central IRB, pertinent study materials, such as study protocols, amendments, initial and updated informed consent forms, advertisements, doctor-to-doctor letters, and patient letters, are already on file within the central IRB's database. Thus, when a new site begins transfer of the study oversight from a local to a central IRB, the process is expedited by allowing the new site to

utilize the materials already on file at the central IRB. The benefits of this situation include IRB knowledge of any major and minor changes to the study and expedited approval of IRB transfer.

While the previous submission of a study to a central IRB allows the board to have access to necessary study materials, sites are still responsible for submitting site-specific material which the central IRB does not have on file. Submission of these materials allows the central IRB to record important information regarding the study, such as the site address and contact information in the ICF, Principal Investigator (PI)/sub-PI contact information and credentials, patient information and safety records, participation rates, and site compliance with federal regulations.

In order to submit any site-specific or study-related materials to the centralized IRB, this process began with converting these documents, records, and forms into an e-records system. This is accomplished by manually scanning and uploading the materials and then properly organizing it within the institution's database. Once the process of uploading site-related and study-related materials is completed, the institution could electronically submit any necessary materials to the centralized IRB online database. This process was completed for eleven studies at Medical City of Fort Worth.

Upon approval of the IRB transfer by the central IRB, the study is officially under the oversight of the central IRB. At this time, submitted study related material, such as revised ICFs, are updated with the central IRB's information. Appendix 18 and Appendix 19 are examples of Informed Consent Form for both a previously approved ICF by local IRB and a revised ICF following central IRB approval.

During the initial review process for a study being transferred to a central IRB, the board reviews the study and the frequency at which a site is required to report information related to the study (i.e. continuing review), which was previously determined by the IRB. This process of Continuing Review provides the IRB with study-related data necessary to oversee the progress of a study at the site.[17] Additionally, continuing review is required by federal agencies and sponsors and must occur at intervals appropriate to the degree of risk of the study, but not less than once per year. In order to provide this site-specific information to the IRB, a site is required to complete a Site Continuing Review Report, at the appropriate intervals decided upon previously. This submission process and IRB approval must be completed before the study's expiration date so the study is in compliance with federal regulation. This form contains questions regarding a number of topics, such as subject enrollment, patient risk-potential benefit assessment, PI/sub-PI performance and compliance, inspections and site compliance with Good Clinical Practices (GCP). Appendix 20 illustrates the Site Continuing Review Report utilized by the research office at Medical City of Fort Worth.

As long as a study remains active within a site, the continuing review process is sustained at the intervals determined during the initial review process. Once a decision has been made to closeout the study at a specific site, the sponsor conducts a closeout visit. During this visit, the sponsor reviews all study related data and files, including patient charts, regulatory approvals, and drug/device inventory to ensure the site is ready for closure. Following this closeout visit, the site is responsible for notifying the centralized IRB of the closure through the completion of a Study Closure Report. However, this site closure process is only possible once the closure criteria provided by the IRB is met. This criteria includes[17]:

1. All subjects at your site have finished their final visits and any follow-up activities (such as phone calls, post-card contacts, or long term follow up required by the protocol) are completed,
2. The sponsor or the sponsor representative has indicated that the study is closed at your site, and
3. If the study was conducted under a Federalwide Assurance, all data analysis at the site is completed

Once the Study Closure is approved by the IRB, the site is responsible for notifying the PI. Only after this process is completed and the Study Closure is on file at the IRB can the site proceed with closing out the study. The Study Closure Report utilized by Medical City of Fort Worth can be seen in Appendix 21.

Revising the audit policy for the regulatory purposes of all research studies

For clinical research studies, it is important to verify that the requirements for compliance of the trial-related activities are fulfilled.[15] One way of accomplishing this task is through an internal audit of the study. Utilized as a quality assurance measure, the internal audit process is a site-driven evaluation that occurs to review, inspect and verify the ethical conduct of human subject research, integrity of previously and current reported data, adherence to the study protocol, and applicable institutional, state and federal regulations and guidances.

When a site undergoes an internal audit, the task is often carried out throughout the duration of the study by a compliance officer at the site. "This process usually involves the review and inspection of informed consent forms, documentation of the consent process, reported data, regulatory records, source documents to ensure protocol compliance and drug accountability records. Furthermore, the internal audit process also includes reviewing the site's copies of the research team's credentials and documentation of training to ensure appropriate delegation of specific research tasks."[16]

At Medical City of Fort Worth, the internal audit process is used to evaluate numerous aspects of a study, including site personnel, IRB oversight, data management, and laboratory conditions. Appendix 15 displays the Internal Regulatory Audit Checklist used by Medical City of Fort Worth when the institution undergoes an internal audit for a study. Once the compliance officer has finished the internal audit and completed the Internal Regulatory Audit Checklist, the site utilizes the evaluation to improve the quality of the study.

Revising the process of reporting adverse events (AE) and serious adverse events (SAE)

The continuing review process is imperative in assuring the protections of the rights and welfare of the human subjects. In order to fulfill this obligation, the site is responsible for obtaining and reporting information regarding any unanticipated problems involving risk to human subjects in the study, such as adverse events (AEs) and serious adverse events (SAEs), to the IRB for review.

For clinical trials, an adverse event is known to be any untoward medical occurrence in a patient or clinical investigation subject associated with the use of a medical product, device, or technique, which does not necessarily have to have a causal relationship with this treatment. Therefore, it can be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product[18]. These adverse reactions may fall under either expected or unexpected AEs.

Serious adverse events, on the other hand, are any adverse event that places the subject, in the view of the investigator, at immediate risk of death from the reaction as it occurred, or it is suspected that the use or continued use of the product would result in the patient's death. According to the FDA, an AE is considered to be serious if it results in death, life threatening harm, hospital admission, congenital anomalies, birth defects, or persistent/significant disability or incapacity.

For any human subject research conducted, there is a potential of AEs. As a result, the responsibility of reporting these AEs falls upon the site, and then subsequently the sponsor and IRB. Due to a study's protocol, however, not all AEs are necessary to be reported. Expected AEs

are considered to be any adverse reaction or event that has been previously observed and documented in package inserts, Investigator's Brochures, protocol and informed consent, and/or drug safety profiles. Thus, when an expected AE is observed, reporting requirements will be compliant with the protocol, IRB, and FDA. Unexpected AEs, on the other hand, are reported if they meet certain criteria based on protocol and regulatory requirements. Unexpected AEs are any adverse events experienced by the subject that is not listed in the documents above. The FDA recommends that these unanticipated problems involving risk to human subjects should be reported to the IRB only if they are unexpected, serious, or would have implications for the conduct of the study (e.g., requiring a significant, and usually safety-related, change in the protocol such as revising inclusion/exclusion criteria or including a new monitoring requirement, informed consent, or investigator's brochure). Listed below are a number of occasions, recommended by the FDA, where AEs should be considered unanticipated problems that must be reported to the IRB[19]:

- A single occurrence of a serious, unexpected event that is uncommon and strongly associated with drug exposure
- A single occurrence, or more often a small number of occurrences, of a serious, unexpected event that is not commonly associated with drug exposure, but uncommon in the study population
- Multiple occurrences of an AE that, based on an aggregate analysis, is determined to be an unanticipated problem. (There should be a determination that the series of AEs represents a signal that the AEs were not just isolated occurrences and involve risk to human subjects)

- An AE that is described or addressed in the investigator's brochure, protocol, or informed consent documents, but occurs at a specificity or severity that is inconsistent with prior observations
- A serious AE that is described or addressed in the investigator's brochure, protocol, or informed consent documents, but for which the rate of occurrence in the study represents a clinically significant increase in the expected rate of occurrence
- Any other AE or safety finding (e.g., based on animal or epidemiologic data) that would cause the sponsor to modify the investigator's brochure, study protocol, or informed consent documents, or would prompt other action by the IRB to ensure the protection of human subjects

The process of reporting an AE varies depending on the IRB utilized by the institution. For institutions with local IRBs, PIs are responsible for reporting unanticipated AEs in a timely manner, through the completion of an "Adverse Event Form", to report the AE to the sponsor and IRB. At Medical City of Fort Worth, the research office utilized an Adverse Event Form formulated by the institution and approved by corporate. This form was completed upon the occurrence of an AE or SAE. Appendix 22 illustrates the Adverse Event Form utilized by Medical City of Fort Worth in reporting AEs/SAEs. Due to IRB requirements, PIs at research sites under local review are urged to report every AE that occurs, regardless of intensity or compliance with the criteria recommended by the FDA. As a result, this is often a less productive and time-consuming process for both the site and IRBs.

For sites utilizing central IRBs, the process for reporting AEs and SAEs differs compared to sites with local IRBs. Once the relationship with a central IRB is established, the site or

institution's AE and SAE reporting process is updated to comply with the rules and guidelines prepared by the new IRB. This usually consists of an Adverse Event Form approved by the central IRB. For Medical City of Fort Worth, following the transition to the Western Institutional Review Board (WIRB), the institution utilizes the "Promptly Reportable Information" form provided by the central IRB in reporting AEs and SAEs[17]. Appendix 23 illustrates the "Promptly Reportable Information" form used by Medical City of Fort Worth in reporting AEs and SAEs under the WIRB.

Establishing a common database for active studies at the institution

Once a site has transitioned its studies from a local IRB to a centralized IRB, it is recommended to establish a common database for active studies at the institution. By creating this database, the site is able to record the regulatory body that will oversee each study. After a study has been transferred to another IRB/centralized IRB, the new IRB is required to report its findings and actions to appropriate officials at the site. Additionally, relevant minutes of IRB meetings will be made available to the site upon request. The site remains responsible for ensuring compliance with the IRB's determinations and with the Terms of its OHRP-approved FWA[11]. Appendix 24 illustrates the database template used by Medical City of Fort Worth.

Reviewing active studies for "exempt determination" in light of updated policies

Under federal regulations, certain types of research studies can be considered Exempt from Full Board (IRB) Review.[21] In order for a study to receive Exempt status, the research study must meet two criteria: being regarded as having minimal risk to subjects and falling under one of the following six exempt categories[5]:

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless: (i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; AND (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.
3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under category (2), if: (i) the human subjects are elected or appointed public officials or candidates for public office; or (ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

4. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.
5. Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine:(i) Public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs.
6. Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

When attempting to receive Exempt status for a study, it is essential for the research study to be classified as having little to no risk to the subjects. While the PI is often tasked with the responsibility of indicating whether a study has minimal risk or not, the OHRP recommends that an institution should refrain from giving PIs this authority because of the potential for conflict of interest. Instead, institutions are advised to utilize a third party for making this determination. Due to this regulatory flexibility regarding exemption determination, institutions

are advised to implement exemption policies that most effectively address the local setting and programs of research, as long as they are compliant with applicable regulations[21].

When a study is considered to meet these two criteria, an Exempt Review Application must be completed and submitted to the institution compliance office for review. If the compliance office determines that exempt review is appropriate for the study, the application will be submitted to the IRB for approval of Exempt status. By becoming Exempt, the study is excused from IRB Review (full and expedited review). However, all modifications to a study's protocol that has been certified exempt must be submitted to the IRB for review and certification of exemption prior to implementation. If there are protocol changes, the PI is required to immediately contact the approving body for more clarification regarding the status of the study. If any of these proposed changes to the protocol increase risk to subjects or change the type of review, the IRB may disqualify the study from exemption. Appendix 25 illustrates the Exempt Review Application used by Medical City of Fort Worth.

CHAPTER V

Limitations of the Study

Limitations Due to Time

Due to the short length of the internship, time was a major hindrance for this practicum project. Currently, there is limited insight from other institutions on the transition from a local to a centralized IRB and the time span this transition requires. As a result, assisting and examining this process for six months did not encompass all aspects of the transition process. Additionally, due to the short time period of the study, the practicum could not gather a full picture of the benefits of this transition.

Limitations Due to Design

Another limitation of this practicum was its scope. With the transition to centralized IRBs for multi-site research, each site must work within itself to modify its day-to-day operations in order to comply with the single IRB. With that being said, my practicum project only focused on a single investigative site. This caused difficulty in establishing a generalized collective analysis of the transition process for a research study. Furthermore, as each research site can utilize different institutions or organizations as their central IRB, there may be slight variations in procedure or forms that differ from Medical City of Fort Worth.

CHAPTER VI

Future Directions

The aim of this practicum was to assist in the implementation of a centralized IRB at Medical City of Fort Worth. Along with completing this task, documentation of the IRB transfer process yielded a guide for other sites to utilize in their transition from a local IRB to a centralized IRB. While this practicum was successful, opportunities for further research are abundant. Following the completion of this practicum, I suggest the following directions for future research:

1. Extending the current analysis to numerous sites and for a longer duration in order to formulate a more comprehensive guide for the IRB transfer process. This includes sites of differing sizes and number of studies.
2. Evaluating the long-term effects of transitioning a site from a local IRB to a centralized IRB

CHAPTER VII

Conclusion

In summary, the operational rules and regulatory processes at Medical City of Fort Worth were updated to comply with the changes in the Common Rule and the institution's transition to a central IRB. This was accomplished by revising numerous aspects of research at the site, including operational research activities, audit policies, adverse event and serious adverse event reporting, and exemption determination, while also establishing a local database and converting local documents to an e-records system.

CHAPTER VIII

General Internship Experience

This internship was completed with the Medical City of Fort Worth Research Department over the course of a six-month period. The Research Department is under the oversight of Dr. Rubina Muzina, MD, MPH, CCRC, whose vast experience with clinical research and medicine was valuable throughout the duration of the practicum project. Working under the management of Dr. Muzina are two research coordinators, Bhagawathy Sarma and Brenda Tapia, whom provided me with much assistance and input. The Research Department is located in the medical professional building adjacent to the main hospital. While a majority of the time is spent in the office, there are studies that require the research staff to conduct their work in the hospital and associated labs. Research subjects are recruited into a number of clinical trials from the patient population.

Prior to the start of my internship, I fulfilled the requirements put forth by Medical City of Fort Worth's IRB and Human Resources department, which included routine TB testing, Collaborative Institutional Training Initiative (CITI) training, and National Institutes of Health (NIH) training for Protecting Human Subject Research Participants. The internship began with getting accustomed to the research office, as well as the hospital and its numerous departments. Following this orientation process, the next few weeks involved familiarizing myself with the policies of both the local IRB, as well as the central IRB to which the site was transitioning. This familiarization process was crucial for my internship as it allowed me to understand the duties of the research staff and lay the foundations of the practicum project. Over the next six months, I assisted the research coordinators on a daily basis throughout the office. This included

organizing study documents both physically and electronically, redacting private information from patient records, scheduling patient visits, recording and filing patient forms, and shipping study samples. During this internship, I was able to gain exposure to multiple aspects of research studies, such as study protocols, informed consent, AEs and SAEs, electronic databases, and IRB policy. Depending on study schedules, I experienced patient contact during on site follow ups, consenting visits, and patient screenings. These patient visits generally involved collecting information on any adverse events and patient progress through tests such as ultrasounds, EK\CG's, and physical exams. The majority of my time during this internship was spent observing the process involved in transferring studies to a central IRB, which involved a variety of procedures such as FWA and IRB number renewal/update, submitting study-related materials, and updating site procedures. Witnessing these procedures allowed me to establish a good understanding of the material that is the basis of my practicum project.

In conclusion, the Medical City of Fort Worth Research Department is an exceptional setting for clinical research to be conducted and my experiences within this institution has provided me with invaluable knowledge and hands-on experience.

BIBLIOGRAPHY

1. Hudson, K. L. and F. S. Collins (2015). "Bringing the Common Rule into the 21st Century." New England Journal of Medicine **373**(24): 2293-2296.

2. Wechsler, Jill. “Central vs. Local: Rethinking IRBs.” *Applied Clinical Trials*. 1 Feb. 2007. Web. 14 Oct. 2016.

3. “Central IRB.” *Clinical Trials Transformation Initiative*. CTTI-Clinical Trials, 2015. Web. 14 Oct. 2016.

4. “Confidence in the Central IRB.” *Applied Clinical Trials*. UBM plc, July 2010. Web. 14 Oct. 2016.

5. “45 CFR 46.” *Office for Human Research Protections*. U.S. Department of Health & Human Services, 1991. Web. 10 Oct. 2016.

6. “Considerations in Transferring a Previously Approved Research Project to a New IRB or Research Institution.” *Office for Human Research Protections*. U.S. Department of Health & Human Services, 2012. Web. 23 November 2016.

7. “The Notice of Proposed Rulemaking (NPRM) for Revisions to the Common Rule.” *National Human Genome Research Institute*. National Institutes of Health, 2015. Web. 23 November 2016.

8. “Using a Centralized IRB Review Process in Multicenter Clinical Trials.” *Food and Drug Administration*. U.S. Department of Health and Human Services, 2006. Web. 14 Oct. 2016.

9. Resnik, D. B. (2012). "Centralized Institutional Review Boards: Assessing the Arguments and Evidence." Journal of Clinical Research Best Practices **8**(11).

10. “Federalwide Assurance (FWA) for the Protection of Human Subjects.” *Office for Human Research Protections*. U.S. Department of Health & Human Services, 2011. Web. 12 Mar. 2017.

11. “Institutional Review Board (IRB) Authorization Agreement.” *Office for Human Research Protections*. U.S. Department of Health & Human Services, 2016. Web. 12 Mar. 2017.

12. “Update or Renew a Federalwide Assurance (FWA).” *Office for Human Research Protections*. U.S. Department of Health & Human Services, 2016. Web. 12 Mar. 2017.

13. “Update or Renew an IRB Registration.” *Office for Human Research Protections*. U.S. Department of Health & Human Services, 2016. Web. 12 Mar. 2017.

14. “Office for Human Research Protections (OHRP) Database for Registered IORGs & IRBs, Approved FWAs, and Documents Received in Last 60 Days.” *Office for Human Research Protections*. U.S. Department of Health & Human Services, 2016. Web. 12 Mar. 2017.

15. “Guideline for Good Clinical Practice.” *ICH Harmonized Tripartite Guideline*. International Conference for Harmonization of Technical Requirements for Pharmaceuticals for Human Use, 1996. Web. 22 Feb. 2017.

16. “Audits.” *OSU Center for Clinical and Translational Science*. The Ohio State University, 2012. 24 Mar. 2017.

17. “A Guide for Researchers.” *Western Institutional Review Board*. WIRB-Copernicus Group, 2017. Web. 8 Mar. 2017.

18. “Clinical Safety Data Management: Definitions and Standards for Expedited Reporting.” *Food & Drug Administration*. U.S. Department of Health & Human Services, 1995. Web. 25 Feb. 2017.

19. “Adverse Event Reporting to IRBs.” *Food & Drug Administration*. U.S. Department of Health & Human Service, 2009. Web. 25 Feb. 2017.

20. “What is Exempt Review.” *University of North .Texas Health Science Center*. University of North Texas System, 2015. Web. 14 Mar. 2017.

21. “Exempt Research Determination.” *Office for Human Research Protections*. U.S. Department of Health & Human Services, 2016. Web. 14 Mar. 2017.

22. Moon RM and Khin-Maung-Gyi F. 2009. “The History and Role of Institutional Review Boards.” American Medical Association Journal of Ethics 11: 311-321.

23. Koski G, Aungst J, Kupersmith J, Getz K, and Rimoin D. 2005. “Cooperative Research Ethics Review Board: A Win-Win Solution?” IRB Ethics & Human Research 27, 3: 1-7.

APPENDIX

Appendix 1: IRB Authorization Agreement

Institutional Review Board (IRB) Authorization Agreement

Institution or Organization Providing IRB Review:

Name (Institution/Organization A):
IRB Registration Number:
Federalwide Assurance (FWA):

Institution Relying on the Designated IRB (Institution B):

Name: _____
FWA#: _____

The Officials signing below agree that _____ (name of Institution B) may rely on the designated IRB for review and continuing oversight of its human subjects research described below: (check one):

(___) This agreement applies to all human subjects research covered by Institution B's FWA.

(___) This agreement is limited to the following specific protocol(s):

Name of Research Project: _____
Principal Investigator: _____
Sponsor/Funding Agency: _____
Award Number, if any: _____

(___) Other (describe): _____

The review performed by the designated IRB will meet the human subject protection requirements of Institution B's OHRP-approved FWA. The IRB at Institution/Organization A will follow written procedures for reporting its findings and actions to appropriate officials at Institution B. Relevant minutes of IRB meetings will be made available to Institution B upon request. Institution B remains responsible for ensuring compliance with the IRB's determinations and with the Terms of its OHRP-approved FWA. This document must be kept on file by both parties and provided to OHRP upon request.

Signature of Signatory Official (Institution/Organization A):
_____ Date: _____

Print Full Name: _____

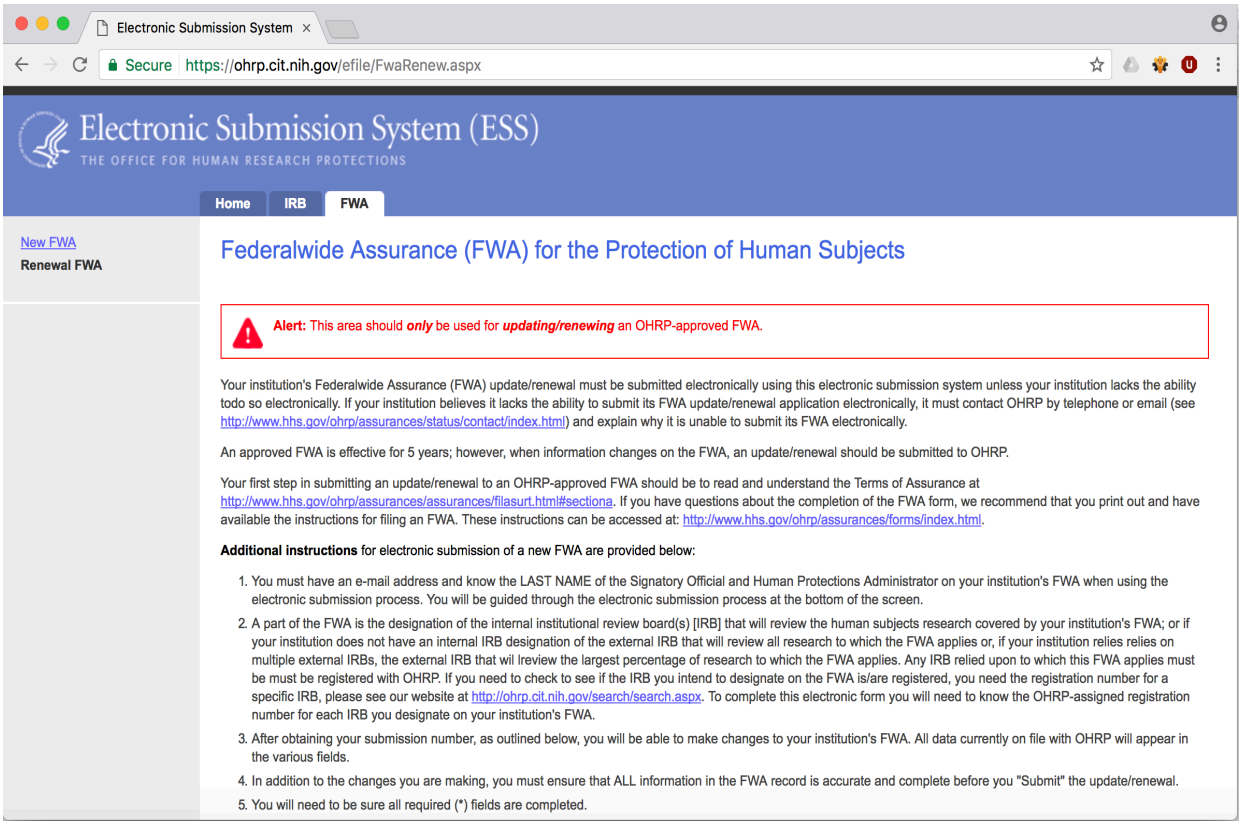
Institutional Title: _____

Signature of Signatory Official (Institution B):
_____ Date: _____

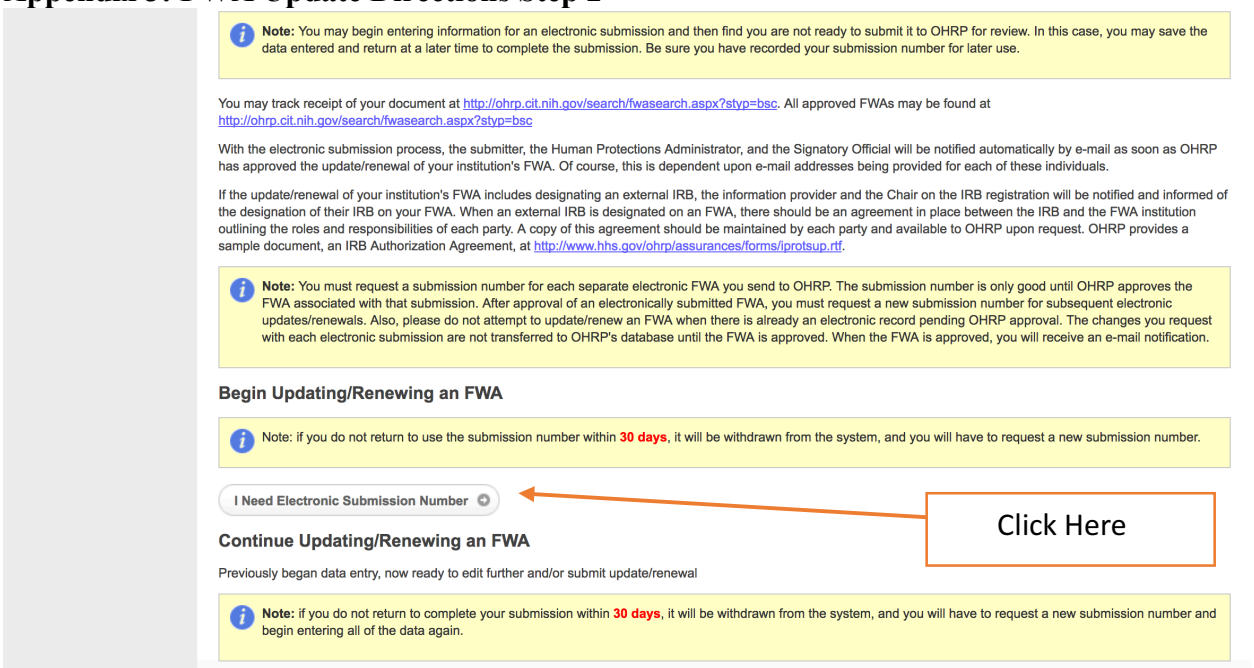
Print Full Name: _____

Institutional Title: _____

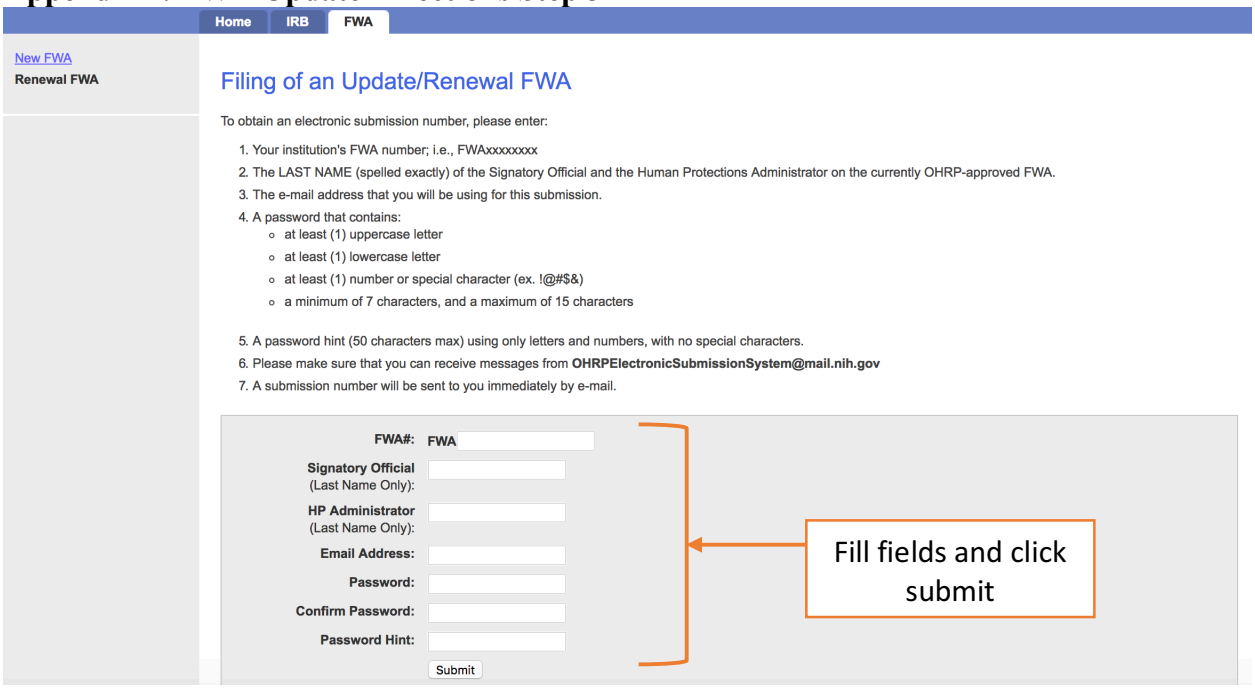
Appendix 2: FWA Update Directions Step 1



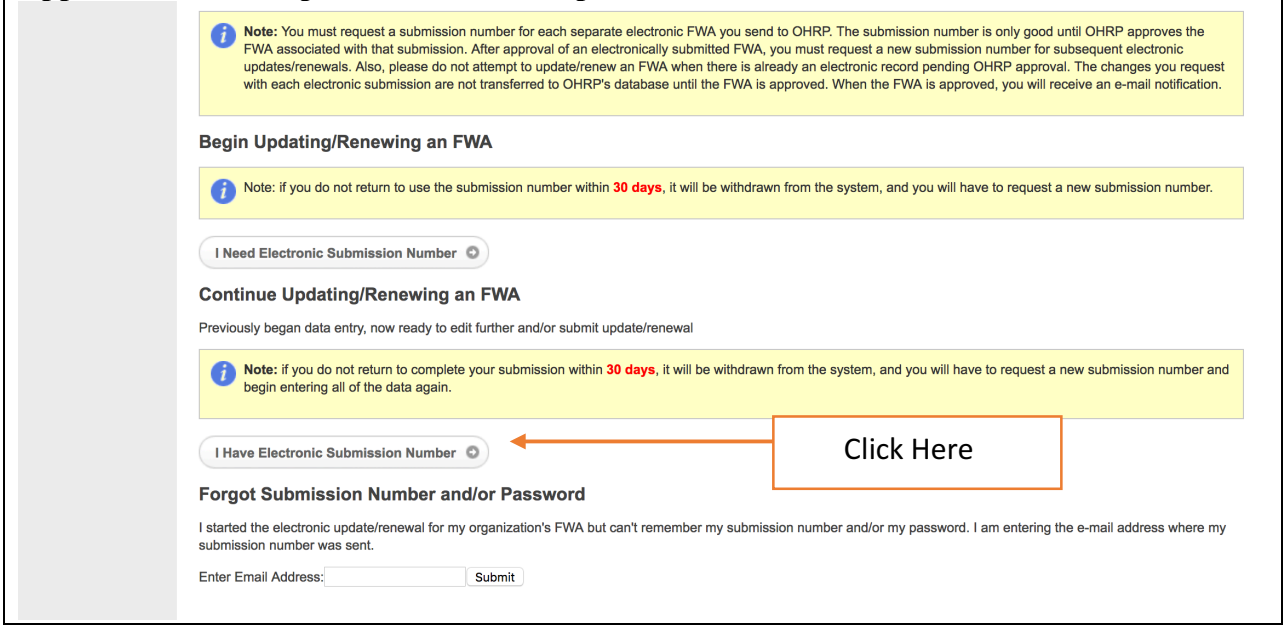
Appendix 3: FWA Update Directions Step 2



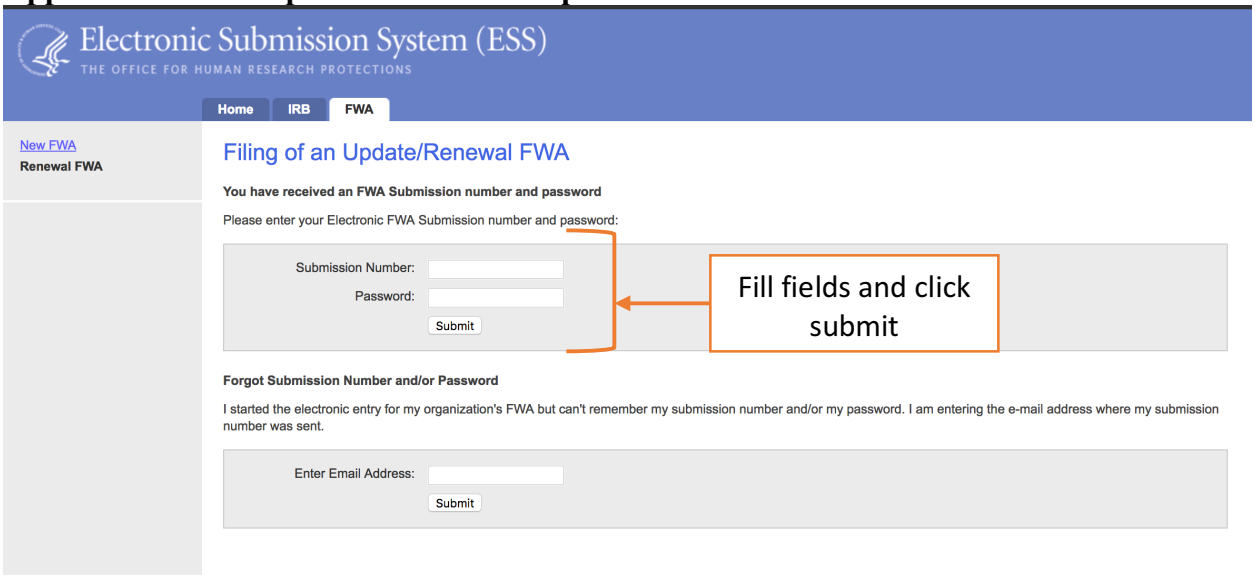
Appendix 4: FWA Update Directions Step 3



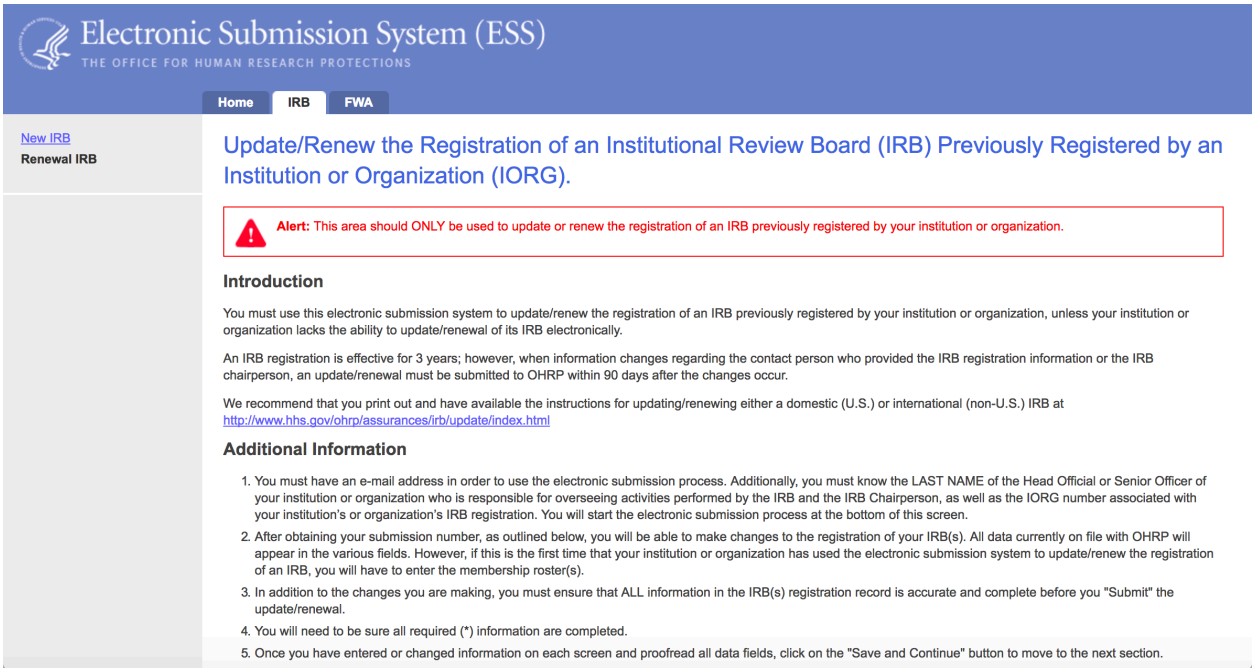
Appendix 5: FWA Update Directions Step 6



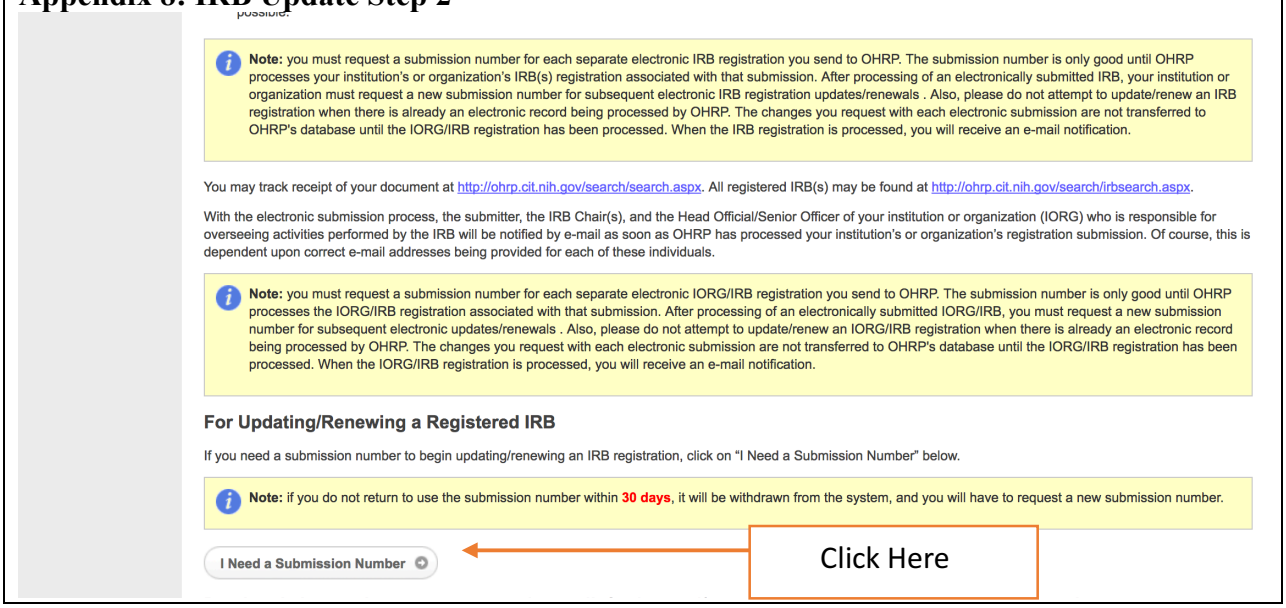
Appendix 6: FWA Update Directions Step 7



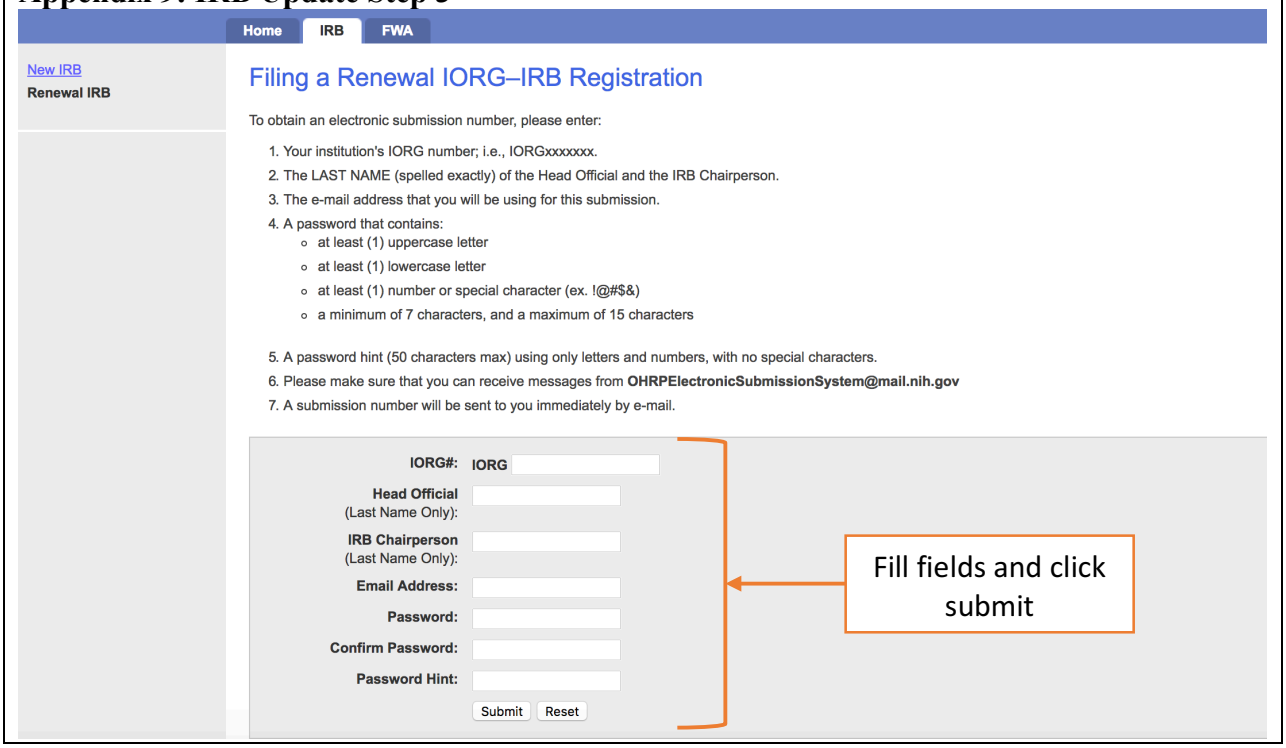
Appendix 7: IRB Update Step 1



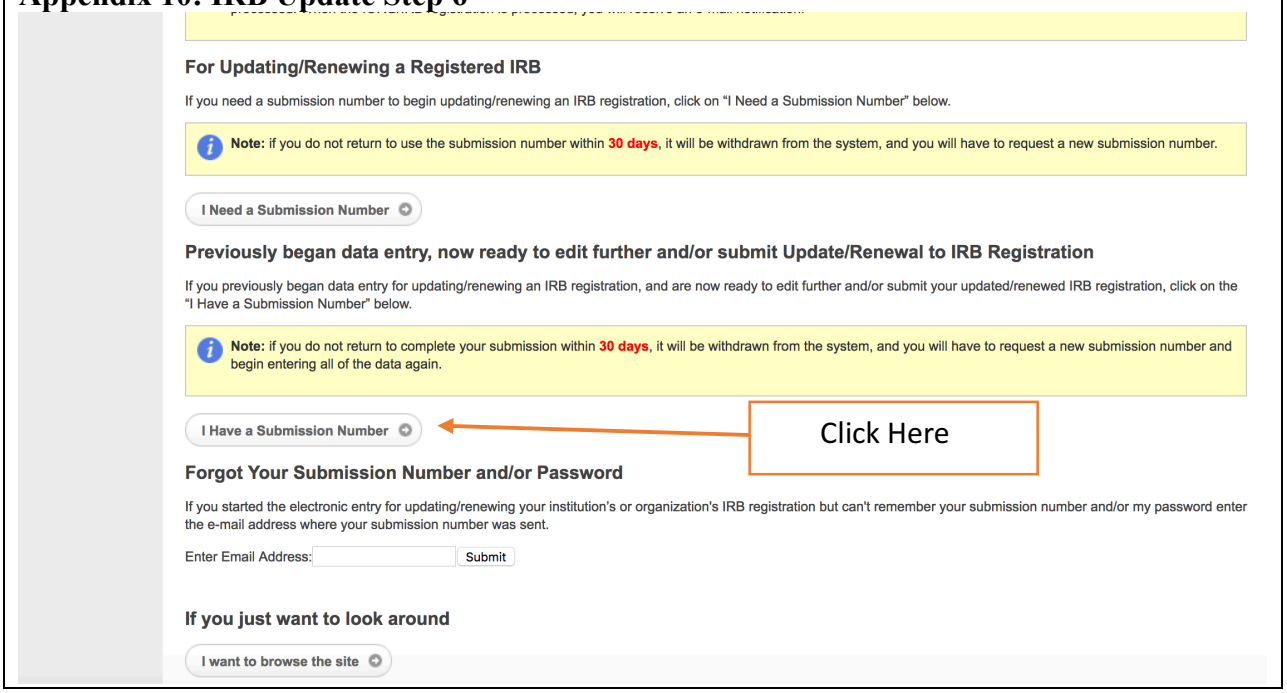
Appendix 8: IRB Update Step 2



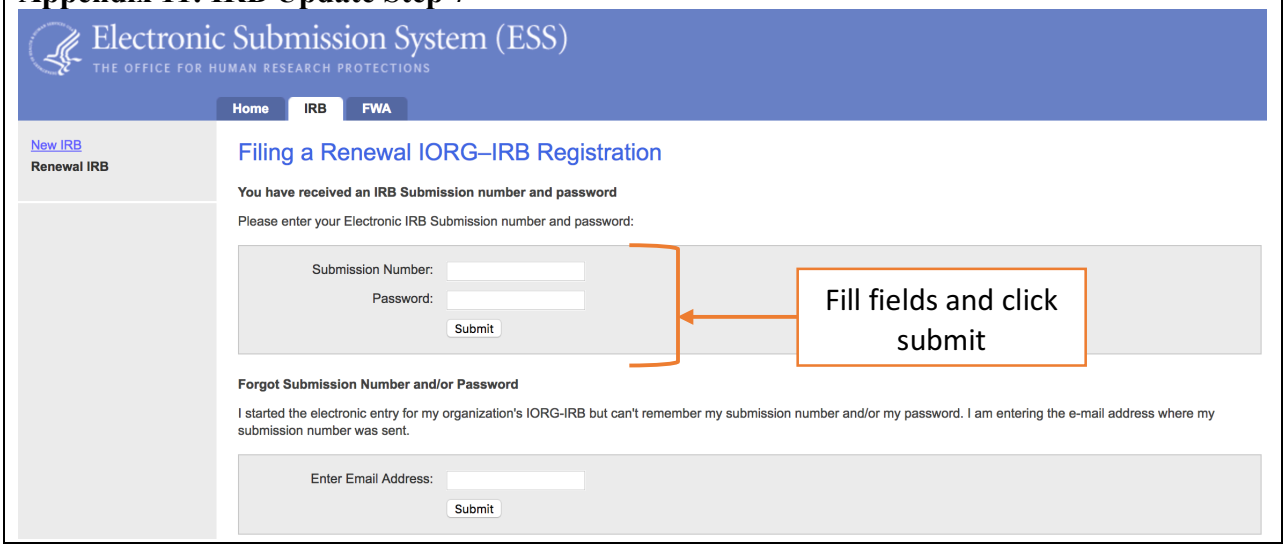
Appendix 9: IRB Update Step 3



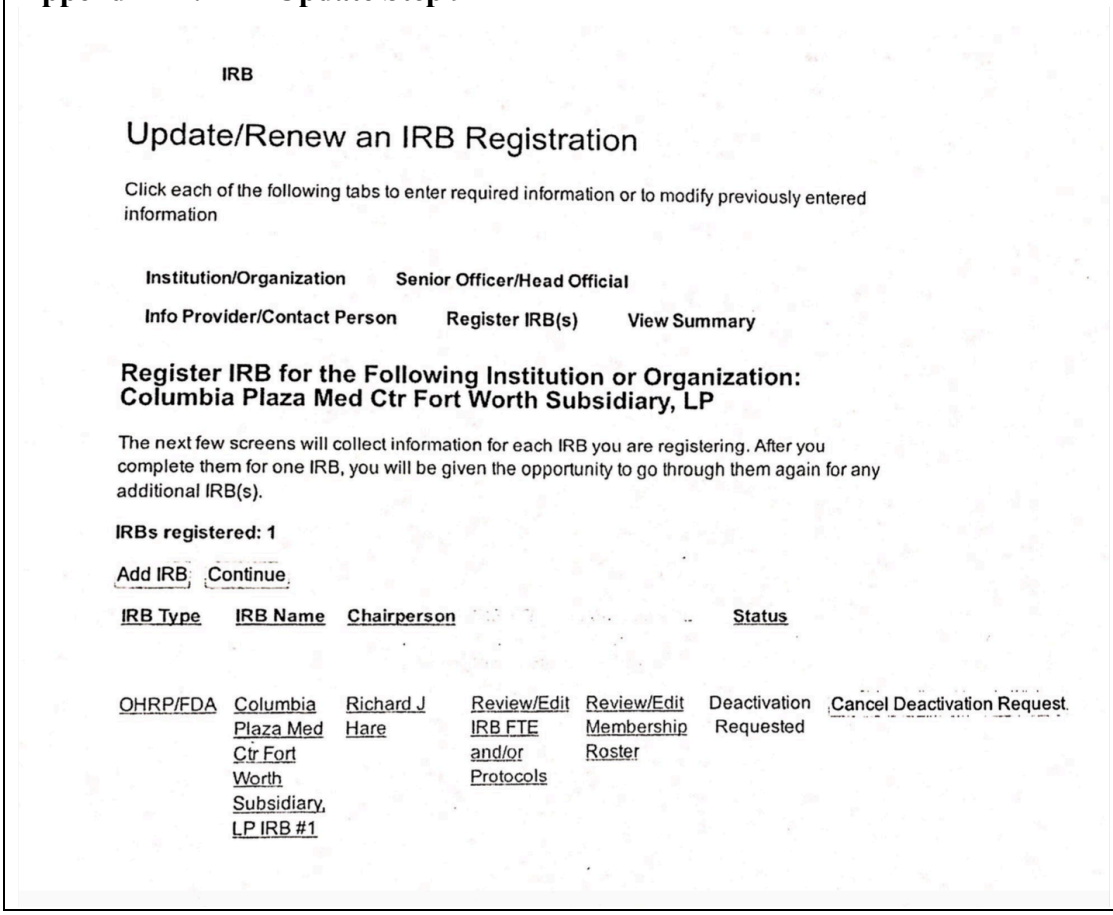
Appendix 10: IRB Update Step 6



Appendix 11: IRB Update Step 7



Appendix 12: IRB Update Step 9



IRB

Update/Renew an IRB Registration

Click each of the following tabs to enter required information or to modify previously entered information

Institution/Organization **Senior Officer/Head Official**

Info Provider/Contact Person **Register IRB(s)** **View Summary**

Register IRB for the Following Institution or Organization: Columbia Plaza Med Ctr Fort Worth Subsidiary, LP

The next few screens will collect information for each IRB you are registering. After you complete them for one IRB, you will be given the opportunity to go through them again for any additional IRB(s).

IRBs registered: 1

Add IRB Continue

IRB Type	IRB Name	Chairperson			Status	
OHRP/FDA	Columbia Plaza Med Ctr Fort Worth Subsidiary, LP IRB #1	Richard J Hare	Review/Edit IRB FTE and/or Protocols	Review/Edit Membership Roster	Deactivation Requested	Cancel Deactivation Request

Appendix 13: OHRP Submission Status Example

New Search

Return to: Search OHRP Database

Documents Received by OHRP in Last 60 Days

Search Results for 'plaza'

Click on any of the column headings to sort by that column.

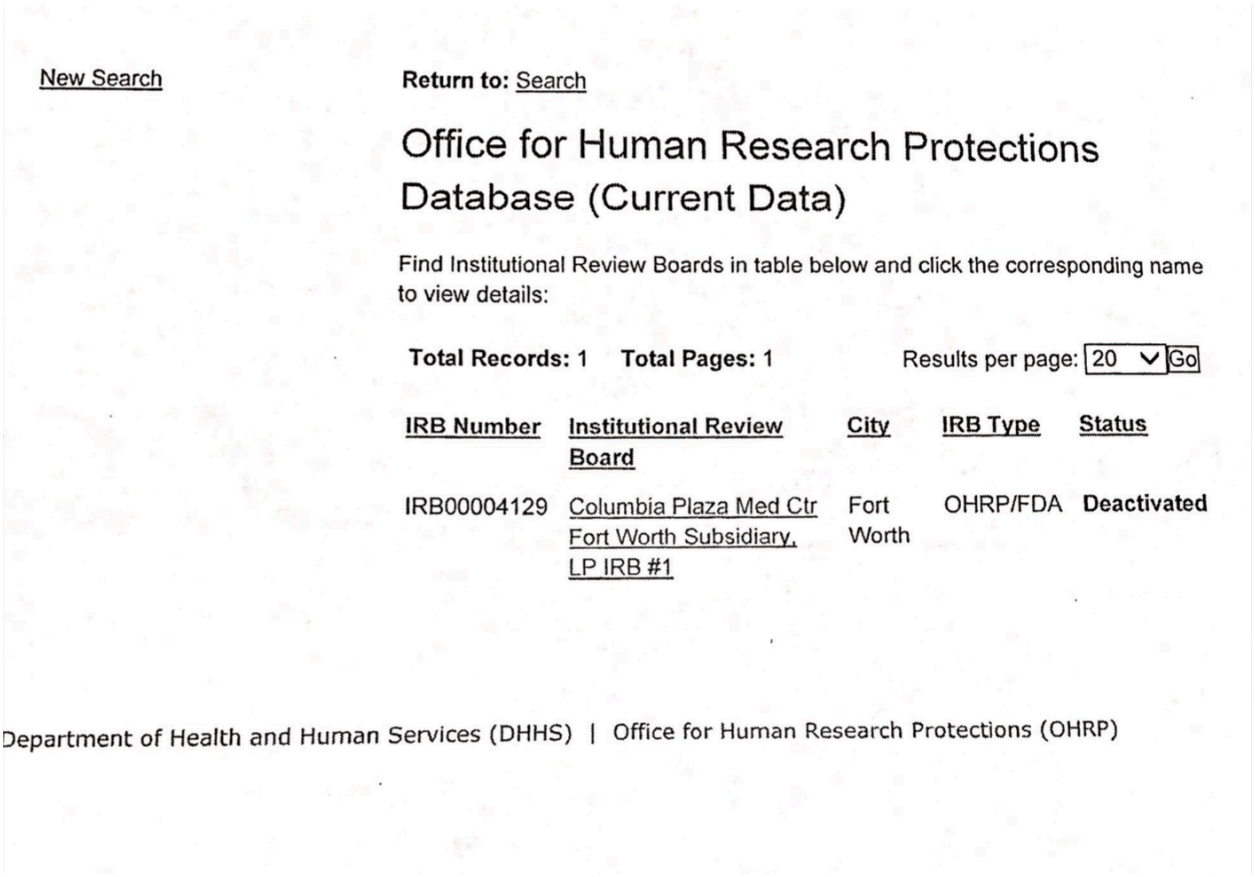
Total Records: 2 **Total Pages:** 1

Date Received	Sender	CITY	State/Country	IORG/FWA #	Type	Additional Data Requested	Completed	OHRP Reviewer
02/27/2017	Columbia Plaza Med Ctr Fort Worth Subsidiary, LP	Fort Worth	TEXAS	IORG0003466	I			Gail Holloway
01/05/2017	Columbia Plaza Med Ctr Ft.Worth Sub. dba Plaza Med Ctr Ft.	Fort Worth	TEXAS	FWA00007115	F		01/11/2017	Christina Lindsay

DOCUMENT TYPE ICON LEGEND

Paper IRB	Paper FWA
Electronic IRB	Electronic FWA
IRB Update	FWA Update
Electronic IRB Update	Electronic FWA Update

Appendix 14: IRB Deactivation Status



New Search

Return to: Search

Office for Human Research Protections Database (Current Data)

Find Institutional Review Boards in table below and click the corresponding name to view details:

Total Records: 1 **Total Pages:** 1 Results per page: 20 Go

IRB Number	Institutional Review Board	City	IRB Type	Status
IRB00004129	Columbia Plaza Med Ctr Fort Worth Subsidiary, LP IRB #1	Fort Worth	OHRP/FDA	**Deactivated**

Department of Health and Human Services (DHHS) | Office for Human Research Protections (OHRP)

Appendix 15: Internal Regulatory Audit Checklist

Internal Regulatory Audit Checklist	
Study Name:	
Site:	**Investigator:**
Monitor:	**Date Reviewed:**

Site Personnel	*Enter dates, or N/A if not applicable.*					
List Names Below	**CV**	**Signature Log**	**Fin. Discl.**	**Inv. Agmnt**	**License Exp.**	**Initiated/ Trained**
1.						
2.						
3.						
4.						
5.						
6.						
7.						
8.						
9.						
10.						

IRB	**Yes**	**Date**	**No**	**N/A***	**Comments**
Are there any additional committees that must review protocol?					
Copy of Original IRB Approval? Version:					
Have there been any amendments or revisions to the original protocol? *List Versions below*					
1.					
2.					
Is there a copy of each IRB Annual Renewal? *List years below*					
Is there a copy of the IRB approval for the original informed consent? 10 Nov 05 Version					
Have there been any revisions to the original informed consent? Specified *below with date of IRB approval.*					
Is there a list of all IRB members? *List years below.*					
1.					
Are any of the investigators members of the IRB? *If so, add memo to file indicating the investigator abstained*					

Appendix 15: Internal Regulatory Audit Checklist

Site:
Date of Review:

IRB	Yes	Date	No	N/A*	Comments
Has the IRB been notified of enrollment completion?					
Has a final report been sent to the IRB?					
Have all Adverse Event Reports been reported to the IRB? *(list events below)*					
1.					
Have all patient advertisements been approved by the IRB? *(list ads below)*					
1.					
Have all other study changes/notifications been approved/reviewed by IRB? *(list specifics below)*					
1.					
Has all IRB correspondence been forwarded to the sponsor?					

Lab (if applicable)	Yes	Exp. Date	No	N/A*	Comments
Is a current copy of the lab certification available for each lab? *List labs below:*					
Are the relevant lab normal reference ranges available for each lab? *List labs below:*					
Has the current lab certification and normal reference ranges been sent to the sponsor?					

Appendix 15: Internal Regulatory Audit Checklist

Site:
Date of Review:

Other	**Yes**	**Last updated**	**No**	**N/A***	**Comments**
Are the patient log(s) complete and up to date?					
Is the Adverse Event Log complete and up to date?					
Is the Device Accountability Log up to date?					
Is the clinical monitor sign-in log complete and up to date?					
Is there a current copy of the protocol available?					
Is there a blank Case Report Form available?					
Is there a current copy of the device manual/Instructions for Use available?					
Are there sufficient supplies to conduct the study?					
Does site maintain all copies of study correspondence? *(HPA Inc., Investigators, IRB)?*					
Have there been any changes in study personnel? *If so, note changes.*					

***N/A** - Not applicable or not done at this visit.

General comments:

-

Signed: _____
Person conducting internal audit

Appendix 16: IRB Transfer Cover Letter/Checklist

Western Institutional Review Board®
1019 39th Avenue SE Suite 120 | Puyallup, WA 98374-2115
Office: (360) 252-2500 | Toll Free: (800) 562-4789
www.wirb.com • clientservices@wirb.com
OHRP/FDA Parent Organization number: IORG0000432
IRB registration number: IRB00000533

A WIRB-Copernicus Group Company

Cover Letter/Checklist
For Transfer of IRB Oversight to WIRB

Date:
Principal Investigator:
Protocol No.:
Title:

Name and Address of Previous IRB:

Indicate the documents that are being submitted for review:

- ☐ WIRB Initial Review Submission Form (required)
- ☐ Most recent version of protocol if one is not on file at WIRB (dated: _____)
- ☐ Amendments (dates of those included: _____), if not incorporated in protocol (required)
- ☐ Complete grant application, if submitted to a Federal agency
- ☐ Most recent IRB approved version of the consent form
- ☐ Advertisements presently being used for recruitment
- ☐ Investigator's Brochure, if applicable and if one is not already on file at WIRB (dated: _____)
- ☐ Curriculum vitae for principal investigator (required)
- ☐ Professional license for principal investigator (required)
- ☐ Medical licenses for all sub-investigators (if applicable)
- ☐ Radiation safety committee approval (if applicable)

Reason for Transfer to WIRB:

Date of initial approval by the previous IRB: _____

Date approval expires: _____

Appendix 16: IRB Transfer Cover Letter/Checklist

Summary of Study Activity Prior to Transfer

At your site:

1. Has the study begun? ☐Yes ☐No
2. Total subjects enrolled (signed consent form): _____
3. Do you intend to enroll any more subjects? ☐Yes ☐No
4. Are subjects coming in for scheduled visits? ☐Yes ☐No
5. Are any subjects still on active treatment? ☐Yes ☐No
   Comments:
6. Is the study completed, but not yet closed out by the sponsor? (Have all subjects at your site completed their final visit?) ☐Yes ☐No
7. Has any new risk or benefit information become available that was not reported to the previous IRB? ☐Yes* ☐No
   *If yes, submit the new risk or benefit information for review.
8. Have there been any unanticipated problems[1] (other than new risk information described in response to question 7 above) related to this research? ☐Yes* ☐No
   *If yes, describe the problem and actions taken, if any, as a result of the unanticipated problem (attach a separate page if necessary) and submit **any IRB correspondence related to the unanticipated problem**.
9. Have there been any subject complaints related to this research? ☐Yes* ☐No
   *If yes, describe the complaint and actions taken, if any, as a result of the complaint, and submit any IRB correspondence related to the complaint (attach a separate page if necessary).

[1] Unanticipated problems include any incident, experience, or outcome that meets **all** of the following criteria:
(1) unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
(2) related or possibly related to participation in the research (in this guidance document, *possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
(3) suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Appendix 16: IRB Transfer Cover Letter/Checklist

10. Did the previous IRB ever suspend or terminate this research at your site? ☐ Yes* ☐ No

*If yes, provide information on the reason for the Board action, the steps taken to resume the research and copies of any IRB correspondence related to the suspension (attach a separate page if necessary).

Prepared and sent to WIRB by:

Printed Name / Title

Date

Appendix 17: Initial Review Submission Form Page 1

wcg WIRB COPERNICUS GROUP

Initial Review Submission Form

Note: Form must be completed in Adobe version 9.1 or later (Reader or Acrobat).
All fields with an asterisk (*) are required.

Submission Source

*Indicate the type of submission

- ○ Sponsor/CRO submitting a new protocol(No PI information)
- ◉ Site being added to active/existing protocol or change of principal investigator
- ○ Investigator submitting a new protocol
- ○ Physician submitting for approval of the on-label use of a Humanitarian Use Device (HUD)

This is a smart form. Some form elements will appear or disappear depending on answers to previous questions.

Protocol Information

*Protocol Title | Sponsor Protocol Number | *Sponsor Name

*To whom are you submitting this application?

- ○ Copernicus Group IRB (CGIRB)
- ○ Western IRB (WIRB)
- ○ New England (NEIRB)

Principal Investigator Information

Prefix | *First | Middle | *Last | Suffix

Degrees | *Company

*Mailing Address: Address Line 1 | Address Line 2 | *City

*State/Province | *Country (United States) | *Postal Code

*Email | *Phone

If this research will be conducted through an organization which has a contract to use WIRB for IRB services, please provide the name of the institution (and the WIRB institution number if known):

Provide the name of the institution:

Provide the WIRB institution number, if known:

Medical Licenses

State | *License Number | Expiration Date

☐ Check this box if this is the person completing this form.

Appendix 17: Initial Review Submission Form Page 2

wcg™ WIRB COPERNICUS GROUP

Initial Review Submission Form

Note: Form must be completed in Adobe version 9.1 or later (Reader or Acrobat).
All fields with an asterisk (*) are required.

*What are the demographics of the PI's patient/subject population?

☐ Pediatric ☐ Adult

What are the specialties of the site?

*Primary specialty

*Secondary specialty

*Indicate which therapeutic area represents the majority of the research studies the PI has:

*What is the name of the disease/condition represented by the majority of the PI's patient population?

What is the average screen failure rate for the PI's prior five clinical trials? (percent)

☐ Mark this box if the PI does not conduct clinical trials or has conducted fewer than five.

What is the average subject drop-out rate for the PI's prior five clinical trials? (percent)

☐ Mark this box if the PI does not conduct clinical trials or has conducted fewer than five.

*Is there a study coordinator/designated contact for this study other than the PI?

◯ Yes ◯ No

PI Transfer

*Are you taking this study over from another PI?

◯ Yes ◯ No

Investigator and Research Personnel History

*Has the principal investigator, any co-investigators, any sub-investigators, or any research personnel been issued any of the following?:

- At any time in the past: One or more of the following: NIDPOE (Noticed of initiation of Disqualification Proceedings and Opportunity to Explain); Suspension by a federal or governmental agency (such as FDA, HHS, or Health Canada; Suspension or termination by an IRB, FDA Warning Letter); OHRP Determination Letter, Health Canada Inspection Letter or similar; or conviction of a crime, or
- Within the past five years: Form FDA 483?

◯ Yes ◯ No

*Has the principal investigator, any co-investigators, any sub-investigators, or any research personnel ever had any of the following denied, revoked, suspended, reduced, limited, placed on probation, not renewed, relinquished, sanctioned, fined, or subject to disciplinary action?
Research privileges at any site; medical licensure in any state, nation, or province; membership on any hospital staff; clinical privileges at any site; professional society memberships or fellowship/board certification; DA licensure or prescribing privileges; or professional sanctions including fines and public reprimands.

◯ Yes ◯ No

Appendix 17: Initial Review Submission Form Page 3

wcg™ WIRB COPERNICUS GROUP®

Initial Review Submission Form

Note: Form must be completed in Adobe version 9.1 or later (Reader or Acrobat).
All fields with an asterisk (*) are required.

*Is any action or investigation currently pending before any state licensing board, federal agency, or court of law concerning the professional conduct of the principal investigator in his capacity as a research investigator or as a clinician?

◯ Yes ◯ No

Financial Interest Disclosure

*Do you, or any of the other research personnel, or your immediate families, have any of the following financial interests in the sponsor, product, or service being tested?

- With regard to any publicly traded entity, a financial interest where the value of any remuneration received from the entity in the twelve months preceding the disclosure and the value of any equity interest in the entity as of the date of disclosure, when aggregated, exceeds $5,000. [For purposes of this definition, remuneration includes salary and any payment for services not otherwise identified as salary (e.g., consulting fees, honoraria, paid authorship); equity interest includes any stock, stock option, or other ownership interest, as determined through reference to public prices or other reasonable measures of fair market value];
- With regard to any non-publicly traded entity, a financial interest where the value of any remuneration received from the entity in the twelve months preceding the disclosure, when aggregated, exceeds $5,000, or when the Investigator (or the Investigator's spouse or dependent children) holds any equity interest (e.g., stock, stock option, or other ownership interest); or
- Intellectual property rights and interests (e.g., patents, copyrights).

◯ Yes ◯ No

Training and Experience

*Indicate the types of training that you and your research staff have had on the protection of human research subjects. Select all that apply.

- ☐ ACRP Certified Clinical Investigator Training
- ☐ Collaborative IRB Training Initiative (CITI)
- ☐ DIA Certified Investigator (CCI)
- ☐ Local Institution's Training
- ☐ Investigator Meeting
- ☐ NIH Protecting Human Research Participants Course
- ☐ OHRP Training Modules
- ☐ SOCRA Clinical Research Professional (CRP)
- ☐ Tri-Council Policy Statement online training (TCPS) Training (strongly recommended for Canadian Investigators)
- ☐ WCG Sponsored Training
- ☐ Other human subject protection training
- ☐ None

*Do you have more than one year of human subject research experience?

◯ Yes ◯ No

How many studies have you conducted as a PI or Sub-investigator?

How many studies are you currently conducting?

*What percentage of your time is devoted to conducting research?

Research Personnel

*Indicate the number of key study staff that will assist in this research:

Appendix 17: Initial Review Submission Form Page 4

wcg™ WIRB COPERNICUS GROUP®

Initial Review Submission Form

Note: Form must be completed in Adobe version 9.1 or later (Reader or Acrobat).
All fields with an asterisk (*) are required.

Subject Recruitment

*How will subjects be recruited for this study? Select all that apply.

- ☐ Existing Patients
- ☐ Referrals
- ☐ Advertisements
- ☐ Telephone Screening Scripts
- ☐ Other

*Indicate the subject populations that will participate in this study. Select all that apply (Note: Individuals from the populations listed below may not be enrolled unless checked.)

- ☐ Adults unable to consent
- ☐ Children
- ☐ Pregnant women
- ☐ Prisoners
- ☐ None of the above

*Indicate the characteristics of populations that will likely participate in this study. Select all that apply.

- ☐ Limited English skills
- ☐ Institutionalized individuals
- ☐ Students or employees of investigators
- ☐ None of the above

*Will the PI or research team receive recruitment bonuses?

○ Yes ○ No

Consent Process

*Indicate the setting for the consent process. Select all that apply.

- ☐ N/A, a complete waiver of consent is requested
- ☐ Private room
- ☐ Waiting room
- ☐ Group setting
- ☐ Group setting with follow-up in a private room
- ☐ Open Ward
- ☐ Emergency situation
- ☐ Online, in public, or over the phone
- ☐ Other

*Which of the following will be true during the consent process? (Note: If you do not select both items, you will be asked for an explanation.)

- ☐ The person conducting the consent process will spend the time needed to thoroughly explain and respond to questions potential subjects and/or their legally authorized representative have about the study.
- ☐ Potential subjects will be allowed as much time as needed to adequately read and consider the consent form, and to decide whether or not to enroll in the study.

Appendix 17: Initial Review Submission Form Page 5

wcg™ WIRB COPERNICUS GROUP®

Initial Review Submission Form

Note: Form must be completed in Adobe version 9.1 or later (Reader or Acrobat).
All fields with an asterisk (*) are required.

Consent Information

*Indicate how you are planning to provide consent information to potential subjects. Select all that apply.

- ☐ Long form consent document
- ☐ Short form consent document and summary
- ☐ Script or information sheet (a waiver of documentation of consent is requested)

*Do you wish to submit site-specific wording for the consent form (other than the PI's name and site address)?

○ Yes ○ No

Subject Payment for Participation

*Will subjects be paid or reimbursed for participation?

○ Yes ○ No

Translations

*Will a translated version of the informed consent form be needed to facilitate a subject's understanding of the research study?

○ Yes ○ No

HIPAA Information

*Select all that apply to this research

- ☐ Request for full waiver of HIPAA authorization
- ☐ Request for partial waiver of HIPAA authorization for recruitment
- ☐ None of the above

Confidentiality

Confidentiality refers to the agreement between the investigator and subject in how data will be managed and used.

*Indicate the procedures that you will follow to maintain the confidentiality of data collected about the subject. Select all that apply.

- ☐ Training of research personnel
- ☐ Study staff will sign confidentiality agreements
- ☐ Storage of paper records in a secure location accessible only to research personnel
- ☐ Coding of data with separate storage of the key and coded data
- ☐ Certificate of confidentiality
- ☐ Removal of identifiers as soon as possible

*Will confidential data be stored on desktop computers?

○ Yes ○ No

*Will confidential data be stored on mobile computers? (e.g., laptops, netbooks, tablets, cell phones)

○ Yes ○ No

Appendix 17: Initial Review Submission Form Page 6

wcg™ WIRB COPERNICUS GROUP*

Initial Review Submission Form

Note: Form must be completed in Adobe version 9.1 or later (Reader or Acrobat). All fields with an asterisk (*) are required.

*Will confidential data be stored on removable media? (e.g., USB drives, removable hard drives, CD, DVD)

◯ Yes ◯ No

*Will confidential data be transmitted over the Internet?

◯ Yes ◯ No

*Will confidential data be transmitted by e-mail?

◯ Yes ◯ No

Privacy

Privacy refers to persons' interest in controlling the access of others to themselves, such as the ability to control who sees them, hears them, touches them, and has access to their private information. Additional privacy interests include the time and place where subjects provide information, the nature of the information provided by the subjects, the nature of the subject's experiences during the trial, and who receives and can use the information.

*What procedures will you follow to protect the privacy of the subject? Select all that apply.

☐ The consent process will be performed in a private setting

☐ Research procedures will be performed in a private setting

☐ Private information collected will be limited to that necessary to conduct the research

☐ Other

Sites

*Are any sites part of an institution that is covered by an OHRP Federalwide Assurance (FWA) for the protection of human subjects?

◯ Yes ◯ No ◯ Don't know

*Indicate if any of the following are involved and have contacts for this study. Select all that apply

☐ CRO (Contract Research Organization)

☐ SMO (Site Management Organization)

☐ Coordinating Group

☐ N/A

Specific Site Information

Sponsor Site Number (if applicable)	*Company Name	
*Address Line 1	Address Line 2	*City
*State/Province	*Country	*Postal Code
	United States	
*Phone	*24 Hour Phone	

Appendix 17: Initial Review Submission Form Page 7

wcg™ WIRB COPERNICUS GROUP®

Initial Review Submission Form

Note: Form must be completed in Adobe version 9.1 or later (Reader or Acrobat).
All fields with an asterisk (*) are required.

Site characteristics

*How would you best describe this site's function? Select one.

- ○ College/University
- ○ Dialysis Center
- ○ Hospital
- ○ Medical Office
- ○ Nursing Home
- ○ Psychiatric Institution
- ○ Research Clinic
- ○ Other

*What are the community attitudes towards the conduct of research in the area around this site? Select one.

○ Neutral ○ Positive ○ Negative

*Are you aware of any state or local laws where you intend to conduct the research that would impose stricter requirements for research than those posed by the regulations?

○ Yes ○ No

*Does a local IRB have jurisdiction over this research site?

○ Yes ○ No

*If this research is federally funded, you may need to send an OHRP IRB Authorization Agreement (or equivalent) for this IRB to provide oversight for this location. Will you include one with this submission?
Contact us for more information about this requirement.

○ Yes ○ No

*Does this study involve medical procedures?

○ Yes ○ No

Indicate any additional resources. Select all that apply.

- ☐ Interpreters
- ☐ Bilingual staff members
- ☐ Counseling services
- ☐ Other
- ☐ Not Applicable

*What is the approximate distance of this site from the main site?

○ N/A, this is the main site ○ 49 miles (79 kilometers) or less ○ 50 miles (80 kilometers) or more

Appendix 17: Initial Review Submission Form Page 8

wcg™ WIRB COPERNICUS GROUP®

Initial Review Submission Form

Note: Form must be completed in Adobe version 9.1 or later (Reader or Acrobat).
All fields with an asterisk (*) are required.

Investigator Agreement

ACKNOWLEDGEMENT
Consistent with AAHRPP's requirements in connection with its accreditation of IRBs, the individual and/or organization submitting this form shall promptly communicate or provide, and where necessary cause each investigator to promptly communicate or provide, the following information relevant to the protection of human subjects to the IRB in a timely manner:

a. Upon request, a copy of the written plan between Client and Site that addresses whether expenses for medical care incurred by Human Subject Research subjects who experience research related injury will be reimbursed, and if so, who is responsible in order to determine consistency with the language in the consent document.
b. Any site monitoring report that directly and materially affects subject safety or their willingness to continue participation. Such reports will be provided to the Review Board within 5 days.
c. Reports from any data monitoring committee, data and safety monitoring board, or data and safety monitoring committee in accordance with the timeframe specified in the study protocol.
d. Any findings from a closed study when those findings materially affect the safety and medical care of past subjects. Findings will be reported for 2 years after the closure of the study.

By submitting this form, I am confirming that I am the Principal Investigator (PI) or the PI's designee authorized to submit on behalf of the PI. The information within this form is accurate and complete with the PI's full awareness of the information submitted.

☐ *I agree

*Name of individual completing this form

*Date *Title

HRP-212 Version 2.0.1 Page 8 of 8

Appendix 18: Informed Consent Form Contact Information (Local IRB)

In the event your study doctor is unable to locate you at the time of the follow-up visits for the limited purpose of collecting necessary follow-up data, you authorize your study doctor to disclose contact information about you, such as your name, last known address, telephone number to a locator company (which may be hired directly by the study sponsor) for the sole purpose of updating the study doctor with your current contact information or vital status.

Withdrawal from this study, for any reason, will not affect in any way the quality of health care you will receive.

You must return all unused study drug to the study doctor.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or a research-related injury, or if you have problems, concerns, questions or suggestions about the research, contact:

Principal Investigator Name: **Amir Malik MD**

Daytime telephone number(s): 817-347-6058

24-hour contact number(s): 817-425-6090

If you have any questions or concerns about your rights as a research subject or want to discuss a problem, get information or offer input, you may contact the Independent Review Board (IRB) at 817-347-1159. An IRB is a group of scientific and non-scientific individuals who perform the initial and ongoing ethical review of the research study with the study subject's rights and welfare in mind. The IRB has reviewed and approved the research study described in this Subject Informed Consent Form. If you have study-related comments, complaints or concerns, you should first contact the study investigator. Please call the IRB if you want to talk to someone other than the study investigator or have difficulty reaching the study investigator.

IRB PROJECT

255

Plaza Medical Center of Ft Worth

IRB APPROVED

DEC 30 2015

PLAZA MEDICAL CENTER OF FT WORTH

Appendix 19: Informed Consent Form Contact Information (Central IRB)

Approved 06Oct2016

Withdrawal from this study, for any reason, will not affect in any way the quality of health care you will receive.

You must return all unused study drug to the study doctor.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?
For questions about the study or a research-related injury, or if you have problems, concerns, questions or suggestions about the research, contact:

Principal Investigator Name: **Amir Malik MD**

Daytime telephone number(s): 817-347-6058

24-hour contact number(s): 817-425-6090

If you have any questions or concerns about your rights as a research subject or want to discuss a problem, get information or offer input, you may contact Copernicus Group Independent Review Board (IRB) at 1-888-303-2224 (toll free). An IRB is a group of scientific and non-scientific individuals who perform the initial and ongoing ethical review of the research study with the study subject's rights and welfare in mind. Copernicus Group IRB has reviewed and approved the research study described in this Subject Informed Consent Form. If you have study-related comments, complaints or concerns, you should first contact the study investigator. Please call the IRB if you want to talk to someone other than the study investigator or have difficulty reaching the study investigator. For further information regarding the clinical trials process and your role as a research subject, you may visit the Copernicus Group IRB website at www.cgirb.com.

Appendix 20: Site Continuing Review Report Page 1

wcg™ WIRB COPERNICUS GROUP*

Site Continuing Review Report

Note: Form must be completed in Adobe version 9.1 or later (Reader or Acrobat).
All fields with an asterisk (*) are required.

Submission Source

*To whom are you submitting this application?

- ○ Copernicus Group IRB (CGIRB)
- ◉ Western IRB (WIRB)
- ○ New England IRB (NEIRB)

This is a smart form. Some form elements will appear or disappear depending on answers to previous questions.

Sponsor Name	*Sponsor Protocol Number	IRB Protocol or Tracking Number

*Indicate the name of the Principal Investigator for whom you are submitting this form

Due Date	Sequence	IRB Report ID

Research Status (Site)

*Indicate the status of the research study:

- ○ Active, **NO** subjects have been accrued
- ○ Active, subjects have been accrued
- ○ Enrollment is closed and site is still open
- ○ HUD use continues

*Provide the current IRB approval date on the main consent document:
(If there are no consent documents or scripts indicate "none")

*Provide the most recent date that a subject signed the main consent document:
(If there are no consent documents or scripts indicate "none")

*Number of subjects enrolled since study startup:
(A subject is enrolled if the subject or representative gave consent to participate in the research. For protocols with a waiver of consent, a subject is enrolled if included in the research.)

*Of the number of subjects enrolled, how many failed screening?
(Enter 0 if the protocol does not involve screening or interventions.)

*Provide the number of subjects who withdrew from the research or were withdrawn/discontinued:
(A subject is considered to have been withdrawn/discontinued from the research when the subject either stopped participation or the research team stopped the subject's participation early for reasons other than reaching a study endpoint. Do not count screen failures.)

Appendix 20: Site Continuing Review Report Page 2

wcg™ WIRB COPERNICUS GROUP®

Site Continuing Review Report

Note: Form must be completed in Adobe version 9.1 or later (Reader or Acrobat). All fields with an asterisk (*) are required.

*Provide the number of subjects who **completed** the research:
(A subject is considered to have completed the research when the subject either completed all research procedures or completed all research procedures up to a study endpoint.)

Number of subjects remaining in the study
0

Site Continuing Review Report: Studies with Subject Accrual

*Have there been any unanticipated study-related problems that involve risks to subjects or others that have not been reported to this IRB?
◯ Yes ◯ No

*Have you received any subject complaints since your last report?
◯ Yes ◯ No

*Has any subject sought compensation for injury associated with this study at your site that has not been reported to this IRB?
◯ Yes ◯ No

Site Continuing Review Report: All Studies

*Are you aware of any scientific publications, reports, or any multi-center trial reports relevant to the risks and benefits of this research?
◯ Yes ◯ No

*Is there new risk or benefit information related to the research not previously reported to this IRB?
◯ Yes ◯ No

*Are there any changes to the protocol or consent form or other materials seen by subjects not previously reported to this IRB?
◯ Yes ◯ No

*Has the PI or any Sub-investigator on this study had a regulatory inspection by the FDA or OHRP since your last report?
◯ Yes ◯ No

*Are there any current investigations or charges involving the principal or Sub-Investigator?
◯ Yes ◯ No

*Has the PI's license been renewed during this reporting period?
◯ Yes ◯ No

*Has the PI received a revocation, sanction, or suspension of his/her state medical license since the start of the study or the last continuing review?
◯ Yes ◯ No

*Have the hospital privileges of the PI or the subinvestigators at the hospital where subjects are seen in case of an emergency been reduced since your last report?
◯ Yes ◯ No

Appendix 20: Site Continuing Review Report Page 3

wcg WIRB COPERNICUS GROUP

Site Continuing Review Report

Note: Form must be completed in Adobe version 9.1 or later (Reader or Acrobat).
All fields with an asterisk (*) are required.

*Have there been any changes in the PI's qualifications?
◯ Yes ◯ No

*Investigators must assure that each member of the research study team/staff has had training in the protection of human subjects, Have you added new study staff since the last report?
◯ Yes ◯ No

*Has the conflict of interest information changed for any of the study team members or their immediate families since the last review?
◯ Yes ◯ No

*Any change at the site where this research is conducted?
◯ Yes ◯ No

*Are you aware of any changes to State or local laws related to research?
◯ Yes ◯ No

*What is the PI's perception of the community's attitude toward research?
◯ Positive ◯ Negative ◯ Neutral

*Is the PI aware of any recent events in his/her community (outside of this study) (such as deaths or serious injuries) related to research?
◯ Yes ◯ No

*Is there any change to the PI's risk-potential benefit assessment based on study results?
◯ Yes ◯ No

Person Completing this form

*Name | *Company

*Title | *Phone number

*E-mail address

Note: The submission of this form means that the Principal Investigator is agreeing to and is responsible for the accuracy of all information on this form.

Appendix 21: Site Closure Report

wcg WIRB COPERNICUS GROUP

Closure Report

Note: Form must be completed in Adobe version 9.1 or later (Reader or Acrobat).
All fields with an asterisk (*) are required.

Submission Source

*To whom are you submitting this application?

- ◯ Copernicus Group IRB (CGIRB)
- ◯ Western IRB (WIRB)
- ◯ New England IRB (NEIRB)

This is a smart form. Some form elements will appear or disappear depending on answers to previous questions.

Submission of this report is appropriate only if all of the following have been accomplished. If not, please submit a Continuing Review Report.

1. All subjects at your site have finished their final visits and any follow-up activities (such as phone calls, post-card contacts, or long term follow up required by the protocol) are completed,
2. The sponsor or the sponsor representative has indicated that the study is closed at your site, and
3. If the study was conducted under a Federalwide Assurance, all data analysis at the site is completed.

☐ *All criteria listed are true

Sponsor Name	*Sponsor Protocol Number	IRB Protocol or Tracking Number

*Indicate the name of the Principal Investigator for whom you are submitting this form

Person Completing this form

*Name	*Company
*Title	*Phone number

*E-mail address

Note: The submission of this form means that the Principal Investigator is agreeing to and is responsible for the accuracy of all information on this form.

Appendix 22: Medical City of Fort Worth AE/SAE Form

APPENDIX 8
Adverse Event Form
Plaza Medical Center of Fort Worth
Institution Review Board for the Protection of Human Subjects

Is the event being reported an AE or an SAE (circle one) AE SAE

Date Principal Investigator Informed : _____ By : _____

Serious: *Death, a life-threatening adverse drug experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect.*
Unexpected: *Any adverse drug /device experience, the specificity or severity of which is not consistent with the current investigator brochure or consent form.*

Complete this form and forward with appropriate attachments to the IRB office. Report to the sponsor and/or FDA as required.

Date: IRB #: _____

Investigator:

Study Title: _____

1. Study is: (circle one) Multi-site Onsite only

2. Is this a follow-up report? Yes No

3. Describe adverse event:

Indicate seriousness: (circle one) a. Serious but not fatal b. Fatal c.AE

Indicate level of severity : (circle one) a . Mild b. Moderate c. Severe

Provide a summary describing the circumstances of the event. Indicate if prolonged hospitalization or medical treatment was required. Include a copy of all notifications and/or letter of adverse event from the study sponsor or other site. INCLUDE A STATEMENT IN YOUR WORDS REGARDING THIS ADVERSE EVENT AND RELATION TO THE STUDY/PATIENTS AT THIS INSTITUTION.

4. In your judgment, was the SAE / AE event caused by the therapy or procedures associated with this protocol? (circle one)

Not Likely Possibly Probably Definitely related

5. Is the risk of this SAE / AE contained in the current consent form? ☐ Yes No

6. Is the risk of this SAE / AE contained in the investigator's brochure? ☐ Yes No

7. Should the consent form or any portion of the study be revised as a result of this event? ☐ Yes No
If yes, please enclose revised documents with all revisions in bold print or highlighted.

8. Will currently enrolled individuals be notified of this event? ☐ Yes No
If yes, describe method of notification:

Signed:_____ Date:_____
(Principal Investigator)

********** For IRB use only**********

Review by IRB chairperson: (initials)_____Date:_____

Appendix 8-ADMIN19/dj

Appendix 23: Promptly Reportable Information Form

wcg WIRB COPERNICUS GROUP

Promptly Reportable Information Submission Form

Use to submit promptly reportable new information

Note: Form must be completed in Adobe version 9.1 or later (Reader or Acrobat). All fields with an asterisk (*) are required.

*To whom are you submitting this application?

- ◯ Copernicus Group IRB (CGIRB)
- ◯ Western IRB (WIRB)
- ◯ New England IRB (NEIRB)

*Indicate the source/type of submission:

- ◯ Sponsor or CRO
- ◯ Study Site / SMO

This is a smart form. Some form elements will appear or disappear depending on answers to previous questions.

Identifying Information

Principal Investigator's Name:

Prefix	*First	Middle	*Last	Suffix

*IRB Protocol or Tracking Number	*Date of this report	Date of occurrence (if known)

Subject ID (if applicable)	*Is the subject still enrolled in the study?	*Submitting body:

Type of Problem (Information not listed below does not require prompt reporting to us)

*Select all that apply:

☐ Audit, inspection or inquiry by a federal agency

Provide the date of the inspection including the beginning and end dates.

Clarify if a study approved by this IRB was audited and identify the study.

For Health Canada inspections, please provide the rating received.

☐ Written report from a federal agency (e.g., FDA Form 483)

Submit a complete copy of all reports and correspondence related to the inspection (e.g. FDA Form 482 and 483, site's response to the 483, FDA letter responding to the site, EIR Summary, FDA WARNING Letter, Health Canada Inspection Notice, Health Canada Exit Notice).

☐ State medical board action

Submit a copy of state medical board licensing documentation [e.g. a physician's (suspended) license, a physician profile, or a physician licensing profile indicating a disciplinary, or even a non-disciplinary action].

☐ Allegation of noncompliance or finding of noncompliance

Submit documents related to the noncompliance allegation or finding.

☐ Suspension or premature termination by the sponsor, investigator, or institution

Submit a copy of correspondence related to the suspension or premature termination and provide additional explanation if applicable.

☐ Incarceration of a subject in a research study not approved to involve prisoners

If a subject becomes incarcerated at any time during a research study, provide details including the date of occurrence or discovery, timeline and actions taken.

Appendix 23: Promptly Reportable Information Form

wcg™ WIRB COPERNICUS GROUP®

Promptly Reportable Information Submission Form

Use to submit promptly reportable new information

Note: Form must be completed in Adobe version 9.1 or later (Reader or Acrobat). All fields with an asterisk (*) are required.

☐ New or increased risk

If the new or increased risk(s) is changing the protocol and/or consent form, please submit as a change in research.

If the new or increased risk(s) will change the protocol and/or consent form in the future, please provide as much detail about the possible change and the expected timeline for that change.

If the new or increased risk(s) is not changing the protocol and/or consent form at this time, please provide the reason why in the "What actions need to be taken" area below.

☐ Adverse events or IND safety reports that require a change to the protocol or consent

If the event is changing the protocol and/or consent form, please submit as a change in research, using the Change in Research Submission Form.

If the new or increased risk(s) will change the protocol and/or consent form in the future, please provide as much detail about the possible change and the expected timeline for that change.

If the event is not changing the protocol and/or consent form at this time, please provide the reason why in in the "What actions need to be taken" area below.

☐ Unanticipated adverse device effect

An unanticipated adverse device effect is defined as follows:
"any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects" (21 CFR 812.3(s))"

☐ Protocol deviation that harmed a subject or placed subject at risk of harm

In the "Describe the problem" section below, please:
• Explain any harm the subject experienced OR how the subject was placed at risk of harm.
In the "What actions need to be taken" section below, please:
• Explain the corrective action taken for this event AND your plans to avoid future occurrences.

☐ Protocol deviation made without prior IRB approval to eliminate an immediate hazard to a subject

In the "Describe the problem" section below, please:
• Describe the subject's situation and why immediate action was required.
• State if sponsor was notified (attach any correspondence)
In the "What actions need to be taken" section below, please:
• Explain your plans to avoid future occurrences, if applicable.

☐ Breach of confidentiality

In the "What actions need to be taken" section below, please state whether this breach has been disclosed to subject(s)

☐ Unresolved subject complaint

This is a complaint that you would like assistance resolving. This would not include subject withdrawals due to expected events.

Appendix 23: Promptly Reportable Information Form

wcg™ WIRB COPERNICUS GROUP®

Promptly Reportable Information Submission Form

Use to submit promptly reportable new information

Note: Form must be completed in Adobe version 9.1 or later (Reader or Acrobat). All fields with an asterisk (*) are required.

☐ Other information the sponsor/CRO/other has directed the PI to report to the IRB, even if not on this list and does not meet any of the reporting requirements.

Please use this when none of the above issues apply, but you are being required to submit to the IRB for filing with the research.

Other events not fitting the criteria above

If you have an event you considered reporting and determined it was not reportable, you may mark the box below, print the form and keep it in your records (DO NOT SUBMIT FOR REVIEW).

☐ Information not listed above does not require prompt reporting to this IRB.

Description and Needed Actions

*Describe the problem (date of occurrence or discovery, timeline, cause, actions taken, changes made):

*What actions need to be taken, or what changes are proposed to protect research subjects or others? (corrective and preventive actions) If none, justify.

*Has the PI reviewed the form?

○ Yes ○ No

Person completing this form:

Prefix	*First	Middle	*Last	Suffix

*Company	*Email	*Phone

Appendix 24: Active Study Common Database Template

TYPE OF STUDY (Drug/ Device)	SPONSOR	PROTOCOL #	TITLE OF STUDY	PI NAME	CURRENT IRB OVERSEEING STUDY	RENEWAL/CLOSURE DATE	COMPLIANCE STATUS

Appendix 25: Exempt Review Application

Medical City Ft Worth
Research Office
Suite 108, Professional Bldg.
900 8th Avenue,
Ft. Worth, Texas 76008
Telephone: (817)347-6094
Email: Rubina.Muzina@medicalcityhealth.com

Exemption Determination Application

NOTE: EXEMPTION CERTIFICATION IS NOT APPROVAL. THE STUDY MATERIALS SHOULD NOT INCLUDE THE STATEMENT THAT HAS REVIEWED AND APPROVED THE STUDY FOR HUMAN SUBJECT PARTICIPATION.

Instructions:

- *Institutional reviewer will determine whether or not your research qualifies for exemption.* ***Do NOT begin data collection prior to reviewer determination.***
- *NIH training https://phrp.nihtraining.com/users/login.php needs to be completed for every study member before the determination of the category pertaining to your research;*
- *DO NOT leave a question blank; write "n/a" if a question does not apply to the application.*

1. Principal Investigator (PI) Contact Information: Name: Phone: E-mail:

2. Study Title:

3. Sub- PI and study members' names: Name: Name: Name:

Name: Name: Name:

SECTION 1. HUMAN SUBJECTS RESEARCH DETERMINATION

Answer the questions below:

1. ❑Yes ❑No Will your investigation gather information about living human individuals?

2. ❑Yes ❑No Will you be interacting with the respondents or intervening in their daily routine, including via the internet or over the phone?

3. ❑Yes ❑No Are you collecting data that would allow you or another researcher to identify the participants (examples: Name, Social Security Number, phone number, mailing address, email, medical record number or any other number or code that pertains specifically to an individual)?

4. ❑Yes ❑No Is the data collected considered to be private information, which the participant expects will not be made public, or in a context which an individual would not otherwise expect to be observed or recorded (such as in their home)?

If you answer "NO" to Each of questions 1-4, your research does not involve human participants and regulatory review is not required.

Appendix 25: Exemption Review Application

If you answer "YES" to one or more of the above questions, your research involves human participants and you need to complete questions below.

5. ❑Yes ❑No Are you conducting an investigation, a searching inquiry to gather facts, or an Examination of a phenomenon?

6. ❑Yes ❑No Is it systematic, involving a system, method, or plan that will be employed consistently throughout data collection?

7. ❑Yes ❑No Will your findings be presented beyond the hospital setting, such as presented at a conference, or published in a peer-reviewed journal or used in a thesis or dissertation?

8. ❑Yes ❑No Will your conclusions be presented as representative of the larger population from which your sample was recruited? (Mark 'No' if the data collected applies only to the sample population)

If you answer "NO" to questions 5-8, your study is not research and regulatory review is not required.
If you answer "YES" to questions 5-8, your study is research. Continue to Section 2.

SECTION 2. SCREENING QUESTIONS

Federal regulations specify that certain types of research pose low risk to participants, and therefore MAY qualify for EXEMPTION under federal regulations. To determine if your study is exempt, answer the following screening questions.

1. ❑Yes ❑No Will participants be asked to report their own or others' sexual experiences, alcohol or drug use, and will their identities be known to you?

2. ❑Yes ❑No Are the participants' data directly or indirectly identifiable, and could these data place subjects at risk for criminal or civil liability, or might they be damaging to subjects' financial standing, employability or reputation?

3. ❑Yes ❑No Are any participants confined in a correctional or detention facility, including involuntary assignment to community-based alternatives to incarceration (drug treatment facilities, etc.)?

4. ❑Yes ❑No Are participants involved who may not be legally/mentally/cognitively competent?

5. ❑Yes ❑No Are personal records (medical, academic, etc.) used with identifiers and without written consent?

6. ❑Yes ❑No Will alcohol or drugs be administered to the subjects?

7. ❑Yes ❑No Will blood/body fluids be drawn from participants?

8. ❑Yes ❑No Will specimens obtained from an autopsy be used?

9. ❑Yes ❑No Are live fetuses subjects in this research?

If you answer "YES" to any of the above questions, then your research is NOT exempt.

Appendix 25: Exemption Review Application

Contact me and I will assist you on submitting the data to Medical City IRB as non-exempt application.

If you answer "NO" to all the above questions, your research may be exempt. Please complete Sections 3-6.

SECTION 3. EXEMPTION CATEGORIES AND DETERMINATIONS

EXCEPTIONS: The exemption categories listed below do not apply when the research includes the following:

- Prisoners
- Survey or interview techniques which include minors as participants (this applies to exemption category #2 only)
- Observation of minors where the investigator participates in the activities being observed (this applies to exemption category #2 only)
- FDA regulated research (this applies to exemption categories 1-5 and includes projects for which the data will be submitted to or held for inspection by the FDA, or research for which the investigator gathers data on participants who serve as controls for participants who receive FDA-regulated drugs or medical devices, other than in the course of medical practice.) **Research activities are exempt from the federal regulation 45 CFR 46.101(b) for the protection of human participants when the ONLY involvement of human participants falls within one or more of the categories below.**

Check the appropriate categories that apply to your research study:

❑ **Category 1 (45 CRF 46.101(b) (1)]** Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as:

i. Research on regular and special educational instructional strategies, **or**
ii. Research on the effectiveness of **or** the comparison among instructional techniques, curricula, **or** classroom management methods.

Will any of the above categories applies to your project?

☐ **Yes (please attach supporting documents** ☐ **No**

If yes, please answer the below question:

Are the education and instructional strategies carried on regardless of your project?
☐ **Yes, they are part of normal activities**
☐ **No , they are part of this research**

❑ **Category 2 (45 CRF 46.101(b) (2)]** Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, **UNLESS**

i. information obtained is recorded in such a manner that human participants can be identified, directly or through identifiers linked to the participants; **and**

ii. any disclosure of the human participants ' responses outside the research could reasonably place the participants at risk of criminal or civil liability; **or**
iii. be damaging to the participants ' financial standing, employability, or reputation.

PLEASE NOTE: According to 45 CFR 46.401(b), this exemption does NOT apply to survey or interview procedures when the participants are children.

Does your project involve any of the above categories?

☐ **Yes** ☐**No**

If yes, please attach supporting documents & answer the question below:

Will the info obtained be recorded in such a manner that participants cannot be identified directly or through identifiers linked to the participants? [Attached you will find the list of HIPPA identifiers -Code of Federal Regulation 45 CRF 164.514(b)]

☐ **Yes** ☐**No**

❑ **Category 3 (45 CRF 46.101(b) (3)]** Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under category (2) of this section, if:

i. the human participants are elected or appointed public officials or candidates for public office; **OR**
ii. federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

Does your project involve any of the above categories?
❑ Yes **If yes, please attach supporting documents;** ❑ No

❑ **Category 4 (45 CRF 46.101(b) (4)]** **Definition:** Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available **Or** if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the participants.

PLEASE NOTE: **According to the Office for Human Research Protections (OHRP), "to qualify for this exemption the data, documents, records, or specimens must be in existence before the project begins.** The principle behind this policy is that the rights of individuals should be respected; participants must consent to participation in research.

Does the research involve the use of data, docs, records, pathological specimen that currently existing? (Means no prospectively collected)

❑**Yes** ❑**No**

Are these documents or specimens publicly available?

❑**Yes** ❑**No**

Does the research involve use of existing pathological specimens?

Appendix 25: Exemption Review Application

❑**Yes** (If yes, please attach source of specimen/description and its origin) ❑ **No**

Will biological specimens be obtained in the future from living individuals?

❑**Yes** ❑**No**

Will the information or samples include any codes with links (directly or indirectly) to the identity of the individuals?

❑Yes ❑No

Will the information or samples collected specifically for this project or they were collected for another purpose?

❑Yes, they were collected for this project

❑No, they were collected for another project

5. ❑ **[Category 5 (45 CRF 46.101(b) (5)]** "Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine:

i. Public benefit or service programs;
ii. Procedures for obtaining benefits or services under those programs;
iii. Possible changes in or alternatives to those programs or procedures;
iv. Possible changes in methods or levels of payment for benefits or services under those programs")

- **Is this research study conducted or approved by a Federal Department or Agency Head? (attach approval documents) ☐ Yes ☐No**
- **Is the aim of the study to study evaluate or examine one or more of the following statements: (Place an X by the following statement(s) that are true):**

❑ **public benefit or service programs;**
❑ **procedures for obtaining benefits or services**
❑ **possible changes in or alternatives to those programs or procedures;**
❑ **possible changes in methods or levels of payment for benefits or services under those programs**
❑

6. ❑ **Taste and Food Evaluation [Category 6 (45 CRF 46.101(b) (6)]** Taste and food quality evaluation and consumer acceptance studies (i)if wholesome foods without additives are consumed or (ii)if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the FDA or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S Department of Agriculture"

Does your project involve any of the above categories: ☐ Yes **If yes attach the supporting documents.** ☐ No

If you mark one or more of the six exemption categories above, complete the remainder of the application and submit to Institutional Reviewer who will determine whether or not your research qualifies for exemption. Do NOT begin data collection without exemption certification from the reviewer.

Appendix 25: Exemption Review Application

SECTION 4. GENERAL INFORMATION

Human Participants Training: Medical City of Ft Worth requires Investigator, Co- investigators, coordinators, and Key personnel involved in this research to complete NIH training in the ethical use of human participants in research. Re-training is required every year.
You will find the link at : https://phrp.nihtraining.com/users/login.php.
For CITI training options, visit the CITI website at http://www.citiprogram.org.
If you have any further questions, please contact Rubina Muzina at 817-980-2938 or Rubina.Muzina@medicalcityhealth.com.

3. Estimated Study Start Date: _____ Duration of the Study: _____

4. ☐ Yes ☐ No Is this research supported in whole or in part by a grant or contract?

   If yes, Grant/Funding Agency(s), Foundation, or Business: _____

5. ☐ Yes ☐ No Does the research require another IRB's review (US and International)?
   If **yes**, complete below.

   Name of the IRB/FWA: _____

6. ☐ Yes ☐ No Does the PI, Co-PI, or any other person responsible for the design, conduct, or reporting of this research have an economic interest in or act as an officer or director of any outside entity whose financial interest would reasonably appear to be affected by the results of the study? If yes, complete below:

   Name of the person with potential conflict of interest (COI): _____

   Explain the potential financial conflict of interest:
   _____

   Explain how the potential conflict of interest will be managed?
   _____

7. ☐ Yes ☐ No Is the proposed research study conducted at an outside (non-medical city fort worth) facility or entity (such as hospitals, clinics, schools, school districts, factories, offices, etc..,)? If yes, complete below.

Appendix 25: Exemption Review Application

Name (s) of the facility or entity: _____

SECTION 5. INVESTIGATOR'S RESPONSIBILITIES AND ASSURANCES

Indicate that you have read and will comply with each statement.

1. ☐ I certify that the information provided in this application, and in all attachments, is complete and correct.

2. ☐ I understand that I have ultimate responsibility for the protection of the rights and welfare of human participants, the conduct of this study, and the ethical performance of this research.

3. ☐ I agree to comply with all HCA policies and procedures, the terms of its Federal Wide Assurance, and all applicable federal, state, and local laws regarding the protection of human participants in research.

4. ☐ I certify that:
   - the study will be performed by qualified personnel according to the this approved application.
   - the equipment, facilities, and procedures to be used in this research meet recognized standards for safety.
   - New information that may affect the risk–benefit assessment for this research will be reported to
   - student and co-investigators on this study have received adequate training and are knowledgeable about the regulations and policies governing this research.
   - I agree to ensure adequate supervision of all research study personnel and to meet with the investigator(s), if different from myself, on a regular basis to monitor study progress.

5. ☐ I further certify that the proposed research has not yet been done, is not currently underway, and will not begin until approval has been obtained.

PI Name: _____ Signature: _____ Date: _____

Appendix 25: Exemption Review Application

How to Submit:

1. Attach the application and supporting materials (survey questions, interview guide, etc.) to an email sent to **Rubina.Muzina@medicalcityhealth.com**. If sent from the PI's HCA e-mail account, a physical signature is not required. Please allow for up to 10 business days to complete exemption determination.

Institutional Reviewer Use Only – Do Not Write or Mark in This Box

☐ **Certified Exempt under 45 CFR 46.101(b)…**
☐ **1** ☐ **2** ☐ **3** ☐ **4** ☐ **5** ☐ **6**
❑**Must be re-submitted on Non-Exempt Application to Medical City Dallas.**

Signature: _____Print Name: _____

Date: _____

APPENDIX 26: Weekly Logs

Week 1

September 27, 2016

- Plaza Medical Center HR orientation
- Received ID badge
- Prepared for the required NIH Human Subject Protection Certificate required by Plaza IRB
- Brain storming for research ideas regarding the topic of the internship

September 28, 2016

- Attended phone call close out visit for PLATINUM study
- Redacted medical records for the cVAD registry
- Checked temperature of study medications within refrigerator
- Redacted medical records for the cVAD registry

September 29, 2016

- Attended COBRA-REDUCE study close out
- Assisted in shipping the study stents back to the sponsor
- Redacted medical records for the cVAD registry
- Checked temperature of study medications within refrigerator
- Worked on researching background literature for thesis proposal

September 30, 2016

- Worked on researching background literature for thesis proposal
- Checked temperature of study medications within refrigerator
- Redacted medical records for the cVAD registry

Student _____ Date _____
Mentor_____ Date_____

Week 2

October 3, 2016

- Prepared pharmacy vouchers to be given to ODYSSEY study patients
- Checked temperature of study medications within refrigerator
- Completed redacting medical information for cVAD registry

October 4, 2016

- Prepared pharmacy vouchers to be given to ODYSSEY study patients
- Checked temperature of study medications within refrigerator
- Prepared storage boxes for close-out of studies and shipment to storage
- Brainstormed for proposal

October 5, 2016

- Scheduled UPS pick up for shipping blood samples to central lab for the ODYSSEY study
- Checked temperature of study medications within refrigerator
- Began transitioning physician CV's and lab certifications to electronic files
- Organized desk and shelf

October 6, 2016

- Assisted in the transition of local to central IRB
- Assisted in categorizing physician CV's and lab certifications to digital folders
- Checked temperature of study medications within refrigerator
- Miscellaneous filing

October 7, 2016

- Brainstorming for proposal
- Checked temperature of study medications within refrigerator
- Meeting with Dr. Muzina to discuss research proposal ideas

Student _____ Date _____
Mentor_____ Date_____

Week 3

October 10, 2016

- Assisted study coordinator to prepare visit checklists for the ODYSSEY study
- Filed Amendment 11 consent forms in study binders for the ODYSSEY study
- Checked temperature of study medications within refrigerator
- Brainstormed for thesis

October 11, 2016

- Assisted study coordinator in gathering study documents for closed studies
- Assembled patient information, manuals, logs, and other pertinent study material for ODYSSEY, COBRA-REDUCE, and SUPERNOVA studies for shipment to storage
- Discussed the committee meeting and created a general plan of attack
- Checked temperature of study medications within refrigerator
- Prepared storage boxes for the close-out study documents

October 12, 2016

- Finalized plans for the committee meeting
- Checked temperature of study medications within refrigerator
- Completed advisory committee meeting
- Transcribed notes from meeting
- Began researching information for thesis proposal

October 13, 2016

- Researched information for thesis proposal
- Checked temperature of study medications within refrigerator
- Discussed local IRB protocol for new and ongoing studies with IRB Coordinator
- Prepared more storage boxes for the close-out study documents

October 14, 2016

- Off site

Student _____ Date _____
Mentor_____ Date_____

Week 4

October 17, 2016

- Checked temperature of study medications within refrigerator
- Assembled patient information, manuals, logs, and other pertinent study material for ODYSSEY, COBRA-REDUCE, and SUPERNOVA studies for shipment to storage
- Began preparing calendars for ODYSSEY patients by adding stickers to dates on which patient is required to take medication
- Searched for sites and resource material for proposal

October 18, 2016

- Checked temperature of study medications within refrigerator
- Continued preparing calendars for ODYSSEY patients
- Continued searching for sites and resource material

October 19, 2016

- Checked temperature of study medications within refrigerator
- Familiarized myself with the COBRA clinical trial for the research site by reviewing the complete study protocol
- Familiarized myself with the cVAD clinical trial for the research site by reviewing the complete study protocol

October 20, 2016

- Checked temperature of study medications within refrigerator
- Familiarized myself with the PLATINUM clinical trial for the research site by reviewing the complete study protocol
- Familiarized myself with the PLATINUM clinical trial for the research site by reviewing the complete study protocol
- Began research proposal draft to be sent to the UNTHSC committee for review

October 21, 2016

- Offsite – out of town

Student _____ Date _____
Mentor_____ Date_____

Week 5

October 24, 2016

- Checked temperature of study medications within refrigerator
- Observed patient follow-up phone call for COBRA study and the process of entering data into the sponsor's database
- Worked on reading and annotating source material for proposal
- Mailed 2017 calendars to ODYSSEY patients

October 25, 2016

- Checked temperature of study medications within refrigerator
- Sat in on office meeting with the hospital's Director of Cardiology
- Worked on reading and annotating source material for proposal

October 26, 2016

- Checked temperature of study medications within refrigerator
- Continued reading and annotating source material for research proposal
- Familiarized myself with the WRAP-IT clinical trial for the research site by reviewing the complete study protocol

October 27, 2016

- Checked temperature of study medications within refrigerator
- Familiarized myself with the COBRA-REDUCE clinical trial for the research site by reviewing the complete study protocol
- Familiarized myself with the SUPERNOVA clinical trial for the research site by reviewing the complete study protocol

October 28, 2016

- Checked temperature of study medications within refrigerator
- Observed coordinator scheduling patient clinic visit over the phone
- Added events to research site calendar regarding patient visits scheduled over the phone
- Began reading policies and regulations of new central IRB, WIRB, which site is transitioning to

Student _____ Date _____
Mentor_____ Date_____

Week 6

October 31, 2016

- Checked temperature of study medications within refrigerator
- Continued analyzing WIRB policies and regulations for studies under their oversight
- Met with Dr. Muzina to discuss updates to the research proposal
- Began redacting subject documents for ODYSSEY registry

November 1, 2016

- Checked temperature of study medications within refrigerator
- Continued redacting subject documents for ODYSSEY registry
- Worked on reading and annotating source material for proposal

November 2, 2016

- Checked temperature of study medications within refrigerator
- Finished redacting subject documents for ODYSSEY registry
- Familiarized myself with the DANCE clinical trial for the research site by reviewing the complete study protocol
- Made copies and uploaded redacted ODYSSEY subject documents within the appropriate study folders online

November 3, 2016

- Checked temperature of study medications within refrigerator
- Worked on background section of research proposal
- Began updating site binders for cVAD study which included getting new binders and labeling them accordingly
- Filed redacted ODYSSEY subject documents within the appropriate study folders

November 4, 2016

- Checked temperature of study medications within refrigerator
- Mailed patient letters to subjects of ODYSSEY study
- Left early to finish medical school secondary essays
- Submitted research proposal to UNTHSC IRB for review

Student _____ Date _____
Mentor_____ Date_____

Week 7

November 7, 2016

- Checked temperature of study medications within refrigerator
- Observed IRB transfer process including updating site FWA and IRB numbers
- Worked on research proposal
- Updated site records of physician CITI training and medical licensure

November 8, 2016

- Checked temperature of study medications within refrigerator
- Scheduled Covance UPS pickup for patient samples to be returned to central lab
- Organized the shared Cath Lab Research folder
- Finished updating site cVAD binders
- Sent draft of research proposal to Dr. Gwirtz

November 9, 2016

- Checked temperature of study medications within refrigerator
- Received Dr. Gwirtz's edits to my research proposal
- Worked on correcting proposal
- Helped retrieve new shipment of study medications from hospital
- Labeled and stored new medication within refrigerator in the hospital pharmacy

November 10, 2016

- Checked temperature of study medications within refrigerator
- Met with Dr. Muzina for input on research proposal and modifications
- Assisted one of the coordinators in updating the IRB submission log
- Learned the process of filling the appendix 7 and 10 required for an expedited review by the IRB

November 11, 2016

- Checked temperature of study medications within refrigerator
- Assisted in centrifuging and transferring blood work to be sent to sponsor
- Coordinated a UPS pick up for patient samples to be sent to central lab

Student _____ Date _____
Mentor_____ Date_____

Week 8

November 14, 2016

- Checked temperature of study medications within refrigerator
- Worked on research proposal for final submission
- Filed paperwork into the appropriate patient binders
- Added patient visit window dates to the shared research calendar for the PLATINUM study

November 15, 2016

- Checked temperature of study medications within refrigerator
- Met with Dr. Muzina to discuss progress on research proposal
- Added Adverse Event Forms to every future visit section in each patient binder in the SUPERNOVA study
- Added Adverse Event Forms to every future visit section in each patient binder in the ODYSSEY study

November 16, 2016

- Checked temperature of study medications within refrigerator
- Converted physician CVs to electronic copies and uploaded into appropriate folders
- Observed clinic follow up visit of research subject
- Submitted patient records from follow-up to health records department

November 17, 2016

- Checked temperature of study medications within refrigerator
- Mailed out reminder letters to patients
- Scheduled UPS pickup of patient samples to central lab, Covance
- Worked on research proposal

November 18, 2016

- Checked temperature of study medications within refrigerator
- Assisted coordinator in updating the patient follow up visit information into the electronic case report forms.
- Obtained necessary signatures from the study PI
- Worked on research proposal

Student _____ Date _____
Mentor_____ Date_____

Week 9

November 21, 2016

- Checked temperature of study medications within refrigerator
- Working on research proposal for final submission
- Observed a clinical patient follow up visit

November 22, 2016

- Checked temperature of study medications within refrigerator
- Met with Dr. Muzina for final review of research proposal
- Left early to finish proposal

November 23, 2016

- Submitted research proposal to committee
- Off site – Thanksgiving break

November 24, 2016

- Offsite – Thanksgiving break

November 25, 2016

- Offsite – Thanksgiving break

Student _____ Date _____
Mentor_____ Date_____

Week 10

November 28, 2016

- Checked temperature of study medications within refrigerator
- Attended office meeting with the Director of Cardiology
- Observed phone follow-up visit for COBRA study
- Began outline for thesis

November 29, 2016

- Checked temperature of study medications within refrigerator
- Began gathering background material for thesis
- Sat in on conference call between office and ODYSSEY sponsor
- Attended the employee forum for the hospital

November 30, 2016

- Checked temperature of study medications within refrigerator
- Logged IRB submissions and sent pertinent study-related materials to study sponsor
- Observed procedures in the Cath lab

December 1, 2016

- Checked temperature of study medications within refrigerator
- Observed COBRA study monitor visit
- Assisted coordinator in copying patient data information on to a DVD
- Continued outlining thesis

December 2, 2016

- Checked temperature of study medications within refrigerator
- Observed process of obtaining informed consent from patient
- Observed phone follow up visit for two patients

Student _____ Date _____
Mentor_____ Date_____

Week 11

December 5, 2016

- Checked temperature of study medications within refrigerator
- Made boxes for future study material storage
- Observed the process of filing the newsletter from the sponsor in the regulatory binder in sponsor correspondence section.
- Redacted patient records for cVAD study

December 6, 2016

- Checked temperature of study medications within refrigerator
- Redacted patient records for cVAD study
- Left early - sick

December 7, 2016

- Off site - Sick day

December 8, 2016

- Checked temperature of study medications within refrigerator
- Redacted patient records for cVAD study
- Observed process of obtaining necessary physician notes from a different facility

December 9, 2016

- Checked temperature of study medications within refrigerator
- Redacted patient records for cVAD study
- Uploaded redacted cVAD patient records to site database
- Organized cath lab research folder

Student _____ Date _____
Mentor_____ Date_____

Week 12

December 12, 2016

- Checked temperature of study medications within refrigerator
- Observed a patient follow up visit on site
- Built more boxes for future study material storage
- Mailed out reminder letters for patients that scheduled follow up visits

December 13, 2016

- Checked temperature of study medications within refrigerator
- Attended a hospital I-care meeting
- Built more boxes for study material storage
- Redacted patient documents for ODYSSEY study

December 14, 2016

- Checked temperature of study medications within refrigerator
- Continued redacting patient documents for ODYSSEY study

December 15, 2016

- Checked temperature of study medications within refrigerator
- Finished redacting patient documents for ODYSSEY study
- Uploaded redacted ODYSSEY patient documents on to site database

December 16, 2016

- Checked temperature of study medications within refrigerator
- Collected literature for thesis
- Began reading and annotating material for thesis

Student _____ Date _____
Mentor_____ Date_____

Week 13

December 19, 2016

- Checked temperature of study medications within refrigerator
- Assisted in gathering study materials that needed to be sent to storage
- Built more boxes for shipping materials to storage

December 20, 2016

- Checked temperature of study medications within refrigerator
- Scheduled a UPS pick up for serum return to central lab.
- Assisted in loading storage boxes for materials department
- Assisted in updating sponsor screen fail database for Odyssey study

December 21, 2016

- Checked temperature of study medications within refrigerator
- Discussed and took notes on IRB transfer process with Dr. Muzina
- Gathered site information on IRB transfer process (FWA number, study records, IRB number)

December 22, 2016

- Checked temperature of study medications within refrigerator
- Observed phone follow-up visit
- Reviewed storage protocol with coordinators
- Marked boxes with closed study materials for shipping to storage

December 23, 2016

- Off site – Christmas break

Student _____ Date _____
Mentor_____ Date_____

Week 14

December 26, 2016

- Off site – Christmas break

December 27, 2016

- Checked temperature of study medications within refrigerator
- Screened hospital patient records for potential inclusion in research studies
- Added new contacts to Heart Center of North Texas Directory
- Assisted in logging injection kits into the regulatory binder for Odyssey

December 28, 2016

- Checked temperature of study medications within refrigerator
- Organized study shelves to make room for new study binders
- Met with Dr. Muzina to discuss AE/SAE reporting process under local IRB
- Obtained local AE/SAE reporting forms

December 29, 2016

- Checked temperature of study medications within refrigerator
- Met with Dr. Muzina to discuss AE/SAE reporting under central IRB
- Assisted in retrieving and filing updated IRB correspondence for COBRA Study
- Observed on site patient follow up visit

December 30, 2016

- Off site – doctor's appointment

Student _____ Date _____
Mentor_____ Date_____

Week 15

January 2, 2017

- Off site- New Years

January 3, 2017

- Checked temperature of study medications within refrigerator
- Faxed patient records to central IRB
- Observed an ODYSSEY study patient screening visit.
- Assisted in screening patients for CMS coverage

January 4, 2017

- Checked temperature of study medications within refrigerator
- Prepared boxes for moving IRB binders from HR
- Began packing IRB binders into boxes for transport to office

January 5, 2017

- Checked temperature of study medications within refrigerator
- Continued packing IRB binders into boxes for transport to office
- Labeled IRB binders and box contents
- Transported IRB binders to research office

January 6, 2017

- Checked temperature of study medications within refrigerator
- Observed phone follow-up visit
- Transported remaining IRB binders to research office
- Unpacked IRB folders and organized them within office

Student _____ Date _____
Mentor_____ Date_____

Week 16

January 9, 2017

- Checked temperature of study medications within refrigerator
- Scheduled UPS pickup for patient samples to sent to central lab
- Assisted in updating sponsor screen fail database for ODYSSEY study.
- Assisted in retrieving and filing updated IRB correspondence for COBRA study

January 10, 2017

- Checked temperature of study medications within refrigerator
- Began introduction section of thesis
- Discussed study database for active studies on site with Dr. Muzina and obtained database template for thesis
- Scheduled UPS pickup for patient samples to be sent to central lab

January 11, 2017

- Checked temperature of study medications within refrigerator
- Observed the process of entering the subject data into the sponsor database
- Observed the process of obtaining the subject information from a different facility
- Looked up patient vial numbers for the DANCE study and recorded them on a log
- Made labels for the ODYSSEY study and placed them in patient binders
- Mailed patient letters and obtained mail for research office

January 12, 2017

- Checked temperature of study medications within refrigerator
- Retrieved patient drinks and snack from kitchen
- Input information for a 3 year follow up into patient folders
- Wrote acknowledgment section of thesis

January 13, 2017

- Checked temperature of study medications within refrigerator
- Filed paperwork in appropriate binders
- Assisted in adding documents to the PROTEGO study regulatory binder
- Worked on thesis introduction

Student _____ Date _____
Mentor_____ Date_____

Week 17

January 16, 2017

- Checked temperature of study medications within refrigerator
- Observed internal audit visit by compliance officer
- Began working on background section of thesis

January 17, 2017

- Checked temperature of study medications within refrigerator
- Scheduled UPS pickup for patient samples
- Observed on site patient follow up visit
- Worked on background section of thesis

January 18, 2017

- Checked temperature of study medications within refrigerator
- Removed study binders that are unnecessary now due to closed enrollment of certain studies
- Archived patient binders no longer needed on site
- Organized Cath Lab Research folder

January 19, 2017

- Checked temperature of study medications within refrigerator
- Worked on background section of thesis
- Met with Dr. Muzina to discuss internal audit policy
- Obtained internal audit checklist used at Medical City of Fort Worth

January 20, 2017

- Checked temperature of study medications within refrigerator
- Faxed patient records to other research sites
- Updated patient contact information for various studies
- Printed new address labels of patients to send patient letters
- Mailed reminder letters for patient follow up visits

Student _____ Date _____
Mentor_____ Date_____

Week 18

January 23, 2017

- Checked temperature of study medications within refrigerator
- Assisted coordinator in sending patient documents to WIRB
- Worked on background section of thesis
- Observed the process of entering information to sponsor database

January 24, 2017

- Checked temperature of study medications within refrigerator
- Observed process of scheduling on site follow up visit with patient
- Started methods section of thesis

January 25, 2017

- Checked temperature of study medications within refrigerator
- Observed how coordinators input IRB meeting minutes into site database
- Discussed continuing review process with coordinators
- Obtained continuing review form

January 26, 2017

- Checked temperature of study medications within refrigerator
- Observed initial and revised informed consent form
- Obtained new informed consent form with updated IRB information
- Gathered more background info for thesis

January 27, 2017

- Checked temperature of study medications within refrigerator
- Observed patient follow up visit in the clinic
- Scheduled UPS pickup for patient samples to send to central lab
- Created methods outline for thesis

Student _____ Date _____
Mentor_____ Date_____

Week 19

January 30, 2017

- Checked temperature of study medications within refrigerator
- Turned in patient records to Health Records department
- Discussed site closure process with coordinators
- Obtained site closure forms used at Medical City

January 31, 2017

- Checked temperature of study medications within refrigerator
- Assisted in verifying that a new shipment of stents was correct
- Called to retrieve medical records for patients that potentially qualify for the ODYSSEY study
- Redacted patient documents for WRAP-IT study

February 1, 2017

- Checked temperature of study medications within refrigerator
- Redacted patient documents for WRAP-IT study

February 2, 2017

- Checked temperature of study medications within refrigerator
- Redacted patient documents for WRAP-IT study
- Uploaded and filed redacted documents into binders and online database
- Updated heart center directory

February 3, 2017

- Checked temperature of study medications within refrigerator
- Prepared vouchers for potential study subjects
- Prepared five new binders for PLATINUM study with appropriate labeling

Student _____ Date _____
Mentor_____ Date_____

Week 20

February 6, 2017

- Checked temperature of study medications within refrigerator
- Created an IRB cover letter for PROTEGO study
- Observed patient follow up visit on site
- Worked on significance section of thesis

February 7, 2017

- Checked temperature of study medications within refrigerator
- Scheduled UPS pickup for patient samples to send to main lab
- Attended monthly meeting with Director of Cardiology
- Put together envelopes for COBRA patients and mailed them

February 8, 2017

- Checked temperature of study medications within refrigerator
- Met with Dr. Muzina to discuss methods section of thesis
- Filed paperwork into appropriate binders
- Continued working out methods section of thesis

February 9, 2017

- Off site - Philadelphia

February 10, 2017

- Off site - Philadelphia

Student _____ Date _____
Mentor_____ Date_____

Week 21

February 13, 2017

- Off site- Philadelphia

February 14, 2017

- Checked temperature of study medications within refrigerator
- Discussed exempt determination process with coordinators and obtained local IRB documents for exempt submission
- Attended mandatory hospital meeting
- Worked on methods section of thesis

February 15, 2017

- Checked temperature of study medications within refrigerator
- Discussed exempt determination process with Dr. Muzina
- Assisted in retrieving shipment for study medication
- Placed new study medication in the refrigerator

February 16, 2017

- Checked temperature of study medications within refrigerator
- Assisted coordinator in scheduling follow up visits with study patients
- Updated site calendar for new scheduled follow-up visits
- Worked on limitations section of thesis

February 17, 2017

- Checked temperature of study medications within refrigerator
- Met with Dr. Muzina to discuss continuing review and site closure
- Worked on methods section of thesis

Student _____ Date _____
Mentor_____ Date_____

Week 22

February 20, 2017

- Checked temperature of study medications within refrigerator
- Observed on site follow up visit
- Observed phone follow up visit
- Worked on thesis

February 21, 2017

- Checked temperature of study medications within refrigerator
- Scheduled UPS pick up of patient samples
- Read over WIRB handbook
- Filed paperwork into appropriate binders

February 22, 2017

- Checked temperature of study medications within refrigerator
- Mailed out reminder letters to patients with scheduled follow up visits
- Assisted coordinator with filing of sponsor newsletter into regulatory binder
- Finished obtaining source material for thesis

February 23, 2017

- Checked temperature of study medications within refrigerator
- Met with Dr. Muzina to discuss methods section of thesis
- Worked on methods section of thesis
- Prepared pharmacy vouchers to be sent to ODYSSEY patients

February 24, 2017

- Checked temperature of study medications within refrigerator
- Prepared pharmacy vouchers to be sent to ODYSSEY
- Mailed out pharmacy vouchers
- Worked on methods section of thesis

Student _____ Date _____
Mentor_____ Date_____

Week 23

February 27, 2017

- Checked temperature of study medications within refrigerator
- Observed a patient follow up phone call
- Met with Dr. Muzina to discuss methods section of thesis
- Worked on thesis

February 28, 2017

- Checked temperature of study medications within refrigerator
- Reviewed methods materials and study protocol
- Filed patient information into appropriate binders
- Worked on thesis

March 1, 2017

- Checked temperature of study medications within refrigerator
- Packaged up closed out study binders for shipment to storage
- Updated the local ODYSSEY screen fail database
- Worked on thesis

March 2, 2017

- Checked temperature of study medications within refrigerator
- Created new cVAD study binders with appropriate labels
- Moved documents from old binders into new binders

March 3, 2017

- Checked temperature of study medications within refrigerator
- Left early - sick

Student _____ Date _____
Mentor_____ Date_____

Week 24

March 6, 2017

- Checked temperature of study medications within refrigerator
- Finished moving cVAD study materials into new binders
- Met with Dr. Muzina to discuss thesis progress
- Worked on thesis

March 7, 2017

- Checked temperature of study medications within refrigerator
- Worked on thesis

March 8, 2017

- Checked temperature of study medications within refrigerator
- Attended monthly office meeting with Director of Cardiology
- Worked on thesis

March 9, 2017

- Checked temperature of study medications within refrigerator
- Scheduled UPS pickup for patient samples
- Worked on thesis

March 10, 2017

- Checked temperature of study medications within refrigerator
- Worked on thesis

Student _____ Date _____
Mentor_____ Date_____