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There is much to consider when managing a multicenter clinical trial. Topics under consideration include a spectrum from budget creation to subject recruitment/retention. THE HEART HOSPITAL Baylor Plano is a participating clinical research site for CABANA, which is sponsored by The National Health Institute, Duke University, and The Mayo Clinic. CABANA will be utilized to elucidate the commencement of a multicenter clinical trial, as well as illustrate issues that may be encountered throughout the process.

The successful execution of a clinical trial such as CABANA needs individuals that are dedicated to the research involved and that the handling of every aspect of the trial is performed with unparalleled proficiency.

MANAGING A MULTICENTER CLINICAL RESEARCH STUDY:
THE CABANA TRIAL: CATHETER ABLATION VERSUS
DRUG THERAPY FOR THE TREATMENT OF
ATRIAL FIBRILLATION

INTERNSHIP PRACTICUM REPORT

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For the Degree of

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By

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I. INTRODUCTION

Managing a multi-center trial is a very meticulous, intricate process. A multi-center trial unquestionably has a plethora of details to consider. One purpose of clinical trials is to prove, disprove, or provide new views on pressing issues in science that have the potential to change the way medicine is practiced across the world. This can be extremely beneficial when addressing a critical question in science. It is of the utmost importance to ensure that the question at hand can be answered, and in this case, that the answer will provide insight on an imperative issue in medicine. The forthcoming explanation of CABANA (**C**atheter **A**blation vs. **A**nti-arrhythmic **D**rug Therapy for the Treatment of **A**trial Fibrillation) will facilitate the later discussion and analysis of the obstacles and unique characteristics associated with managing a multi-center clinical trial.

Catheter ablation is a medical procedure used to treat arrhythmias, which can be characterized as a problem with the speed or rhythm of the heartbeat (12). The electrical system of the heart controls the speed and rhythm of how the heart beats. With each heartbeat, an electrical signal disperses from the base of the heart to the apex, causing the heart to contract and pump blood. A problem with any portion of this process can cause an arrhythmia (8). Catheter ablation, a minimally invasive procedure, involves advancing several flexible catheters into the patient's blood vessels, usually either in the femoral vein, internal jugular vein, or subclavian vein (1).

In an effort to correct arrhythmias of the heart, an electrophysiologist will conduct an Electrophysiology (EP) Study. This will test the electrical conductivity of the heart and ultimately indicate the origin of the abnormal heart rhythm (2). This procedure is performed in a catheterization lab which contains a video x-ray machine to provide the physician with live images of the heart, as well as large magnets (2-3 tesla, 2 ft diameter) for manipulating the electrodes located at the tips of the catheters once they are placed in the heart (3). A metal plate is placed underneath the torso of the patient, directly under the heart, in order to facilitate the manipulation of the electrodes.

The X-ray machine provides the physician with a view of the heart and the location of the electrodes. The electrophysiologist proceeds to move the electrodes along the conduction pathways of the heart, measuring the electrical activity during the process (2). The electrophysiologist then alters the speed of the heart by placing the electrode at certain points along the conductive pathways of the heart to control its rate. The physician will then attempt to provoke arrhythmias within the patient's heart by injecting electrical current into the conductive pathways of the heart (2). This electrical current is a low-voltage, high-frequency form of electrical energy known as radiofrequency energy (RF). The electrical impulses caused by the RF energy then ablate the abnormal tissue where the origin of the arrhythmia is identified. This produces small, homogeneous, necrotic lesions and ideally restores healthy heart rhythm. The relative safety of this energy source contributed to the widespread adoption of catheter ablation as a restorative treatment for atrial fibrillation (10).

The clinical conditions for which catheter ablation may be recommended by physicians are as follows: if drug therapy does not control the arrhythmia, if the patient cannot tolerate the

medicines prescribed for the treatment of the arrhythmia, or if the patient has a certain type of arrhythmia, such as atrial fibrillation, atrial flutter, supraventricular tachycardia (SVT) or Wolff-Parkinson-White syndrome (10). Risks associated with catheter ablation include bleeding, infection, and pain where the catheter is inserted. More serious problems include blood clots, stroke, esophageal injury, puncture of the heart, and even death (10). It is also important to mention that catheter ablation alone may not restore a normal heart rate and rhythm indefinitely. Furthermore, catheter ablation is not for everyone and is not necessarily the first line of defense against arrhythmias. This alludes to the purpose of CABANA Pivotal Trial: to determine what the difference in outcome may be, if any, when comparing catheter ablation to anti-arrhythmic drug treatment for the management of atrial fibrillation.

Anti-arrhythmic agents are pharmaceutical drugs that are used to suppress cardiac arrhythmias, such as atrial fibrillation, atrial flutter, ventricular tachycardia, and ventricular fibrillation (7). Failure of these agents to suppress arrhythmias in patients may lead to implantation of an implantable cardioverter-defibrillator (ICD) (7).

Classification of anti-arrhythmic agents is often difficult. The problem arises from the fact that many of the anti-arrhythmic agents have multiple mechanisms of action, often making classification imprecise. For CABANA, patients will be given Class III anti-arrhythmic drugs, which include (but are not limited to) heart rate controlling drugs such as metoprolol, atenolol, carvedilol and propranolol, and rhythm control drugs such as sotalol, amiodarone, and dronedarone (7). The precise dose for therapy must be carefully titrated for each subject to minimize the risk of toxicity (7).

A very important question regards which treatment for atrial fibrillation is superior. It is proposed that the treatment strategy of percutaneous left atrial catheter ablation for the purpose of eliminating atrial fibrillation (AF) is superior to current state-of-the-art therapy with either rate-control or anti-arrhythmic drugs with regards to reducing total mortality (primary endpoint) and decreasing the composite endpoint of total cardiovascular mortality, disabling stroke, serious bleeding, and cardiac arrest (secondary endpoint), in patients with recent onset AF requiring treatment.

II. SPECIFIC AIMS

Throughout the duration of the internship, critical aspects integral to the successful operation of clinical trials have been observed. The specific aims pertinent to this practicum are as follows:

1. Comprehend the various elements necessary to initiate a multi-center clinical research trial.
2. Learn how physicians are recruited to participate in a research study.
3. Participate in the formation of documents and literature required for a research study.
4. Observe the cardiovascular research study creation process from initial consult through subject recruitment, consent, treatment, data collection, and follow-up.
5. Learn about general research study processes such as:
 - How study budgets are developed
 - How to create documents for Institutional Review Board (IRB) review
 - Regulatory requirements for ongoing studies
 - How correspondence is handled between the a study sponsor and a research site
 - Regulatory Binder auditing
 - Completion of case report forms

III. SIGNIFICANCE

Since CABANA is a multi-center study including sites in Europe, it will facilitate answering the pressing research question of which method to correct arrhythmias is superior, if any. An important issue to consider is that the comparative long term outcomes of ablative treatment remain unclear, and often patients may need to undergo ablative treatment a second time a few years later. However, smaller scale trials of the past that have compared drug and ablative treatment for atrial fibrillation have shown favor towards ablative intervention. These trials include the Catheter Ablation for the Cure of Atrial Fibrillation Study (CACAF), First Line Radiofrequency Ablation Versus Anti-arrhythmic Drugs for Atrial Fibrillation Treatment (RAAFT), A Controlled Randomized Trial of Circumferential Pulmonary Vein Ablation Versus Antiarrhythmic Drug Therapy in for Paroxysmal AF (APAF), and A Comparison of Antiarrhythmic Drug Therapy and Radiofrequency Catheter Ablation in Patients With Paroxysmal Atrial Fibrillation (A4) (6).

In an effort to validate the need for a multi-center clinical trial as expansive as CABANA, a pilot study was initially conducted. Sixty (60) patients were enrolled in ten (10) centers and randomized to ablation versus drug therapy groups. The CABANA Pilot Study suggests that the larger scaled CABANA Pivotal Trial will provide relevant information for a broad spectrum of atrial fibrillation patients. The Pilot Study demonstrated that recruiting and

enrolling patients for the trial could be achieved, and it identified the expected demographics of CABANA subjects, which has been beneficial in optimizing the study design of CABANA (6).

The significance of CABANA is multifaceted. Clinically, this trial will optimistically determine if the emerging role of catheter ablation as the superlative treatment for atrial fibrillation is legitimate (6). Scientifically, the trial will determine whether the achievement of normal sinus rhythm is a mortality advantage. No trial to date has prospectively addressed this issue, nor will any other current study have the statistical power to do so. Computed Tomography/ Magnetic Resonance (CT/MR) imaging will also elucidate structural abnormalities contributing to the occurrence of atrial fibrillation in a diverse population of patients and the modulation of these factors by drug or ablative treatment (6).

With the previous discussion, along with the explanation of all of the intricacies and fine points that must be accounted for in order to launch a study of this stature, the ubiquitous nature of clinical trial management must be illustrated. Proper management of trials is integral to ensuring that the specific research question of interest can be adequately addressed without excessive delay or interference. If managed properly, this multi-center study will provide a thorough answer to the question proposed in atrial fibrillation treatment with an approach that could possibly not be accomplished in a small-scaled study.

IV. LITERATURE REVIEW

In order to initiate a multi-center study, a catalog of issues must be addressed to ensure the comprehensiveness of the clinical trial. Topics to take into consideration include how to screen and recruit subjects for the trial, as well as how to recruit for potential sites to participate in the trial. It is imperative to include sites that desire to participate in the trial because of the ambition to make the same great contribution to scientific knowledge as the other sites involved in the study, including the sponsor. Simultaneously, a clinical research site should not exhaust itself by trying to recruit more subjects than it can reasonably handle. This will potentially leave subjects feeling neglected and causing follow-up to be difficult. The goal of a clinical trial is to collect accurate data and ensure the safety of research subjects. Participation as a study site is a meticulous endeavor and a certain standard of commitment is imperative. With this commitment, appropriate site education is a requirement to ensure that all sites involved in the study know what is expected from them. Potential sites should understand what the duration of participation will be, the purpose of the study, potential hurdles that may be faced within the study, and anticipated outcomes. Before discussion proceeds further, there is one question that the sponsor must address prior to any other action: what is the nature of the trial.

First and foremost, the reason for conducting the trial must be determined. For this purpose, the field of science that the trial would be conducted in has to be established; in this case, it is Cardiology. There also must be an incongruity or gap in the knowledge of a particular

topic of interest (7). Although catheter ablation and drug therapy are current methods for the treatment of atrial fibrillation, the question still exists whether one of these techniques is superior (4). From literature review, support for establishing research to address the need for CABANA can be achieved.

CABANA is a product of previous clinical studies, such as Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM), A Comparison of Rate Control and Rhythm Control in Patients With Recurrent Persistent Atrial Fibrillation (RACE), Randomized Trial of Rate-Control Versus Rhythm Control in Persistent Atrial Fibrillation: The Strategies of Treatment of Atrial Fibrillation (STAF), Atrial Fibrillation and Congestive Heart Failure (AF CHF) Investigations of Rate vs. Rhythm Control Therapy, and the International Atrial Fibrillation Ablation Registry. The aforementioned trials offered a great deal of information concerning treatment for atrial fibrillation, but evaluating overall mortality in a population at increased risk will provide the most persuasive evidence for determining the superlative treatment for this condition (6). Establishment of interest in the medical community facilitates determining the potential number of sites to be involved. Once this is established, the physician population of interest (i.e., of a certain specialty) must be determined (11). After identifying the potential physicians for the trial, formal letters should be sent to them in an effort to spread the word about the importance of the trial and that their participation is integral to the success of the trial. Before the discussion proceeds further, it should be noted that involvement of the Institutional Review Board (IRB) is essential.

The IRB is a committee that has been formally designated to approve, monitor, and review biomedical and behavioral research involving humans with the aim to protect the rights and welfare of the research subjects (9). IRBs are empowered to approve, require modifications

in planned research prior to approval, or disapprove research (9). There are rules and regulations that must be accounted for with IRB submissions, such as financial disclosures of anyone that is considered study staff for the trial, step by step procedures for what is required from subjects, how subject information will be stored, and a proper assessment of risk to the subjects. Once IRB approval has been achieved and a site has received the approval from the sponsor, it is time to start subject recruitment.

Subject recruitment is an involved process and requires immense attention to detail. There are certain guidelines that must be followed by the research personnel. However, this should not shadow the fact that clinical research study staff impose on the lives of others. For this reason, it is essential to exude ethical competence. Recruitment is a complicated process because there are certain inclusion/exclusion criteria that must be adhered to in order to ensure that the ideal patient population is targeted for the trial. The ideal subject for a clinical study often varies depending on whether or not the trial is a drug or device study. Pre-existing conditions that a patient may have may qualify or exclude them from participating in a study as well. Often, when consenting potential subjects, they may be in a vulnerable state. Especially with the majority of the trials THE HEART HOSPITAL Baylor Plano (THHBP) is involved in, the potential subjects approached about research are about to have procedures performed on them, ranging from open heart surgery to the placement of stents in various arteries. There is a natural insecurity and trepidation that may be expressed by patients. It is the job of the research staff to not be coercive, but simultaneously inform patients that they will be making a contribution to science that ideally will enhance the quality of their lives and others in the future. Compassion is another attribute that should be displayed by research staff. It is the research staff

that should be available to answer any questions the potential research subjects may have, or direct them to the proper individual who can answer their questions.

When screening a patient to participate in a clinical trial, adherence to the inclusion/exclusion criteria established by the sponsor of the study is crucial. Often, these criteria are established from previous studies. This will ensure that the correct population of patients is targeted that will also guarantee that data obtained is valid. For CABANA, the inclusion/exclusion criteria are as follows:

Inclusion Criteria:

- Have the capacity to understand and sign an informed consent form.
- Be ≥ 18 years of age.
- Have documented Atrial Fibrillation (AF) episodes ≥ 1 hour in duration; with ≥ 2 episodes over 4 months with electrocardiographic documentation of 1 episode or at least 1 episode of AF lasting more than 1 week.
- Warrant active therapy beyond simple ongoing observation.
- Be eligible for catheter ablation and ≥ 2 sequential rhythm control and/or ≥ 3 rate control drugs.
- Be ≥ 65 yrs of age, or < 65 yrs with one or more of the following risk factors for stroke: hypertension, diabetes, congestive heart failure, prior stroke or traumatic ischemic attack (TIA), left atrium (LA) size ≥ 5.0 cm (or volume index ≥ 40 cc/m²), or ejection fraction (EF) ≥ 35 . Subjects < 65 yrs of age whose only risk factor is hypertension must have a second risk factor or left ventricular (LV) hypertrophy to qualify.

Exclusion Criteria:

- Lone AF in the absence of risk factors for stroke in patients < 65 years of age.
- Patients who in the opinion of the managing clinician should not yet receive any therapy for AF.
- Patients who have failed ≥ 2 membrane active anti-arrhythmic drugs at a therapeutic dose due to inefficacy.
- More than one week of amiodarone treatment in the past 3 months.
- An efficacy failure of full dose amiodarone treatment ≥ 12 weeks duration at any time.
- Reversible causes of AF including thyroid disorders, acute alcohol intoxication, recent major surgical procedures, or trauma.
- Recent cardiac events including myocardial infarction (MI), percutaneous coronary intervention (PCI), or valve or bypass surgery in the preceding 3 months.
- Hypertrophic obstructive cardiomyopathy.
- Class IV angina or Class IV congestive heart failure (including past or planned heart transplantation).
- Other mandated anti-arrhythmic drug therapy.
- Heritable arrhythmias or increased risk for torsade de pointes with class I or III drugs.
- Prior LA catheter ablation with the intention of treating AF.
- Prior surgical interventions for AF such as the Maze procedure.
- Prior atrioventricular (AV) nodal ablation.

- Patients with other arrhythmias requiring ablative therapy.
- Contraindication to warfarin anti-coagulation.
- Renal failure requiring dialysis.
- Medical conditions limiting expected survival to < 1 year.
- Women of childbearing potential (unless post-menopausal or surgically sterile).
- Participation in any other clinical mortality trial.
- Unable to give informed consent.

There also has to be a quality assurance plan in effect to ensure that all participating sites are following the rules set forth by the sponsor of the study, Food and Drug Administration (FDA), and/or IRB (9). This will ensure that good clinical practices are in fact being followed, providing an efficient means of tracking all of the necessary information associated with the trial. The most important aspect of ensuring a multi-center trial is successful is communication. A unique concern to consider is that everyone participating in the trial is not in one location. This requires persistent collaboration and contact between all of the sites to ensure that the most updated information is accessible to everyone involved in the study.

The press release for CABANA occurred the first week of June, 2009. Thus far, a physician letter has been created to send to skilled cardiologists in the North Texas area in an effort to educate physicians about CABANA and have them refer some of their atrial fibrillation patients to us to participate in the study. In addition, inclusion/exclusion cards have been created to send to physicians, as well as delivered to local practices in an effort to educate others about the trial and generate interest throughout the area. A CABANA checklist has also been created

in an effort to facilitate the screening of subjects. When a patient arrives at the office/clinic of one of the investigators participating in CABANA, they will fill out a one page questionnaire that will allow physicians to decide whether or not to refer the patient to us as a potential research subject. The goal is to make the recruitment process more efficient and thorough, resulting in maximizing the opportunities to enroll into the trials at the hospital. Copies of the aforementioned documents can be found at the end of this thesis in the section entitled:

APPENDIX A: Documents Created for CABANA.

Start-up documents were received by THE HEART HOSPITAL Baylor Plano in early July of 2009 from the National Institutes of Health, Mayo Clinic, and Duke University (the sponsors of the study). The documents included the protocol, informed consent form, and case report forms. Soon thereafter, immediate revision of the documents to fit Baylor Research Institute (BRI) guidelines occurred. The Informed Consent Form and the Protocol required modification. It is also a requirement that an IRB Financial Disclosure Form, known as a FORM 14, is completed by everyone participating in the study. The conflict of interest (COI) forms, which the investigators typically complete for the sponsor, disclose any financial interests they may have that are associated with the current research project. Various documents are needed to be sent to the IRB prior to the study review date. One document is the IRB FORM 1:

Application and Project Summary. This document provides a thorough explanation of what the prospective study entails. By reading the FORM 1, members of the IRB can find valuable information about the sponsor of the study, the purpose of the study, and what drugs/devices are to be used. Also, if radiation is to be used, the quantity and duration must be designated as well. Thus, the FORM 1 provides a brief overview of the components of the study and at the same

time informs members of the IRB that the best interest of the subject is being considered by the investigators. Copies of the aforementioned forms have been included in this thesis under the section entitled: APPENDIX B: IRB Forms.

Another requirement of the IRB that must be completed prior to approving a clinical study is that every member of study staff must complete Human Subject Training located on the Baylor Learning Network. An individual will simply sign onto the Baylor Network using their own special login assigned to them by the IRB. Eight (8) modules exist that consist of questions dealing with proper treatment of subjects, as well as rules and guidelines set forth by the IRB for research. Scores of 100% must be achieved on all modules in order to pass. Once this is accomplished, the individual is permitted to participate as study staff. The first time CABANA proposal was submitted to the Baylor IRB, it was approved pending modifications on August 6, 2009. The IRB requested that two changes be made; one dealing with the formatting of the consent form, and one clarifying whether a medical procedure qualifies as standard of care or research. The appropriate changes were made to the consent form and the study was resubmitted to the IRB on September 21, 2009.

Another important aspect of the trial that must be considered when using devices is whether or not an Investigational Device Exemption (IDE) is needed. An IDE enables the device to be used in a clinical study in order to collect safety and efficacy data. Investigational use also includes clinical evaluation of certain modifications or new intended uses of legally marketed devices (4). With regard to CABANA, the majority of the catheters that have been selected for use in this study have been approved by the FDA for the ablation of cardiac tissue, not specifically for the treatment of atrial fibrillation. Therefore, this discrepancy requires that

the sponsor of the study obtain an IDE in order to use the catheters for this purpose. All clinical evaluations of investigational devices, unless categorized as exempt, must have an approved IDE before the study commences (4).

Once approved by the FDA, an IDE permits a device to be shipped lawfully for the purpose of conducting investigations of the device (4). Since catheter ablation can be considered a procedure possessing significant risk, the sponsors of CABANA were required to submit a complete IDE application to the FDA. When completing an IDE application, the sponsor must demonstrate that the risk to benefit ratio for human subjects from the proposed investigation are outweighed by the anticipated benefits to subjects and the importance of the knowledge to be gained, that the investigation is scientifically sound, and that there is reason to believe that the device, as proposed for its use, will be effective (4).

Another valuable aspect of a multicenter trial is trust. Sponsors reach out to investigators and sites with hopes and aspirations that there will be no issue with compliance to the rules and regulations associated with research. Great risks are involved when giving responsibility to others, knowing that the results obtained from the study can reflect positively or negatively on the sponsor(s). Depending on the nature of the study, sponsors may require documentation that qualifies an investigator and a site to handle study specific tasks and ensure that procedures that are performed take place at an institution that is qualified to do so. For the purpose of CABANA, it is necessary to document that the Principal Investigator is qualified to perform catheter ablations on the subjects that are randomized to the ablation arm of the study. Also, five first-time catheter ablations need to be sent to the sponsor with pre and post EKGs showing that the atrial fibrillation was corrected successfully. Once all of the necessary documentation is sent

to the sponsor, an Investigator's Meeting is scheduled to provide investigators and coordinators training by the sponsor of the study.

The Investigator's Meeting for CABANA occurred in Philadelphia, Pennsylvania on October 2nd through October 3rd, 2009. The first day consisted of an overview of the trial and training of the investigators on the electronic data capture (EDC) website. In conjunction with training, multiple presentations occurred describing the history of atrial fibrillation, disparities in its treatment, and past studies that have attempted to answer questions concerning the success of drug therapy and ablative therapy for the treatment of atrial fibrillation. Once ample background was provided emphasizing the importance of this trial, discussions commenced concerning the protocol to ensure that the investigators and coordinators from across the U.S. were on the same accord in terms of what to expect from this trial, and that any questions that might have arisen were answered adequately by qualified individuals. Recruitment and retention of subjects were also discussed. This is a vital component of any trial, because without subjects, there cannot be a trial. Therefore, it is imperative that subjects enrolled in the trial are retained and that they understand how important their participation is. This presents a very important consideration that must be dealt with when handling a clinical trial of this size: different rules exist depending on the location of the site. In addition to IRBs deciding what can and cannot be done in a trial, it is also dictated by state law. It is important to realize how difficult this can be when trying to coordinate efforts towards a common goal in different sites around the world. The limitations presented by different IRBs and state laws may also dictate how many subjects a site may be able to recruit.

Investigators were trained on how to sign onto the EDC database, known as INFORM, and electronically sign the electronic case report forms (eCRFs). This is of the utmost importance since the Principal Investigator must sign off on any case report forms associated with the trial. Full responsibility lies with the PI and it is important that he/she knows exactly what occurs at the site. Therefore, requiring that the PIs sign off on data ensures that the PI knows what is going on with every subject enrolled, as well as reassures the sponsor that they are receiving valid data.

The second day of training focused on training the coordinators on INFORM and how to enter data into eCRFs. The majority of the day dealt with eCRFs because it is the coordinator that enters all of the subject information into the database. Proper eCRF training is essential for being a compliant study site. Once data is entered into the database, it is reviewed by the sponsor. Data must be entered into the database correctly in order to decrease any delay in processing the data and increase turn around associated with results. Also, with the potential of being audited by the FDA in the future, proper documentation of study related documents is imperative.

Attending the Investigator's Meeting has allowed THE HEART HOSPITAL Baylor Plano to realize what tasks still need to be completed before the site can commence enrolling subjects. The Principal Investigator for CABANA from THHBP, Electrophysiologist J. Brian DeVille, decided that the site is to have bimonthly meetings to discuss enrollment, adverse events, and any other topics that may be associated with the trial to ensure everyone involved is working together efficiently and effectively. This is a vital aspect of research to guarantee compliance with the approved protocol for the study and abidance with the rules set forth by the

IRB to ensure the protection of research subjects. Communication is extremely significant.

Without it, THE HEART HOSPITAL Baylor Plano would not survive as a research site with any of the studies currently ongoing at the site.

V. METHODOLOGY

The research question of the practicum project consists of an in depth overview of what managing a multi-center clinical trial entails, and does not necessarily pose a problem requiring scientific rationale to answer. This project is an attempt to provide a thorough analysis of what is needed to successfully initiate a clinical trial that has the potential to answer a very pressing issue in medicine that ultimately can change medical practices in the future.

This multi-center study will involve approximately 3000 patients (1500 patients assigned to drug therapy and 1500 patients assigned to catheter ablation) and will include a 6 month start up, 3 years of enrollment, a minimum of 2 years of follow-up with each subject, and 6 months for close out and data analysis. Patients meeting the inclusion criteria will be randomized in a 1:1 fashion in an unblinded, parallel arm treatment format to either drug therapy directed at rate or rhythm control or catheter ablation. Efficacy with respect to atrial fibrillation will be established from long term follow up beginning after the 3 month initiation phase. Patients will be followed for 2.5-5 years.

VI. LIMITATIONS

A major limitation of any clinical trial includes subject recruitment and subject retention. Without subjects, clinical research is nothing more than a prodigious notion. There must be criteria that are adhered to in order to ensure that subjects are recruited efficiently to get the necessary results, and also that subjects are treated fairly to ensure that they continue to participate throughout the duration of the entire study. It must also be noted that although subjects participating in the trial will have the commonality of suffering from atrial fibrillation, individuals may come from different ethnic and or religious backgrounds. This variable can severely influence recruitment and retention efforts. Also, since this is a multi-center trial, multiple IRBs will be utilized from different states and even countries. Although the main goal of the IRB is the protection of human subjects, it is necessary to consider limitations that may be enforced depending on where a study site may be located. This is an issue that must be addressed and can ultimately dictate how well a site may enroll in a trial.

It is of the utmost importance that subjects comply with the 2.5-5 year follow up for the CABANA trial. By participating in this trial, although there is no monetary compensation for the participants, they are receiving more care than an individual with the same condition may receive that is not participating in the trial. They will be closely observed for the duration of the trial to examine the status of their condition. The majority of our subjects will be over sixty (60) years old, and by participating in the study, it can be assured to them that their health will be monitored very closely, which should alleviate any worries the subject may have concerning

their health, in particular, the increased risk of stroke involved with the catheterization procedure (13).

Budgeting poses another limitation to a clinical trial. In order to conduct the research, adequate funding is essential. The potential study needs to be satisfactorily innovative in order for a sponsor to want to financially support the study. Without the proper funding, the clinical trial will remain idle. The last details of the budget are being finalized for CABANA. It was beneficial to complete the budget after attending the Investigator's Meeting because critical questions were addressed at this meeting. Baylor actually has two research sites participating in CABANA with two separate PIs. The lead research coordinator from the other Baylor site, Baylor Heart and Vascular Hospital (BHVH), has a great deal of experience developing budgets for trials, specifically for trials of this nature. Therefore, THHBP is going to reference the BHVH budget since we anticipate accruing similar expenses. Also, both sites being associated with Baylor allowed collaboration in completing this task quickly. The next obstacle to accomplish will be to brainstorm the best methods for subject recruitment.

Limitations specific for the internship practicum project include the short duration of the internship in order to observe the many aspects of managing a clinical trial come to fruition. Also, concerns such as inexperience with handling the aforementioned limitations innate to any trial undeniably introduce another variable to take into consideration when attempting to comprehend the complexity of clinical trials.

Due to the delays encountered with the commencement of CABANA within the timeframe designated for the internship, certain aims that were anticipated to be experienced and resolved in association with CABANA were not accomplished. These include observing the

cardiovascular research study creation process from initial consult through subject recruitment, consent, treatment, data collection, and follow-up, as well as dealing with the regulatory requirements for ongoing studies such as how correspondence is handled between the a study sponsor and a research site, self auditing Regulatory Binders, and the completion of case report forms. It should be noted, however, that despite the fact these aforementioned aims were not accomplished in association with CABANA, they were fulfilled with involvement in many other trials at THHBP.

VII. INTERNSHIP EXPERIENCE

My time at THE HEART HOSPITAL Baylor Plano has been extremely beneficial.

THHBP is a gorgeous, four (4) floor hospital that is the only freestanding, full service hospital in the area dedicated solely to heart and vascular health. It is evident that patient care and comfort are of supreme importance. Rather than staying at the hospital, it appears as if patients are more like vacationers staying in a posh hotel, with hardwood floors in every patient room and flat screen televisions (just to name a couple of the amenities). Beyond the aesthetics of the hospital, the staff is great as well. I have had the pleasure of working with a great group of people that take the time to thoroughly explain details to me and ensure my understanding of vital topics pertinent to research. Learning about clinical research in a classroom is completely different than actually dealing with it as a profession. The classes I took in my Master of Science program helped develop a solid foundation for me, but nothing compares to having hands on experience. Interacting with the physicians has been a tremendous experience as well. My ultimate goal is to become a cardiologist plus an investigator on various trials, just like many of the physicians at THHBP. Before starting the internship, I did not know how a physician would get involved in such a process. At this point, I know how to get the information I would need to become an investigator on a clinical trial, as well as every step in between. This reinforces my excitement for the future as a physician, knowing I will have the opportunity to make great contributions to research. It is also amazing to see how efficient research needs to be in order to be effective and worthwhile. THHBP has 20+ trials underway and this requires a paramount level of dedication,

as well as the innate ability to multi-task. It is easy to lose track of vital aspects of the various trials and developing a game plan to tackle this task is necessary. In an effort to alleviate the confusion associated with managing a multicenter clinical trial, I have created a flow chart which can be found at the end of this thesis in the section entitled: APPENDIX C: Clinical Trial Flow Chart.

Also, as part of my curriculum during this internship, I kept a daily journal of my activities associated with the internship. This information can be found in its entirety at the end of this thesis entitled: APPENDIX D: Daily Journal.

APPENDIX A

Documents Created for CABANA

PHYSICIAN TO PHYSICIAN LETTER

Dear Cardiologists,

THE HEART HOSPITAL Baylor Plano is eager to announce the commencement of The Catheter Ablation vs. Anti-arrhythmic Drug Therapy for Atrial Fibrillation Trial (CABANA). This is a multi-center study encompassing 140 sites worldwide involving patients requiring treatment for atrial fibrillation (AF).

It is anticipated that The CABANA Trial will prove that the AF treatment strategy of percutaneous left atrial catheter ablation is paramount to the current state-of-the-art therapy with either rate-control or anti-arrhythmic drugs in patients with recent onset AF requiring treatment.

Study design elements include:

- Multi-center study participation
- Enrollment of 3000 patients (1500 patients assigned drugs and 1500 patients assigned ablation)
- A 1:1 randomization scheme that is an unblinded, parallel arm treatment of drug therapy directed at rate or rhythm control vs. catheter ablation
- Start up of 6 months, 3 year enrollment, a minimum of 2 years of follow-up and 6 months for close out and data analysis

Participating Cardiologists include:

- Dr. J. Brian Deville, MD; Principal Investigator
- Dr. Thomas Beveridge, MD
- Dr. Hafiza Khan, MD

If you have evaluated patients that require treatment from atrial fibrillation and would like to refer them for screening evaluation for this study, please contact the study team at 469.814.4712 or by email at lisa.plummer@baylorhealth.edu. Participation in this study will help answer an imperative question in medicine which can potentially change the routine clinical care for AF patients, as well as further enhance their quality of life.

Attached you will find a CABANA fact sheet which provides more information regarding the trial. We would also be delighted to entertain any questions you may have and provide more specific details regarding this study.

Thank you so much for your consideration of this momentous trial!

Sincerely,

THE HEART HOSPITAL Research Department

Pocket Inclusion/Exclusion Card

CABANA Catheter Ablation Versus Anti-arrhythmic Drug Therapy for Atrial Fibrillation

CABANA is designed to provide insight into whether RFCA or drug therapy (rate control or anti-arrhythmic) is superior in the treatment of atrial fibrillation (AF)

Inclusion Criteria

- Documented AF which warrants active drug or ablative treatment
- Eligible for both catheter ablation and at least 2 sequential anti-arrhythmic drugs and/or 3 sequential rate control drugs.
- The patient must be > 65 yrs of age, or <65 yrs with any one or more of the following risk factors for stroke:
 - Hypertension
 - Diabetes
 - Congestive heart failure (including systolic or diastolic heart failure documented in either the inpatient or outpatient setting)
 - Prior stroke or TIA
 - Left atrium >4.5 cm
 - Ejection fraction <35% by echocardiogram, radionuclide evaluation or contrast ventriculography

At a minimum, paroxysmal AF episodes must be at least 1 hour in duration with 2 episodes occurring in the past 3 months. At least one qualifying episode must be documented by ECG or rhythm strip recordings. Patients with persistent or chronic AF will require at least one documented episode which is of sufficient importance that drug or ablative therapy is required. Patients with a history of only one episode of AF would not typically meet the “requiring therapy” litmus test.

CABANA Catheter Ablation Versus Anti-arrhythmic Drug Therapy for Atrial Fibrillation

CABANA is designed to provide insight into whether RFCA or drug therapy (rate control or anti-arrhythmic) is superior in the treatment of atrial fibrillation (AF)

Exclusion Criteria

- Previously failed 2 or more membrane active anti-arrhythmic drugs
- Efficacy failure of a full dose Amiodarone trial of ≥ 12 weeks duration
- Any amiodarone therapy in the past three months
- Reversible causes of AF including thyroid disorders, acute alcohol intoxication, recent major surgical procedures, or trauma
- Lone atrial fibrillation in the absence of risk factors for stroke in patients <65 years of age
- Recent cardiac events including MI, PCI, or valve or coronary bypass surgery in the preceding 3 months
- Hypertrophic Obstructive Cardiomyopathy
- Class IV angina or congestive heart failure
- Planned heart transplantation
- Other mandated anti-arrhythmic drug therapy
- Heritable arrhythmias or increased risk for torsade de pointes with class I or III drugs
- Prior LA catheter ablation with the intention to treat AF.
- Patients with other arrhythmias requiring ablative therapy
- Prior surgical interventions for AF such as the MAZE procedure
- Prior AV nodal ablation
- Medical conditions limiting expected survival to <1 year
- Contraindication to warfarin anti-coagulation
- Renal failure requiring dialysis
- Women of childbearing potential
- Participation in any other clinical mortality trial
- Unable to give informed consent

CABANA CHECKLIST

CABANA Patient Participation Checklist

CABANA is designed to provide insight into whether RFCA or drug therapy (rate control or anti-arrhythmic) is superior in the treatment of atrial fibrillation (AF).

Are you 65 years of age or older? <input type="checkbox"/> yes <input type="checkbox"/> no								
If you are younger than 65 years of age, do you have: <table style="width: 100%; margin-top: 5px;"> <tr> <td style="width: 60%;">High Blood Pressure</td> <td style="width: 40%; text-align: right;"><input type="checkbox"/> yes <input type="checkbox"/> no</td> </tr> <tr> <td>Diabetes</td> <td style="text-align: right;"><input type="checkbox"/> yes <input type="checkbox"/> no</td> </tr> <tr> <td>Congestive Heart Failure</td> <td style="text-align: right;"><input type="checkbox"/> yes <input type="checkbox"/> no</td> </tr> <tr> <td>Suffered a prior stroke</td> <td style="text-align: right;"><input type="checkbox"/> yes <input type="checkbox"/> no</td> </tr> </table>	High Blood Pressure	<input type="checkbox"/> yes <input type="checkbox"/> no	Diabetes	<input type="checkbox"/> yes <input type="checkbox"/> no	Congestive Heart Failure	<input type="checkbox"/> yes <input type="checkbox"/> no	Suffered a prior stroke	<input type="checkbox"/> yes <input type="checkbox"/> no
High Blood Pressure	<input type="checkbox"/> yes <input type="checkbox"/> no							
Diabetes	<input type="checkbox"/> yes <input type="checkbox"/> no							
Congestive Heart Failure	<input type="checkbox"/> yes <input type="checkbox"/> no							
Suffered a prior stroke	<input type="checkbox"/> yes <input type="checkbox"/> no							
When was your first atrial fibrillation diagnosis? _____								
Have you been on any medications that are used to treat atrial fibrillation previously? If yes, please list. <input type="checkbox"/> yes <input type="checkbox"/> no _____								
Have you ever had surgery or catheter ablation? If so, when and where? What was the diagnosis? <input type="checkbox"/> yes <input type="checkbox"/> no _____								
Are you treated with Coumadin/Warfarin? If so, when did you start? <input type="checkbox"/> yes <input type="checkbox"/> no _____								
Have you taken Amiodarone within the past three months? <input type="checkbox"/> yes <input type="checkbox"/> no								
Have you had any major surgeries within the last year? If yes, please list procedure. <input type="checkbox"/> yes <input type="checkbox"/> no _____								
Have you recently had a heart attack, stent placement, or valve or heart bypass surgery within the past 3 months? <input type="checkbox"/> yes <input type="checkbox"/> no								
Have you been diagnosed with any other heart conditions? If yes, please list. <input type="checkbox"/> yes <input type="checkbox"/> no _____								
Do you have any other family members with arrhythmias? <input type="checkbox"/> yes <input type="checkbox"/> no								
Are you currently undergoing dialysis? <input type="checkbox"/> yes <input type="checkbox"/> no								
If you are female, are you pregnant or able to have children? <input type="checkbox"/> I am pregnant <input type="checkbox"/> I am not pregnant, but able to have children <input type="checkbox"/> I am not pregnant and I am not able to have children								
Are you participating in any clinical trials at this time? <input type="checkbox"/> yes <input type="checkbox"/> no								

APPENDIX B

IRB FORMS

FORM 1

Baylor Research Institute
Institutional Review Board
Application and Project Summary
This form must be TYPED – Handwritten copies not accepted

Project Title: _____

Principal Investigator: _____

Clinical Department: _____

Telephone Extension: _____

FAX: _____

Mailing Address: _____

Email Address: _____

Contact Person (if different from PI): _____

Department: _____

Telephone Extension: _____

FAX: _____

Mailing Address: _____

Email Address: _____

THIS BOX FOR IRB USE ONLY	
DATE RECEIVED:	IRB MEETING ASSIGNMENT:
PRIMARY REVIEWER:	
PRIMARY REVIEWER:	

Instructions: All sections must be completed. All questions must be answered. It is NOT acceptable to answer *see attached* or *see protocol* – the one exception is that you may attach a copy of the schedule of events to the form to supplement the information provided in that section. This portion of the document is to summarize the protocol and provide supplemental information to the IRB to assist in conducting a thorough review. DO NOT DELETE ANY QUESTIONS ON THIS FORM OR ALTER ANY OF THE TEXT WITHIN THE QUESTIONS. If a question does not apply to your study – answer N/A.

Sponsor of Study - Resources	
1	Funding Source:
	<input type="checkbox"/> Industry: Name of Sponsor: _____
	<input type="checkbox"/> NIH: Specific Institute: _____
	<input type="checkbox"/> National Science Foundation
	<input type="checkbox"/> Public (Federal, State or Local): _____
	<input type="checkbox"/> Baylor Department: _____
	<input type="checkbox"/> Baylor Foundation
	<input type="checkbox"/> Private Foundation: _____
2	Are resources for conducting this research being provided from other sources? <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, please specify what resources are being provided: _____ If yes, please specify the source: _____

	Contracts for industry sponsored studies must be negotiated through the BRI Office of Sponsored Research. Grants must be submitted through BRI Office of Sponsored Research. Funding from the BHCS Foundation or from within the Baylor department also require the completion of specific forms. These must be submitted to the BRI Office of Sponsored Research.
	Purpose and Background
3	OBJECTIVES OF THE STUDY: _____
4	SUMMARIZE THE STUDY DESIGN: _____
5	PROVIDE THE SCIENTIFIC RATIONALE: _____
6	HISTORICAL INFORMATION – ANIMAL STUDIES: _____
7	HISTORICAL INFORMATION – HUMAN STUDIES: _____
	<i>This section applies only to studies involving drugs:</i> <input type="checkbox"/> Section N/A
8	Phase of the trial: <input type="checkbox"/> I <input type="checkbox"/> II <input type="checkbox"/> III <input type="checkbox"/> IV <input type="checkbox"/> Other: _____
9	Provide the following information for each drug used in this study (If additional drugs are used, please attach separate list and check here <input type="checkbox"/> :
A	Drug name: _____ Is this drug approved by the FDA? <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, is it being used in accordance with current approval? <input type="checkbox"/> Yes <input type="checkbox"/> No If the answer to either question is no, provide IND#: _____ IND number is indicated on which sponsor document (protocol, IB, Letter, etc.): _____ Where will drug be stored?*: _____
B	Drug name: _____ Is this drug approved by the FDA? <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, is it being used in accordance with current approval? <input type="checkbox"/> Yes <input type="checkbox"/> No If the answer to either question is no, provide IND#: _____ IND number is indicated on which sponsor document (protocol, IB, Letter, etc.): _____ Where will drug be stored?*: _____
C	Drug name: _____ Is this drug approved by the FDA? <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, is it being used in accordance with current approval? <input type="checkbox"/> Yes <input type="checkbox"/> No If the answer to either question is no, provide IND#: _____ IND number is indicated on which sponsor document (protocol, IB, Letter, etc.): _____ Where will drug be stored?*: _____
D	Drug name: _____ Is this drug approved by the FDA? <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, is it being used in accordance with current approval? <input type="checkbox"/> Yes <input type="checkbox"/> No If the answer to either question is no, provide IND#: _____ IND number is indicated on which sponsor document (protocol, IB, Letter, etc.): _____ Where will drug be stored?*: _____
	*For all drugs stored in your facility, you are responsible for following guidelines set forth in BRI Policy 118 regarding storage and control of investigational drugs in outpatient settings.
	<i>This section applies only to studies involving devices:</i> <input type="checkbox"/> Section N/A
10	Provide the following information for each device being used in this study (If additional devices are used, please attach separate list and check here <input type="checkbox"/> :
A	Device name: _____ Is the device used in this study approved by the FDA? <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, is the device being used in accordance with current approval? <input type="checkbox"/> Yes <input type="checkbox"/> No If the answer to either question is no, provide IDE #: _____ HCFA Category: <input type="checkbox"/> A <input type="checkbox"/> B

	FDA Letter indicating IDE # and HCFA Category must be provided. Where will device be stored?*: _____
B	Device name: _____ Is the device used in this study approved by the FDA? <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, is the device being used in accordance with current approval? <input type="checkbox"/> Yes <input type="checkbox"/> No If the answer to either question is no, provide IDE #: _____ HCFA Category: <input type="checkbox"/> A <input type="checkbox"/> B FDA Letter indicating IDE # and HCFA Category must be provided. Where will device be stored?*: _____
C	Device name: _____ Is the device used in this study approved by the FDA? <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, is the device being used in accordance with current approval?: <input type="checkbox"/> Yes <input type="checkbox"/> No If the answer to either question is no, provide IDE #: _____ HCFA Category: <input type="checkbox"/> A <input type="checkbox"/> B FDA Letter indicating IDE # and HCFA Category must be provided. Where will device be stored?*: _____
D	Device name: _____ Is the device used in this study approved by the FDA? <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, is the device being used in accordance with current approval? <input type="checkbox"/> Yes <input type="checkbox"/> No If the answer to either question is no, provide IDE #: _____ HCFA Category: <input type="checkbox"/> A <input type="checkbox"/> B FDA Letter indicating IDE # and HCFA Category must be provided. Where will device be stored?*: _____
	*You are responsible for control of investigational devices in accordance with BRI Policy 113 Investigational Device and Radiologic Accountability.
	<i>Study Subjects</i>
11	Age Range: _____ to _____
12	Number of subjects: Locally: _____ Nationally/Internationally (multi-center trials): _____
13	Gender: <input type="checkbox"/> Male <input type="checkbox"/> Female <input type="checkbox"/> Both
	<i>Special Populations</i>
14	<input type="checkbox"/> Children (age<18) – Complete IRB Form 23 Authorization to Enroll Children. Are any (or all) of the potential subjects in this study considered to be Wards of the State? <input type="checkbox"/> Yes <input type="checkbox"/> No. If you answer yes to this question, special provisions must be made to comply with 45 CFR 46.409. Please contact the IRB Office Directly for further guidance.
15	<input type="checkbox"/> Neonates – please check all that apply (See BRI Policy 856 for definitions) <input type="checkbox"/> Viable Neonates – Complete IRB Form 23 Authorization to Enroll Children <input type="checkbox"/> Non-Viable Neonates – Contact the IRB Office for Special Instructions <input type="checkbox"/> Neonates of Uncertain Viability – Contact the IRB Office for Special Instructions
16	<input type="checkbox"/> Pregnant women - Complete IRB Form 24 Authorization to Enroll Pregnant Women Are any (or all) of these pregnant woman under the age of 18? <input type="checkbox"/> Yes <input type="checkbox"/> No. If so, complete IRB Form 23 Authorization to Enroll Children.
17	<input type="checkbox"/> Prisoners or parolees – NOT ALLOWED - If you have a research subject who becomes a prisoner while on the research study, they must be removed from the study, except for follow up activities to assure safety. Please contact the IRB Office immediately if this occurs during the study for guidance.
18	<input type="checkbox"/> Spanish speaking subjects – please specify which document you will use <input type="checkbox"/> Spanish translation of the entire consent document <input type="checkbox"/> Spanish version of the short form document –bilingual witness required With either of these documents you must also have a translator available who will facilitate the translation process. This translator can NOT be a family member/friend of the research subject. It can be a member of the research team, physician practice group, certified translator from the hospital guest services department or other comparable individual.

	<p>Translator: _____</p> <p><input type="checkbox"/> Other non-English speaking subjects – please specify which document you will use</p> <p><input type="checkbox"/> Translation of the entire consent document</p> <p><input type="checkbox"/> Translated version of the short form document –bilingual witness required</p> <p>Specify language(s): _____</p> <p>With either of these documents you must also have a translator available who will facilitate the translation process. This translator can NOT be a family member/friend of the research subject. It can be a member of the research team, physician practice group, certified translator from the hospital guest services department or other comparable individual.</p> <p>Translator: _____</p>
19	<p><input type="checkbox"/> Terminally Ill</p> <p>Protocol specific rationale for enrolling these subjects: _____</p> <p>Special provisions to protect these subjects: _____</p>
20	<p><input type="checkbox"/> Elderly (>64)</p> <p>Protocol specific rationale for enrolling these subjects: _____</p> <p>Special provisions to protect these subjects: _____</p>
21	<p><input type="checkbox"/> Cognitively Impaired (mentally challenged, alzheimers, etc) (See BRI Policy 857 for guidance)</p> <p>Protocol specific rationale for enrolling these subjects: _____</p> <p>Special provisions to protect these subjects: _____</p> <p>How will you assess the capacity of these individuals to provide informed consent: _____</p> <p>Special Consent Requirements:</p> <p><input type="checkbox"/> Informed consent will be obtained from legally authorized representative (See BRI Policy 857 for individuals who qualify under Texas Law)</p> <p><input type="checkbox"/> Assent of the subject will be obtained. Provide specific information on method and timing: _____</p>
22	<p><input type="checkbox"/> Medically Unable to Consent (comatose, head trauma, etc) (See BRI Policy 857 for guidance)</p> <p>Protocol specific rationale for enrolling these subjects: _____</p> <p>Special provisions to protect these subjects: _____</p> <p>Special Consent Requirements:</p> <p><input type="checkbox"/> Informed consent will be obtained from legally authorized representative (See BRI Policy 857 for individuals who qualify under Texas Law)</p> <p><input type="checkbox"/> Informed consent will be obtained from the subject as soon as they are physically able to provide such and they will be informed that they can withdraw from the study if they so choose. Provide specific information on method and timing: _____</p>
23	<p><input type="checkbox"/> Employees (BHCS)</p> <p>Protocol specific rationale for enrolling these subjects: _____</p> <p>Special provisions to protect these subjects: _____</p>
24	<p><input type="checkbox"/> Students (this only applies to students from institutions working with BHCS)</p> <p>Protocol specific rationale for enrolling these subjects: _____</p> <p>Special provisions to protect these subjects: _____</p>
25	<p><input type="checkbox"/> Educationally/Economically Disadvantaged</p> <p>Protocol specific rationale for enrolling these subjects: _____</p> <p>Special provisions to protect these subjects: _____</p>
26	<p><input type="checkbox"/> Other (be specific): _____</p> <p>Protocol specific rationale for enrolling these subjects: _____</p> <p>Special provisions to protect these subjects: _____</p>
	Inclusion/Exclusion Criteria

27	Inclusion Criteria: _____
28	Exclusion Criteria: _____
29	Protocol specific rationale for the exclusion of any group of individuals for whom this treatment could potentially benefit (i.e., women, children, non-English speaking): _____
Recruitment of Subjects	
30	Subjects will be recruited from the following sources (check all that apply): <input type="checkbox"/> my private practice <input type="checkbox"/> physician referral sources <input type="checkbox"/> posters/flyers within the local community <input type="checkbox"/> copies of these items are available and are included with this submission <input type="checkbox"/> copies of these items are NOT available and will be submitted prior to use <input type="checkbox"/> advertise with the local media (newspaper, radio, television) <input type="checkbox"/> copies of these items are available & are included with this submission <input type="checkbox"/> copies of these items are NOT available & will be submitted prior to use <input type="checkbox"/> listing on Baylor internet site <input type="checkbox"/> listing on www.clinicaltrials.gov <input type="checkbox"/> other (be specific): _____
31	Describe methods that will be used to identify potential subjects, obtain and record subject PHI (i.e. BCON search, medical records query, database query, etc). This section should specifically state what records will be searched, who will conduct the search, what (if any) data will be recorded for future contact with subjects, what relationship the individuals who review the data have with the potential subject: _____
32	Recruitment incentive offered: <input type="checkbox"/> Cash or Visa/American Express Gift Card How much? \$ _____ (total for entire study) How frequently will payments be made? _____ (Payments must be made to the subject at least every six months and bonus payments cannot be given for completion of the study.) <input type="checkbox"/> Store or Other type of Gift Card: _____ (location) How much? \$ _____ (total for entire study) How frequently will payments be made? _____ (Payments must be made to the subject at least every six months and bonus payments cannot be given for completion of the study.) <input type="checkbox"/> Other (be specific): _____
Study Procedures	
33	Procedures involved in the study – Be sure to include at least the following information: study schedule; study procedures; number of visits; duration of participation. Procedures, tests or activities that are not considered standard of care and are being done for research purposes only should be differentiated from any procedures, tests or activities that are already being performed for diagnostic or treatment purposes. _____
Potential Risks to Research Subjects	
34	Physical Risks: _____
35	Psychological Risks: _____
36	Social Risks: _____
37	Legal Risks: _____
38	Economic Risks: _____
39	RADIATION SAFETY ISSUES: If this study involves the use of any the following procedures for either <i>diagnostic</i> or <i>therapeutic</i> purposes, provide the following information: <input type="checkbox"/> Section N/A
A	Simple Diagnostic x-ray: <input type="checkbox"/> Yes <input type="checkbox"/> No Specify type (i.e. chest, abdominal, extremity): _____

	If yes, is it for Standard of Care* <input type="checkbox"/> or Research ** <input type="checkbox"/> (see definitions below)
	How many procedures will be done: _____ What is the estimated dose per procedure: _____
	Where (facility) will the above procedures be performed? _____
B	CT Scanning: <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, what part of body: _____
	If yes, is it for Standard of Care* <input type="checkbox"/> or Research ** <input type="checkbox"/> (see definitions below)
	How many procedures will be done: _____ What is the estimated dose per procedure: _____
	Where (facility) will the above procedures be performed? _____
C	Fluoroscopy: <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, what part of body: _____ minutes of fluoroscopy per procedure _____ minutes of digital cine pre procedure _____
	If yes, is it for Standard of Care* <input type="checkbox"/> or Research ** <input type="checkbox"/> (see definitions below)
	How many procedures will be done: _____ What is the estimated dose per procedure: _____
	Where (facility) will the above procedures be performed? _____
D	Radionuclide Studies: <input type="checkbox"/> Yes <input type="checkbox"/> No Specify type (liver scan, bone scan, HIDA scan, PET, etc): _____
	If yes, is it for Standard of Care* <input type="checkbox"/> or Research ** <input type="checkbox"/> (see definitions below)
	How many procedures will be done: _____ What is the estimated dose per procedure: _____
	Where (facility) will the above procedures be performed? _____
F	Therapeutic Radiation (external beam or other): <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, what part of body: _____
	If yes, is it for Standard of Care* <input type="checkbox"/> or Research ** <input type="checkbox"/> (see definitions below)
	How many procedures will be done: _____ What is the estimated dose per procedure: _____
	Where (facility) will the above procedures be performed? _____
G	Other administration or use of Radioactive Substances: <input type="checkbox"/> Yes <input type="checkbox"/> No
	If yes, is it for Standard of Care* <input type="checkbox"/> or Research ** <input type="checkbox"/> (see definitions below)
	How many procedures will be done: _____ What is the estimated dose per procedure: _____
	Where (facility) will the above procedures be performed? _____
H	Will women of child-bearing potential be exposed to radiation (including any diagnostic or therapeutic radiology or nuclear medicine procedure) as part of this study? Yes <input type="checkbox"/> No <input type="checkbox"/>
	If YES, then pregnancy status might need to be evaluated prior to each radiation procedure. Please indicate what provisions for pregnancy status are proposed for your study. This should include (but is not limited to) such information as when study required pregnancy tests are done and what type of birth control is required per protocol. _____
	*Standard of Care: Use of radiation or radioactive substances that would be part of the routine care or follow-up of patients with disease as part of current standard of care (examples: radiation therapy for certain tumors, follow-up CT scans after chemotherapy, spiral CT scan of chest in patients with suspected pulmonary embolism). If the number or frequency of such procedures is greater than, or the manner in which such procedures are performed is different from, the same procedures that would be performed in these patients if they were not part of this research, then this does not qualify as Standard of Care.
	**Research: Use of radiation or radioactive substances in normal individuals or in patients that

	would <u>not</u> routinely be indicated or done as part of current standard of care (examples: fluoroscopy to place tube in small bowel in normal subjects for research study, additional heart catheterization to assess patency of coronary artery stent in asymptomatic patients, MUGA scans to evaluate cardiac function after novel chemotherapy, novel use of implanted radioactive seeds to treat tumor). This also includes standard of care procedures that would not be performed on these patients unless they were in this research or standard procedures that are done more often for research purposes.
	<i>Provisions to Minimize Risks</i>
40	Based on your knowledge of the subject matter, do you believe that this study involves the alternative of least risk for the potential subjects to be enrolled in the study? <input type="checkbox"/> Yes <input type="checkbox"/> No If no, provide justification for conducting the study: _____
41	Have evaluations of less risky alternatives been done? <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, summarize: _____
42	What provisions are in place for monitoring study related data to assure the protection of the rights, welfare and safety of the research subjects. This would include (but is not limited to) such information as protocol compliance, adverse events, serious adverse events, complaints by subjects, and other risks to subjects? If your study involves greater than minimal risk, at least one of these options must be chosen. Check all that apply: <input type="checkbox"/> Data Safety Monitoring Board (DSMB), Data Monitoring Committee or other committee _____ provided by sponsor. Process to provide reports to the PI and IRB: _____ <input type="checkbox"/> Medical Monitor, Data Monitor or other monitor _____ provided by sponsor. Process to provide reports to the PI and IRB: _____ <input type="checkbox"/> Review of AE's, problems and other data by investigator on a regular basis. Frequency of review: _____ <input type="checkbox"/> Review of AE's, problems and other data by another researcher or physician on a regular basis. Identify who will review the information: _____ and frequency of review: _____ <input type="checkbox"/> Other (provide details): _____
43	If the study has the potential for research related injuries or problems (physical or psychological) – please describe any procedures that are in place to provide medical/psychological care to the subjects if these problems occur. This explanation should not simply address who will pay for the care, but should address how the care will be provided: _____
	<i>Potential Benefits</i>
44	Potential direct benefits to research subjects: _____
	Potential future benefits to individuals with the condition being studied: _____
	Potential benefits to society in general: _____
	Potential benefits to others involved in the research: _____
	<i>Risk to Benefit Analysis</i>
45	Protocol specific information justifying the risks of the study in relation to the anticipated benefits and importance of the knowledge that may reasonably be expected to result from the study: _____
	<i>Privacy and Confidentiality</i>
46	Provisions in place to protect confidentiality of research related information: _____
47	Provisions in place to protect the privacy of the research subjects: _____
48	Provisions in place to protect the PHI collected during the study: _____

	Key Personnel
	<i>The Principal Investigator must be current on the IRB education modules on the Baylor Learning Network before this project will be put on the IRB agenda. All other members of the research team must be current on the lessons before the final approval will be granted. Provide name and credentials/qualifications (MD, PhD, CCRC, RN, etc.) of all members of the study team. If a CV/Resume is not on file with the IRB Office for an individual, one must be provided.</i>
49	Principal Investigator: _____
50	Other Investigators*: _____
51	Research Coordinators*: _____
52	Other Research Staff*: _____
53	Support Staff (no interaction with research subjects) *: _____
54	Collaborators with outside institution(s): _____ Will any of these individuals interact with BHCS subjects or have access to their BHCS PHI? <input type="checkbox"/> Yes <input type="checkbox"/> No
	*Please attach contact information for all individuals listed in 49 -52. This should include business address, phone number and email.
	Location of Research Activities :
55	<input type="checkbox"/> Baylor Facility a. Location: _____ Bldg: _____ Room: _____ Specific research activities to take place at this location: _____ b. Location: _____ Bldg: _____ Room: _____ Specific research activities to take place at this location: _____ c. Location: _____ Bldg: _____ Room: _____ Specific research activities to take place at this location: _____ d. Location: _____ Bldg: _____ Room: _____ Specific research activities to take place at this location: _____ e. Location: _____ Bldg: _____ Room: _____ Specific research activities to take place at this location: _____ <input type="checkbox"/> Non-Baylor Facility a. Address: _____ Specific research activities to take place at this facility: _____ b. Address: _____ Specific research activities to take place at this facility: _____ c. Address: _____ Specific research activities to take place at this facility: _____
	If additional locations, please attach separate list and check here <input type="checkbox"/>
	Informed Consent Process
56	Location of obtaining informed consent. <i>Provide a specific location, such as clinic office, surgical suite, and/or patient's hospital room. If more than one location is possible, please list a summary of the types of places that you would expect to obtain the informed consent:</i> _____
57	Timing of obtaining informed consent. <i>Include specifics and such details as when in relation to the beginning of the study procedures you will obtain informed consent, and the amount of time the subject has to make the decision. It is important that you allow the subject sufficient time to make an informed decision prior to beginning the study and that they have the opportunity to discuss this with family or other significant individuals in their lives. If the nature of the study requires that consent be obtained immediately prior to the beginning of the research, give the rationale:</i> _____
58	Individuals designated to obtain informed consent (all must be listed as key personnel): _____

59	Consent as an ongoing process: _____
60	Describe steps taken to minimize the possibility of coercion or undue influence. : _____
61	If additional tools, handouts, other written materials are used (other than the IRB approved consent forms) these must be listed here and provided to the IRB for review and approval prior to their use. If you will use these materials, please list here: _____
For Studies involving medications: <input type="checkbox"/> Section N/A	
62	Where will the medications be administered? (Check all that apply) <input type="checkbox"/> BUMC <input type="checkbox"/> BIR <input type="checkbox"/> Baylor Irving <input type="checkbox"/> Baylor All Saints Fort Worth <input type="checkbox"/> BSH <input type="checkbox"/> Baylor All Saints Cityview <input type="checkbox"/> Baylor Garland <input type="checkbox"/> OCH <input type="checkbox"/> Baylor Waxahachie <input type="checkbox"/> Baylor-Plano <input type="checkbox"/> BHVH <input type="checkbox"/> Baylor Grapevine <input type="checkbox"/> Baylor Irving Coppel <input type="checkbox"/> Outpatient <input type="checkbox"/> Clinic <input type="checkbox"/> Other: <input type="checkbox"/> Physician's Office
63	The sponsor will supply all medications for this study. <input type="checkbox"/> Yes <input type="checkbox"/> No
64	Some or all medications for this study will need to be purchased by the hospital pharmacy. <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, which medications will need to be purchased: _____
65	If inpatient, all medications will be dispensed from hospital stock. The patient or the insurance company will be billed for the product. <input type="checkbox"/> Yes <input type="checkbox"/> No
Supplemental Review – Other Committees	
66	Radiation Safety Committee: Radiation Safety Committee: If you answered yes to any of the questions outlined in #38, you must obtain approval from the Committee on Radiation Safety and Radioisotopes (CRSR). Please contact CRSR at 214-820-7133 for specifics on submission process. All protocols involving the following types of radiation exposure must be approved by the CRSR at a full Committee meeting: 1. use of novel (non-FDA approved) radioactive materials, devices, or therapies; 2. novel uses of approved radioactive materials; any type of radiation that exceeds 50 rem to any organ or body part and is delivered in a manner, dose, or frequency that is beyond that which would be employed in standard clinical practice if the patient were not on the protocol. The CRSR committee meets quarterly. Protocols involving radiation exposure that meets “Standard of Care” criteria and/or involves lower radiation doses MAY be approved at more frequent intervals by appropriate subcommittees of the CRSR.
67	Institutional BioSafety Committee: Does this study involve the use of recombinant DNA? <input type="checkbox"/> YES <input type="checkbox"/> NO Does this study involve the use of Select Agents*? <input type="checkbox"/> YES <input type="checkbox"/> NO Does this study involve the use of Select Agent Toxins*? <input type="checkbox"/> YES <input type="checkbox"/> NO If you answered “YES” to any of the questions above, your study must be submitted to the Institutional Biosafety Committee (IBC) for review. Send a copy of the protocol and IRB Application to: Steven J. Phillips, Ph.D., BRI Biosafety Officer, Baylor Research Institute 214-820-9993 (Phone) 214-820-4952 (Fax) steveph@baylorhealth.edu
<i>*A list of Select Agents and Select Agent Toxins can be viewed at the website of the Centers for Disease Control. www.cdc.gov/od/sap/docs/salist.pdf</i>	
68	Tissue Bank Committee: Does this study involve the use and/or collection of human tissue, either in the form of glass slides or fresh/fresh-frozen tissue? <input type="checkbox"/> YES <input type="checkbox"/> NO If yes, further review may be required by the BRI Tissue Bank Utilization Committee. To facilitate

	this process, please complete the BHCS Tissue Bank/Fresh Tissue Procurement Application (ADM012) and submit to: BHCS Tissue Bank, Hoblitzelle Bldg., Suite 326
69	Nursing Research Committee: Does this project study nursing in the area of practice, professional issues, education, or management? <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, this must be submitted to the Nursing Research Committee at: John Dixon, MSN, RN, The Center for Nursing Education & Research, Baylor University Medical Center
70	Credentials Committee Do all members of the research team hold appropriate medical staff and/or allied health professional credentials required to perform any standard procedures that are being done as a part of this study? <input type="checkbox"/> Yes <input type="checkbox"/> No If no, please explain: _____

INVESTIGATOR COMMITMENT:

I understand that as Principal Investigator, I have ultimate responsibility for the conduct of the study, the ethical performance of the project, the protection of the rights and welfare of human subjects, and strict adherence to the IRB approved protocol and any additional stipulations imposed by the IRB. I assure the IRB that I have sufficient time to conduct and complete the research in accordance with IRB guidelines. I agree to comply with all Baylor Research Institute IRB policies and procedures, as well as with all applicable federal, state, and local laws regarding the protection of human subjects in research. I certify that no similar proposal has been disapproved by another IRB. I agree to maintain strict confidence of information that may be disclosed including subject/patient, data, employee, institution proprietary, industry trade secrets, and any other form of confidential information.

I agree to report immediately to the IRB any non-compliance, unanticipated problems involving risks to subjects or others, complications or adverse incidents with respect to human subjects.

I agree to perform the project with qualified personnel according to the approved protocol. I agree that I am to implement no changes in the approved protocol or consent form without prior IRB approval (except in an emergency, if necessary to safeguard the well-being of human subjects). I agree to obtain the legally effective informed consent from human subjects or their legally responsible representative, and use only the currently approved, date-stamped consent form. I agree to evaluate on an individual subject basis, whether or not an individual subject understands the information presented during the informed consent process. I agree that informed consent is an ongoing process and it is my responsibility to determine over a period of time that all research subjects continue to be willing to participate.

I understand that I have the responsibility to make the Department Administrator aware of all protocols that are submitted to the IRB.

The Institutional Review Board of the Baylor Research Institute will suspend approval of all research projects of investigators who are non-compliant with the above requirements. The Chief-of-Service will be notified of the suspension as will the Chairman of the Medical Board and other Institutional Officials. Non-compliance of IRB requirements could result in Institutional Officials reporting these actions to the Office of Human Research Protections, the US Food and Drug Administration, the Study Sponsor or other agencies.

Investigator Signature

Date

STATEMENT OF BAYLOR ADMINISTRATOR:

I have reviewed the proposal to be submitted to Baylor Research Institute and understand that by signing below I have committed the resources needed by my department to conduct this study. It is my responsibility to assure that

budget issues related to this study are resolved. If this study involves the resources of another Baylor department, I have contacted that department administrator for input regarding their department. If applicable, I will ask the investigator to obtain a second signature for said department administrator.

Baylor Administrator

Date

(If the study is funded solely by a Baylor department, must be signed by VP)

Name and Title of Baylor Administrator: _____

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FORM 14

IRB/IACUC #: _____ Date: _____

Project Title: _____

Name: _____ Department: _____

Address: _____ Phone: _____ E-Mail: _____

Sponsor: _____

Significant Financial Interest includes the following:

- anything of monetary value of \$10,000 or more, including but not limited to, salary or other payment for services (e.g., consulting fees or honoraria); equity interests (e.g., stocks, stock options or other ownership interests); and intellectual property rights (e.g., patents, copyrights and royalties from such rights)
- ownership interest less than \$10,000 whose value could not be referenced to publicly available prices or other measures of fair market value
- ownership interests of any value that could be affected by the outcome of the research
- ownership interests greater than 5% interest in any single entity
- compensation related to the research in any amount that would be affected by the outcome of the research
- board or executive relationship related to the research, regardless of compensation

Family member means a spouse or dependent child or stepchild.

List below any relationships in which you or your family members are involved that constitute a significant financial interest as defined above, with any institution sponsoring this research project.

Institution/Company	Relationship/Role (explain)	Amount of Financial Interest
		<input type="checkbox"/> \$10,000 - \$25,000 <input type="checkbox"/> \$25,001 - \$50,000 <input type="checkbox"/> \$50,001 - \$100,000 <input type="checkbox"/> >\$100,000 _____ (record amount)
		<input type="checkbox"/> \$10,000 - \$25,000 <input type="checkbox"/> \$25,001 - \$50,000 <input type="checkbox"/> \$50,001 - \$100,000 <input type="checkbox"/> >\$100,000 _____ (record amount)
		<input type="checkbox"/> \$10,000 - \$25,000 <input type="checkbox"/> \$25,001 - \$50,000 <input type="checkbox"/> \$50,001 - \$100,000 <input type="checkbox"/> >\$100,000-_____ (record amount)

If you have nothing to disclose, please confirm such by checking the below statement and sign at the bottom of the form.

☐ I hereby certify that none of the financial interest or arrangements listed above exists for myself, my spouse, or my dependent children.

-----**Signature**

Acknowledgement

I have read the Financial Conflict of Interest requirements as outlined in 42 CFR 50, Subpart F. I hereby agree to report immediately in writing to the BRI Vice-President any new situation with the potential for a conflict of interest that may develop before the completion of my next Statement of Disclosure.

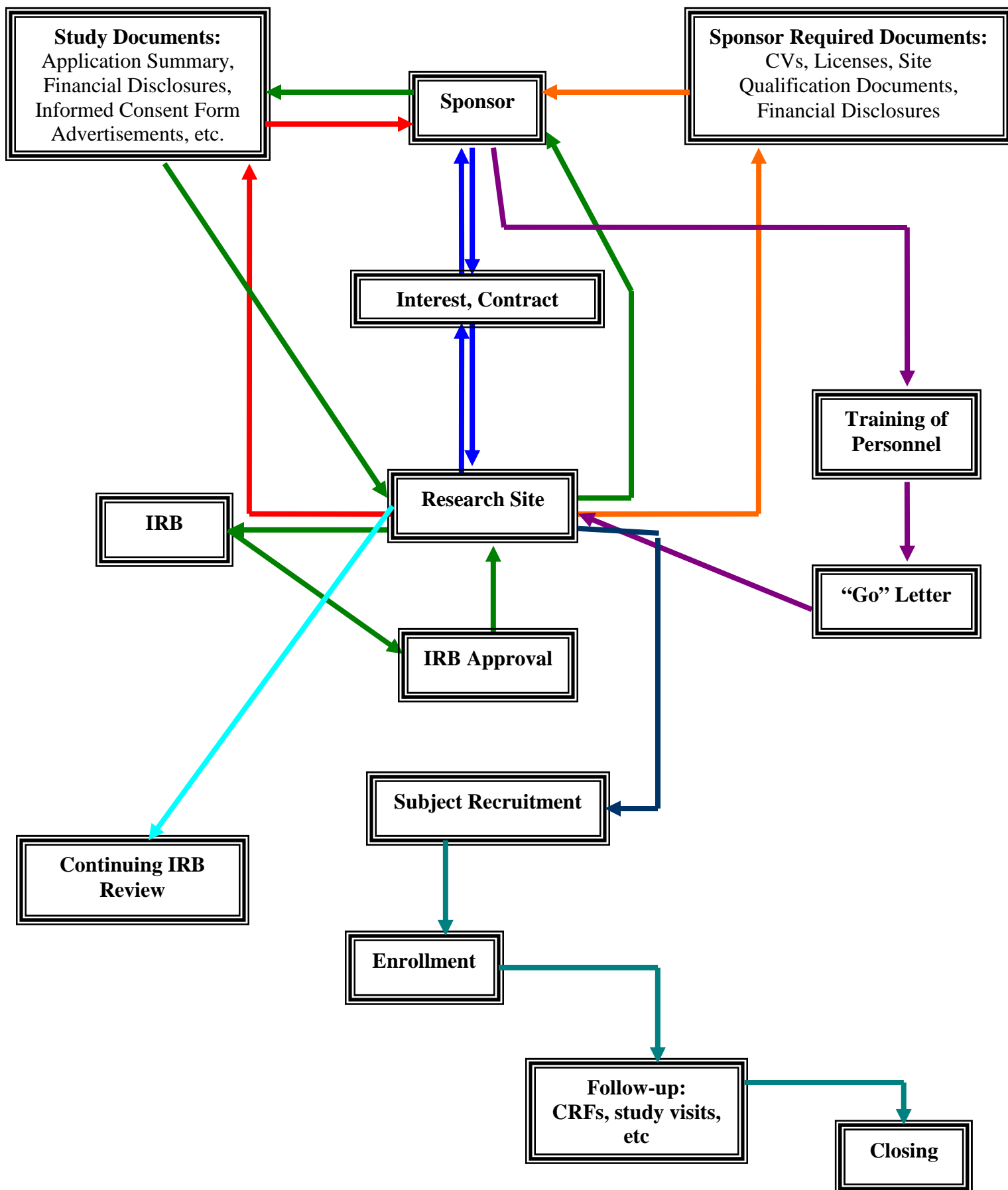
The answers above are true and accurate to the best of my knowledge as of the date of this disclosure.

Signature: _____ Date: _____

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APPENDIX C

CLINICAL TRIAL FLOW CHART



APPENDIX D
DAILY JOURNAL

WEEK 1

6/01/2009: Today was the first day of the internship. I arrived in the morning and completed training modules dealing with IRB processes, as well as consenting potential subjects. Once I was done with training, I met up with Lisa and we proceeded to track down a couple of doctors who are co-investigators for a trial that is comparing surgical ablation vs. catheter ablation in the treatment of atrial fibrillation. We discussed changes to their protocol that need to be completed prior to submission to the IRB. After lunch, Lisa, two other research coordinators (Ilene and Amy) and myself met with individuals about another trial that is about to start which focuses on the use of a vest which, to my understanding, doubles as a pacemaker for subjects. The meeting lasted for the rest of the afternoon.

6/02/2009: Today I helped organize our open study reference binder by including pages that listed the follow up schedules for subjects depending on which trial they are involved in. On Thursday, there is supposed to be training on a program known as Study Manager that will allow us to enter subject data and alerts will be sent to us to prompt us when to contact subjects to ensure that they continue to be a part of the study. Later in the day, I went through spreadsheets of all the subjects involved with our various trials and checked start dates of enrollment. Based off of these dates, I was able to let the other coordinators know if it was time to contact subjects for their next study visit.

6/03/2009: The day started off with a meeting at 7:00 a.m. where we discussed protocol development for a study that is comparing different techniques for endoscopic vein harvesting. After the meeting, I sorted through subject folders for two of the trials going on right now in an effort to make a list of which subjects need to be contacted about changes made to the Informed Consent Form. I was also able to participate in two consenting processes today for two different trials: one comparing two different aortic valves in subjects undergoing aortic valve replacement, and the other is a prospective study to see what happens with a certain type of stent used to repair coronary arteries. With the second subject, I was fortunate enough to participate in the consenting process, observe the angiography/stent placement, and then follow up with the subject after the procedure.

6/04/2009: Today I started off the day with a training session about new software (Study Manager) that we plan to use in order to help us organize subject info for the various trials. Next, I went to Baylor's Downtown campus to sit in on an IRB meeting for 2 studies we are trying to get approved. Once we made it back to Baylor Plano, I organized trial information on spreadsheets.

6/05/2009: Once I arrived today, I began working on a letter to send to cardiologists in the North Texas/South Oklahoma area about the CABANA trial, which is what my thesis will be on. The trial is going to compare catheter ablation to drug therapy for the control of atrial fibrillation. After I completed the letter, I sent it to my mentor Lisa as well as the Principal Investigator Dr. DeVille for critiquing. Around mid-day, I watched an aortic stent placement on a patient with a

thoracic aneurysm for one of our trials that is a data registry study. I believe it is referred to as this type of study because the patient was going to get a stent regardless of his participation in the trial. The manufacturers of the stent used in the trial just want to collect data on it (short and long term). This way, the follow-up on the patient will shed light onto many different aspects of the stent.

WEEK 2

6/08/2009: I spent the majority of the day working with the Study Manager program. I was trained for a few hours in the morning and then for the rest of the day I entered data from different studies into the program in an effort to make subject follow-up easier.

6/09/2009: Today I started off working with Study Manager again and entered 2 more studies into the program. Around mid-morning, I attended an architecture meeting discussing the addition of 2 floors to THE HEART HOSPITAL Baylor Plano. Once the meeting was done, I helped organize data for various studies and continued to work on adding studies to Study Manager.

6/10/2009: Today I was able to participate in another consenting process and I watched another catheterization. The patient was being consented to participate in a stent study, but didn't meet all of the criteria. The patient that had the catheterization did consent to participate in the stent study, however, during the preliminary angiogram it was discovered that she had no blockage in any of her arteries. Considering this fact, the woman was no longer qualified to participate in the study. At the end of the day, I attended a meeting with the CEO of Heart Test Laboratories where we discussed having THE HEART HOSPITAL Baylor Plano (THHBP) create a clinical trial to check the efficacy of a new piece of technology known as a Myocardial Ischemia Electrocardiogram (MIECG) which would ideally identify individuals that may have heart disease sooner.

6/11/2010: Today I added 2 more studies into Study Manager throughout the day. I also typed up notes in regards to the meeting I attended yesterday pertaining to the MIECG. I organized the notes because tomorrow Lisa and I are supposed to meet with Dr. Brown, an Interventional Cardiologist and a prestigious person associated with THHBP, about his viewpoint on the potential of the MIECG trial. Later in the day, Dr. DeVille, the Principal Investigator for the CABANA trial stopped by the office to discuss the physician letter we are going to send out to cardiologists across Texas in an effort to recruit physicians to participate in the trial. He approved the letter I had written, therefore the next step is to create a list of potential physician participants and then send it out to them.

6/12/2009: The morning started off with a meeting on the 3rd floor with the Electrophysiology Dept. Lisa and I met with the staff in their break room to give them updates on the types of trials we are conducting that are relevant to Electrophysiology. A little later in the morning, I had my first meeting with Nanette and Lisa to talk about how things are going and what the outlook for the next week looked like. It was a very positive meeting and has motivated me even more; a lot

of exciting things are about to take off. In the early afternoon, Lisa and I met with Dr. Brown in between a couple of his cases to get his feedback and input pertaining to the questions we have in regard to the MIECG. The day wrapped up with me making calls to participants in one of our trials because the sponsor of the trial decided that it wanted to compensate subjects for participating in the clinical trial. It was really nice to call people and tell them they were getting more money; that's always good news.

WEEK 3

6/15/2009: The day started off with me watching a catheter ablation to correct atrial fibrillation. Unfortunately, while the patient was intubated, his blood pressure skyrocketed and his PCO₂ was also exceptionally high. With the best interest of the patient in mind, it was decided to abort the surgery and try again at a later date. At the time of the procedure, the reason for the high pressures was unknown and I don't know what the resolution on the situation is. I later made copies of consent forms, scanned some documents and faxed some documents as well. The day wrapped up with me calling some more patients letting them know that they were going to be compensated for their participation in one of our studies.

6/16/2009: Today I worked on gathering more information on the rest of the patients that need to be re-consented for the two studies I have been referencing over the past few days. Two people actually came in today in response to my phone calls about re-consenting, which is really good because I figured it would take people longer to get out here. Tomorrow I will be ready to follow up with the last few patients that have past due appointments and reschedule them. I also attempted to get a grasp on our fax problems we've been having over the last week.

6/17/2009: Today started off with a meeting with the Cath lab staff. Lisa and I updated them on what is going on in the Research Dept. and what future plans/projects we have at this point. Next, I watched an ablation on a patient suffering from supraventricular tachycardia. The surgery seemed very laidback, but I am sure it is because of the skill the doctor and nurses have. The source of the patient's arrhythmia was localized and then destroyed. The ablation portion of the procedure was accomplished by applying radiofrequency energy in this case (however there are many ablation techniques). A small scar is created that is electrically inactive and thus incapable of generating heart arrhythmias. The ablation was a success. After lunch, I called subjects of one of our studies that are past due on follow-up appointments in an attempt to schedule a time for them to come in.

6/18/2009: Today consisted of my weekly meeting with Nanette and Lisa and an IRB meeting. At the weekly meeting, we discussed new options for using Study Manager in regards to helping us keep track of our finances for our studies. We also discussed my progress and the activities of the last week. Once I made it to the IRB meeting, it was very interesting to see how efficient the process of approving/disapproving/tabling a study really is. One thing that I learned from our IRB class with Dr. Gladue is that different IRBs can be like night and day, and that some

meetings drag on for hours upon hours. It was really nice to see an example of an IRB that in my opinion is very proficient, fair, and thorough in their reviews.

6/19/2009: Today started with an early meeting to discuss the formulation of a protocol for the endoscopic vein harvesting study I mentioned two weeks ago. It was interesting to see the brainpower of everyone working together to make sure they were creating a solid study that would get approved by the IRB. I later sat in on another meeting with Lisa and Nanette discussing the possibility of doing a drug trial at THHBP, as opposed to the customary device trials we have under way. The rest of the day consisted of contacting the “hard to reach” subjects about the ICF updates and organizing the financial data for next week’s meeting about Study Manager.

WEEK 4

6/22/2009: Today was a fairly relaxed day. It consisted of copying and faxing various documents, as well as getting packets ready to send out to subjects consisting of W-9 forms and ICFs. I also attempted to contact the last subject on my list of individuals that have to either sign the new ICF or are late for one of their follow-up visits. This particular subject has not been home the last 3 times I have called. Hopefully they will return my call soon.

6/23/2009: Today I worked on my research proposal in the morning. Next, I sat in on a meeting with Lisa and Nanette to discuss the formulation of budgets for certain trials. I was also able to finally mail out the necessary documents to subjects pertaining to the updated ICFs. The second half of the day started off with me putting together research trial overviews for physicians. The goal is to have a system where we have our physicians critique trials that we have aspirations of participating in at THHBP and determining the validity of our participation and whether or not “good science” is being done. The day ended with a meeting about handling hazardous materials.

6/24/2009: Today started off with a Study Manager meeting to learn how to include financial information for studies. After the meeting, I had my weekly meeting with Nanette and Lisa to discuss the progress of the CABANA trial and where I stand in terms of my research project. The day wrapped up with me working on my research proposal again. I initially was having a hard time developing how I would write the proposal since my project is evolving around the management of a research study, but with today’s discussion with Lisa and Nanette, I have a better grasp of where to start.

6/25/2009: It has been another “low stress” day here at THHBP. Lisa graciously allowed me to work on my research proposal, which I believe I have finally completed. It still is rough around the edges, but I think I have a good skeleton to mold as the internship progresses. I will definitely be able to learn a lot about managing a multi-center clinical trial and the rest of the thesis will hopefully not be challenging to write. At this point, I am still trying to learn what a feat like this entails. Nanette has provided me with some magazines and books to read about some of the things involved and issues to consider with such a venture. I also helped Ilene, one

of the research coordinators, with paperwork for one of the trials she is responsible for. I finished up the day conducting a 6 month telephone follow-up with a subject in one of our trials. Despite the overall low intensity of activities of this week, Lisa has implied that this may be the calm before the storm, and that things will pick up soon.

6/26/2009: The morning began with me making a few phone calls, both for 6 month follow-ups. One subject, whom I have been trying to contact for a week, is in Australia. This is good news because it means post-surgery the subject is feeling well enough to leave the country; a very positive sign. The other subject didn't answer the phone. I received feedback from Nanette and Lisa on my research proposal. I took heed in their suggestions and incorporated them into the proposal and will send it off to Dr. Gwartz before I go home for the day. The end of the day wrapped up with me observing Amy, one of the coordinators, obtain consent from a patient for a stent data registry study.

WEEK 5

6/29/2009: Today started off with me performing a 6-month telephone follow-up with one of our subjects for one of our trials. Next, I sent an e-mail to cardiologists that have plans on participating in one of our studies dealing with percutaneous mitral valve repair. It is required by the IRB that the participating physicians have at least 100 procedures under their belt before they can participate in the trial. I then organized a couple of Regulatory Binders for a couple of our studies. My next task was to fill out the evaluation forms electronically that were sent to physicians in order to critique potential research taking place at THHBP. In the early afternoon, we received one of the signed updated ICFs in the mail from one of the subjects I sent the new ICF to last week. That's a good sign and hopefully the rest will come pouring in soon. The day wrapped up with some minor clerical tasks.

6/30/2009: In the morning, I worked with Study Manager in an attempt to update some of our studies with financial information. Close to midday, I helped package food collected from a food drive the THHBP was having. I worked with a few other individuals to make sure the goods would be easily transported to The Salvation Army. The afternoon consisted of a Research Department meeting where we discussed our current projects and outlook for the near future.

7/01/2009: This morning began with me searching the CDC website for information pertinent to Coronary Artery Disease for a potential study. I then helped Lisa update our communication board outside of the office. Periodically new information is placed inside of it highlighting what is going on at a particular time in the research department. This time around, we will be focusing on one of the new studies we will be starting soon. Later in the day, I proof-read a grant for grammatical errors and gave my novice opinion on parts that I found to be a little confusing.

7/02/2009: Once I arrived this morning, I helped Ilene with some paperwork for one of the trials she is in charge of. The rest of the morning was spent working on inputting financial

information into Study Manager. The day wrapped up with me watching Dr. DeVille correct an atrial fibrillation by means of catheter ablation.

7/03/2009: Fourth of July Holiday

WEEK 6

7/06/2009: The morning started off with me doing another search of the CDC website for CAD statistics again. The information I found last week is over 10 years old and I am trying to find some more recent data. I then looked at the History and Physical (H&P) sections of 2 patient's charts in an effort to see if they qualified to participate in one of our trials. There is a lot to consider as far as exclusion and inclusion criteria. I find it easy to get lost in all of the details when deciding if a patient can potentially participate or not. The rest of the day consisted of me continuing my efforts to find CAD statistics and also reviewing past proposals to see if I am on the right track with writing my proposal.

7/07/2009: Today began with me working on my research proposal. Receiving some past proposals yesterday has really helped me with my efforts in writing my own proposal. I see that my initial approach to writing the proposal is fairly consistent with the examples I have seen; therefore I anticipate having a solid thesis once everything is all done. The rest of the day consisted of me helping Ilene enter information for screen failures for one of the trials she is in charge of. I also filled out research overview spreadsheet critiques for one more physician. The rest of the day I continued working on my proposal, with me wrapping up my last hour of the day helping Lisa get materials ready for our meeting tomorrow morning.

7/08/2009: The morning started off with a Research Advisory Meeting that occurs on the first Wednesday of the month, every other month. Various topics were discussed, such as trial status at the hospital, potential new trials, ways to obtain funding for upcoming trials, and much more. The afternoon consisted of me working on my proposal some more, filling in gaps, referencing text properly and things of that nature. I did escape for a little with Ilene to watch a consenting of a patient for one of our trials at the end of the day too.

7/09/2009: Today started off with some clerical tasks. I then worked on my proposal some more and attempted to put together a subject recruitment checklist for two of our studies that deal with atrial fibrillation. At our meeting yesterday morning, one of the physicians mentioned that it would be a great idea to have a checklist for potential subjects to fill out when they come to the doctor for appointments. This will ideally allow us to catch more participants for our studies and increase our enrollment. With that being said, I am putting together a rough draft of a questionnaire that patients can fill out, and based on their responses, we will know whether or not they qualify for the study or not. At the end of the day, I went with Amy to consent a patient for one of our studies.

7/10/2009: The morning started off with me performing a literature search for two of the physicians at THHBP. I needed to locate 3 of each of their publications to be sent to the AHA. After completing the literature search, I helped Amy get documents together for an auditor from one of our sponsors. Also, it just so happened today that the protocol and informed consent for CABANA finally arrived. Therefore, THHBP has to fill out/adjust the documents so that they pertain to our site.

WEEK 7

7/13/2009 -7/17/2009: Lisa and Nanette were kind enough to allow me to take the week off in order to focus on the MCAT that I will be taking on Friday, 7/17/2009. Some correspondence via e-mail did take place throughout the week. Over the weekend I worked on the IRB Form I for CABANA. It provides details about the purpose of the study, the investigators of the study, where the trial will be taking place, plus many other topics that are necessary for the IRB to get a solid idea of what the study will be about. A Form 1 can be viewed as the overall “summary” of what to expect for a trial. It provides the members of the IRB with the background they need to make the best decisions when reviewing potential research trials.

WEEK 8

7/20/2009: I did not come in to work today because I had car problems and had no means of making it in.

7/21/2009: The morning started off with me reviewing the ICF and Form 1 that was created specifically for THHBP in regards to the CABANA trial. Certain questions were still unanswered and needed our research team to provide the proper information, so I worked with Lisa to accomplish this. I also organized a subject binder for one of our trials. After lunch, the research staff took a tour of a different floor where we could potentially relocate during the expansion of THHBP. Due to the need for more space, additional floors will be added to THHBP. Lastly, I made a trip downtown to Baylor Research Institute (BRI) and Baylor Heart and Vascular Hospital (BHVH) in order to deliver some documents that need physician signatures.

7/22/2009: The day commenced with me attempting to locate patient information for 5 different patients that have undergone a left atrial catheter ablation. This documentation is needed in order to ensure that the Principal Investigator for the CABANA trial, Dr. DeVille, meets the requirements set forth by the Sponsor and that he is qualified to perform the surgeries. Unfortunately I wasn't able to find the nurse I need to assist me, so I will try to find her later. Next, I proceeded to start another Form 1 for another CABANA trial, but this one deals with carotid stents, not atrial fibrillation. After lunch, I went downtown to the Baylor Heart and Vascular Hospital (BHVH) with Lisa to speak with a physician about a study we will be starting soon. I also continued to edit the CABANA (afib) Form 1 and ICF.

7/23/2009: Today started off with a meeting with one of the physicians, Dr. Brown, concerning the material that will be presented tonight at a meeting for all of the financial partners of THHBP. Also, the status of a couple of our trials was discussed. Next, I ran a few errands. First, I picked up a video of a patient from a doctor's office and took it downtown for another doctor to look at. Then, I stopped by Baylor Research Institute Downtown to drop off some documents. Once I made it back from my trip, I organized forms for IRB submissions and continued working on the Form 1 for the CABANA (carotid stent) trial.

7/24/2009: The morning started full throttle because we have 4 IRB packets for different studies that need to make it downtown by midday. Therefore, there has been a lot of copying and sorting of documents in order to make sure we finish in time. I also had to get Dr. Deville's signature for various documents dealing with the CABANA trial. After lunch I went with Ilene to consent a patient for a carotid stent trial.

WEEK 9

7/27/2009: The day started out with a meeting with representatives from one of the sponsors of a few of our studies. With one of the aforementioned studies, THHBP has reached our recruitment goal/allotment determined and agreed upon by the IRB. Therefore, we need permission to continue to recruit for the trial. This topic was discussed as well as recent protocol amendments. Next, I helped Ilene enter information into the website for one of our sponsors for a few subjects.

7/28/2009: The morning consisted of me dealing with car problems. My alternator had gone bad so I had to take it to the shop. Once I returned to THHBP, I worked on my research paper a little and went with Ilene to place a Holter monitor on one of our subjects. For their 6 month follow up visit, a portable monitor is placed on the individual to record the electrical impulses of their heart for 24 hours. Then, they return the device and the results are sent to be processed. The day ended a little early because I had to go pick up my car.

7/29/2009: Yesterday Nanette expressed the importance of making sure the appropriate study information is in Study Manager to allow easier maintenance of budgetary items for different studies. Therefore, today I am spending the majority of my time re-familiarizing myself with the program and I will collaborate with our Research Assistant, Jared, to create a checklist of items that we know how to do with the program and certain things we need to be "re-trained" on. The rest of the afternoon consisted of me doing some personal research on some terms I have heard here and there and didn't fully understand.

7/30/2009: Today consisted of me putting together folders for different studies. The folders include any questionnaires that are to be filled out by coordinators when screening potential subjects, as well as consent forms and inclusion/exclusion criteria. For many of the studies, we do not have the IRB approved consent forms, so I must wait until we receive them to finish the folders. In the afternoon, I went over a preliminary budget for CABANA (afib) with Nanette and

Lisa. It was interesting to see how a budget is developed. I also did some filing and scanning of documents today.

7/31/2009: In the morning I sent the CABANA Pivotal Investigator Agreement to Duke University. I also sent one copy to Baylor Research Institute Downtown and kept one for our records. It is necessary for the PI to sign one of these to assure that he/she will follow GCP. I also created 2 more regulatory binders for 2 of our trials and filed documents in them. In the afternoon, I watched an aortic valve repair done by Dr. Ryan.

WEEK 10

8/03/2009: Today started off with me sending protocols and ICFs to doctors that will be having their studies reviewed at the IRB meeting this Thursday. Also, we had a new coordinator start today named Sandi. I gave her a brief tour of the facility and introduced her to a few people. After lunch, I sent another e-mail to a select few physicians that need to be trained in trans-septal puncture techniques for the participation in one of our new trials. Dr. DeVille, an Electrophysiologist, will be doing the training. The latter part of the day consisted of some clerical work.

8/04/2009: In the morning I watched Amy consent a patient for one of our studies. Next, I worked on trying to ensure that case report forms were filled out for our subjects with one of our studies. A 6 month EKG is part of the follow up procedure and the Case Report Forms (CRFs) need to be filled out accordingly with information from the EKG. Therefore, I tried to make sure the forms were filled out completely but didn't get to finish today. After lunch, I watched an atrial fibrillation ablation performed by Dr. DeVille.

8/05/2009: The morning started off with a Study Manager meeting to iron out some of the kinks. Our Research Assistant, Jared, is going back to college next week and I will temporarily be in charge of inputting information into the program. After the meeting I put together study folders which consist of worksheets and consent forms that the coordinators use when consenting patients. I also continued to work on completing the CRFs that I had started yesterday. After lunch I ran to Medical City to drop off a patient's EKG disk.

8/06/2009: When I arrived today, I had to promptly change and go to one of our ORs. A subject for one of our studies was undergoing an aortic valve repair. As part of the protocol, the patient isn't randomized to one of the valves until the surgeon is ready. Therefore, I had to be in the room to open the envelope that decides which valve the physician is going to use. Once that was done, I went to consent a patient with Sandi, our new research coordinator. Lisa had already talked to the patient last night, but she gave her enough time to read the consent. Fortunately, the patient wanted to consent to be in the study. There was an IRB meeting downtown where 4 of our studies were being reviewed, one of which is the study my thesis is going to be over (CABANA). Fortunately, all 4 studies were approved. This is a big deal because now we can start enrolling patients. Actually, we are still awaiting FDA approval for the use of one of the

catheters as a tool for the treatment for atrial fibrillation for the study. Once this is accomplished, things will really pick up.

8/07/2009: Today started with some minor clerical duties. I also went with Ilene to consent a patient for one of our studies. This particular study is a carotid stent registry. The day wrapped up with some more clerical tasks and further organization of some study-specific folders. Lisa, Nanette and I had a brief meeting to talk about the internship and how things are going.

WEEK 11

8/10/2009: Early in the day I met with Lisa and Dr. DeVille to overlook Patient Checklists for 2 of our atrial fibrillation cases. The goal is to screen patients when they come in for doctor appointments to try to catch as many participants as possible. Amy also taught me how to screen patients for participation in our studies. I also made a trip to Medical City to get a physician to sign some IRB forms.

8/11/2009: The morning started with me printing out History and Physical (H&P) documents for potential research candidates. After I browse the patient list and look for keywords that identify potential research subjects, the research coordinators look through the H&P's of patients to make sure they qualify before they attempt to consent them. We also found out that CABANA was actually approved, with minor modifications with the consent form. Therefore we will adjust accordingly and resubmit to the IRB. The afternoon consisted of me editing the patient checklists that Dr. DeVille, Lisa, and I looked over yesterday.

8/12/2009: The day consisted of checking the hospital schedule for any potential research subjects that have a case that may have been added on since the last time I checked. I also tracked some physicians down for signatures and helped Sandi with some clerical duties.

8/13/2009: The day consisted of reviewing the hospital schedule for next week and creating the new list of potential research subjects. I also made the final edits to the patient checklists for two of our atrial fibrillation trials and did some more clerical duties.

8/14/2009: Today I started off by checking the schedule for any add-on cases for today and next week. I then had to scan some documents and get them to a research nurse downtown. The documents include some patient information regarding an individual we are trying to screen for one of our trials. Dr. Grayburn who works downtown at BHVH is taking the lead with this patient to see what he can do. I also did some paperwork for one of our trials. I had to transfer information from EKGs to CRFs for one of our studies. I also attempted to go through Study Manager to find any gaps and try to fill them in the best that I can.

WEEK 12

8/17/2009: The day started off with me checking the patient schedule to see if there have been any add-on cases over the weekend. My next task was to gather IRB forms that need to be signed by investigators for one of our studies. I believe the study is up for continuing review. Therefore, I created financial disclosure and sub-investigator agreement forms to have investigators sign. The day wrapped up with me continuing to fill out subject worksheets for one of our studies and I checked the patient schedule for any last minute add-ons for tomorrow.

8/18/2009: This morning I checked the patient schedule for add-ons when I first arrived. My next task was to browse through Study Manager and try to fill in any gaps that our research assistant may not have completed before he left to go back to college. After lunch, I helped Amy enter data on one of our study sponsor's website for a patient. I also took some time to fill in gaps in my thesis. I realize that the internship is halfway done and that a lot of questions I had a couple of months ago can be answered. I am learning a lot and realize just how intricate and meticulous of a task it is to make sure research runs smoothly.

8/19/2009: I started the day by screening for any additional cases that may have been added. My big task of the day was to get information situated for the compensation some of our subjects are going to receive for their participation in a couple of our studies. I had to make copies of consent forms and gather W-9s for the subjects, as well as make some calls and follow up with a few people who we need to sign W-9s or sign the updated consent forms. After lunch, I also attempted to go through some studies on Study Manager and close any gaps that I can. The day wrapped up with me making copies of updated consent forms and replacing out-dated ones in some of our study binders.

8/20/2009: The morning started out with me finishing up some filing of documents and filing. I also faxed some information to various locations. We currently have 2 monitors here from 2 separate studies reviewing study information. This morning, I helped Ilene get one of the monitors situated so she could review our study binders. After lunch, I helped our volunteer, Bhavani, make copies of documents for one of our studies that is up for continuing review. The day wrapped up with me getting a head start on looking at the patient schedule for next week and screening for studies.

8/21/2009: Today consisted of a trip to Medical City to pick up 2 copies of an echo that was performed on a patient. Then, I had to deliver one to Baylor Vascular Heart Hospital Downtown for Dr. Grayburn and then return the other copy to Lisa. The rest of the day consisted of trying to contact subjects that need to send in W-9 forms so they can be reimbursed for their participation in our study.

WEEK 13

8/24/2009: This morning I watched an aortic valve replacement done on one of our research subjects. It was my job to be in the OR and when the time was right, open an envelope to see what type of aortic valve the patient has been randomized to. Once this is determined, I collect data pertaining to the valve and then the principal investigator fills out the rest of the data. Once that was complete, I spent the rest of the day gathering IRB documents for the reimbursement of our subjects for participating in our study. We are still waiting on about 7 W-9s. As for the rest, the necessary forms were taken to the IRB downtown for processing. The day ended with me delivering a physician agreement document to a private practice of some of the physicians that have privileges at THHBP. We need them to be signed and returned to the IRB.

8/25/2009: The day started off with some filing, copying, and scanning of documents. I also decided to look through our patient schedule and screen for any add-on cases for potential research participants a littler earlier than usual. I also had to call San Antonio and request records for one of our research subjects that had surgery there. As standard protocol, anything that happens to our subjects, especially surgeries, must be reported to us and then to our IRB. It then needs to be determined if the occurrence was due to the services rendered to them as a study participant. In the afternoon I watched a case for one of our trials. It is a superficial femoral artery (SFA) stent study; however, the patient did not need a stent once the physician had the opportunity to assess the condition of the artery.

8/26/2009: Today I created a document for physicians to easily assess whether or not their patients may qualify for a study. Based off of the patient's diagnosis, the physician can see what trial the patient may qualify for. From that point, the criteria for the particular study that the patient may qualify for can be looked at more closely to see if the patient truly qualifies. This will ideally make subject recruitment more efficient. I also made some phone calls to our subjects that need to return W-9s to us so they can get paid for their participation in our study. All of the necessary paperwork has been sent out; now we must wait to get it back in the mail.

8/27/2009: The day started off with me trying to contact the last few individuals who need to turn in W-9s to us. The few I talked to, I went ahead and sent out the document to them; I only have one left to send tomorrow. We also had a Billing Compliance meeting this morning. It is important to make sure that charges incurred during a research study are paid for by the right entity. For instance, if a certain procedure is standard of care vs. research will indicate from which budget the procedure will be paid for, or if it is to be covered by the patient's insurance. I also started screening for next week's cases to get a head start on things.

8/28/2009: This morning I sent the last W-9 forms out to our patients to sign. I also scheduled an echo for one of our research subjects as part of their follow up for being research subjects. I completed screening patients for next week and also helped Ilene fill out some CRFs on a subject. The Research Department also had a meeting today to discuss our game plan for when Nanette goes on Maternity leave and tie up some loose ends with some projects.

WEEK 14

8/31/2009: Today a new research nurse started named Jennifer. I started off by giving her a brief tour of the hospital until Lisa was ready to take her to HR to sign some papers and finish giving her a tour. I then started to work on filling out CRFs for a subject of ours. Doing so has really emphasized how important patient records are, as well as how multifaceted research really is. Paperwork is essential. I also filled out eCRFs for a subject in another study that had a deadline of close of business today. The day wrapped up with me checking to see if any add on cases were put on the weekly schedule.

9/01/2009: The day started off with me working on my proposal a little. I realize that if I want to defend by the end of this semester, I need to make sure I stay on top of things. I am fortunate because I feel like I have a good foundation and I just have to fill in gaps. Tomorrow is our Research Advisory Board meeting that occurs on the first Wednesday of every other month. Therefore, I am helping Lisa get documents ready for the meeting.

9/02/2009: Today started off with our Research Advisory Board meeting in the morning, where we discussed updates in research over the past 2 months. Later, I attended another meeting where we discussed the status of one of our studies that may potentially be reviewed by the FDA. I also opened the randomization envelope during an aortic valve replacement for one of our studies. The patient is randomized to one of two types of valves, both which are FDA approved. The day wrapped up with me screening for new cases for tomorrow.

9/03/2009: Today started off with a trip to Legacy Heart Center to get some signatures from a physician on some CRFs. Later I made some phone calls to try to get some medical records on some of our subjects that were hospitalized recently. Also, I followed up on a subject for their 12 month review since their procedure. The rest of the day involved working on some Form 7's and 14's to add myself to some studies so I can start consenting patients and helping out with cases. I also screened for additional cases tomorrow.

9/04/2009: Out of Office

WEEK 15

9/07/2009: Labor Day Holiday

9/08/2009: Out of Office

9/09/2009: Today started off with me swinging by Legacy Heart Center to pick up signed documents that I dropped off a couple of weeks ago. When I got to the office, I made copies of ICFs and tried to retrieve some medical records for some of our subjects. After lunch, I worked on completing some Form 7's and 14's to add myself to some studies so I can start consenting patients and helping out with cases. I also screened for additional cases tomorrow.

9/10/2009: Today began with making some more calls to patients in an attempt to gather medical records. I also tentatively scheduled times to follow-up with some patients for one of our studies. I was also trained by the sponsor of one of our studies so I could be added on as study staff and help consent subjects and do other study tasks. The rest of my day consisted of finishing up screening cases for tomorrow and completing Form 7s and Form 14s.

9/11/2009: The day consisted of phone calls to patients for follow ups and trying to track down records for patients as well. When I had time, I tried to track down physicians to sign Form 14s for continuing reviews that we have coming up, as well as to expedite the process of getting me added to studies so I can start consenting patients. We had a lunch meeting with Jennifer Thomas who has temporarily replaced Nanette while she is out on maternity leave. The research department simply discussed our status and enjoyed some pizza. The day ended with me screening the schedule for potential research subjects for next week.

WEEK 16

9/14/2009: This morning I attempted to find a regulatory binder for one of our studies that is approaching continuing review, but I did not have any luck. I then proceeded to attempt to request more records for patients and follow up on some requests I made last week. I also found some physicians and had them sign some forms for us. I also did some typical clerical duties today such as filing and scanning. The day wrapped up with me organizing some information and writing summaries on articles pertaining to Thromboelastography. Many Baylor physicians are trying to decide whether TEG is a valid technique to use in regards to the heart. I am merely organizing some info so they can have something easy to read to facilitate their assessment. The day ended with me screening for additional cases tomorrow and swinging by Legacy Heart Center to pick up some documents.

9/15/2009: The morning started off with me tracking down a couple of physicians for signatures, which was successful. The rest of the day consisted of me continuing to work on the TEG summaries as well as attempting to start creating inclusion/exclusion cards for CABANA. Last week, Microsoft Publisher was finally added to my computer and now I can make the cards. As usual, my last task of the day was screening for additional cases for tomorrow.

9/16/2009: The day included me pursuing physicians for signatures and putting the finishing touches on the inclusion/exclusion cards for CABANA. If I haven't already mentioned, I am tracking down physicians to get their signatures on documents such as Form 14s (Financial Disclosures) for continuing reviews and Form 7s to add myself and other coordinators to some of our existing studies. I also tried to get a good start on my NIH Stroke Scale training. For some of the trials I will be a coordinator for, I will have to assess if individuals have had strokes and if so, how severe they were. The day wrapped up with me screening for any additional cases for tomorrow.

9/17/2009: The day included a lot of preparation for our potential FDA audit. I had to track down physicians for signatures and ensure that we have updated CVs and medical licenses for all physicians. I ended the day by screening cases for tomorrow.

9/18/2009: Today I tracked down more physicians for signatures and gathered documents for CABANA. We had to fix our consent form again and we have just sent it off to the sponsor for review. Close to noon, we had a meeting about FDA audits and what to expect. It was very beneficial to learn what I can say, shouldn't say and can't say, amongst other things. The day ended up with me screening for next week.

WEEK 17

9/21/2009: Today started off full throttle. Lisa is out of town attending a conference in San Francisco and we had a lot of things to accomplish early on in the day pertaining to IRB approvals for a few of our studies under the status "Approved Pending Modifications". I also tracked some more physicians down for signatures. The day wrapped up with me screening cases for tomorrow.

9/22/2009: Today I tracked more physicians down for signatures and filed documents that we received back from the IRB. I also tracked physicians down for CVs and updated medical licenses. It seems like a little, but somehow it was enough to fill up 8 hours.

9/23/2009: Once again the day was more of a wild goose chase, finding doctors and asking them for more signatures and contacting doctor offices in an attempt to get up to date CVs and medical licenses. I also helped get Dr. DeVille registered to attend the Investigator's Meeting for CABANA next week in Philadelphia. The day wrapped up with me screening for any cases for tomorrow.

9/24/2009: Lisa is on her way back into town from San Francisco and this morning I helped her tie up a few loose ends with some items pertaining to a potential subject for one of our studies and ensuring that some of our staff are up to date with their Human Subject Training. Once again, I spent a chunk of the day strategically finding physicians for more signatures. My time to defend is fast approaching, so I am hoping to utilize any free time to finish up my thesis. The day wrapped up with me screening for tomorrow's cases.

9/25/2009: The day consisted of gathering signatures on documents that our sponsor needs signed in order for THHBP to start enrolling subjects in the CABANA trial after the Investigator's Meeting that is taking place this Thursday through Saturday. I also worked on my thesis a little and wrapped up the day by screening for cases next week.

WEEK 18

9/28/2009: The day started off with me finding physicians for signatures. I also made phone calls to request updated medical licenses for some of the physicians that participate in clinical trials with us. I utilized a little free time to continue working on a project I started a couple of weeks ago which involves me organizing/summarizing journal articles about Thromboelastography. The day wrapped up with me screening for any new cases tomorrow.

9/29/2009: The morning consisted of me trying to find some documents that I misplaced. After an hour, I was able to find them. I mistakenly thought I had put them on Lisa's desk. However, on my way to her desk, I mixed the documents in with some CVs that I was sorting through. Once I found them, they were Fed-Ex'd to the sponsor of the corresponding study. We also had a meeting after lunch to discuss our plan of action since we have many trials that are about to start, and we need to devise a plan of how we are going to tackle them, as far as our responsibilities and expectations. The rest of the day consisted of tracking down updated physician licenses and screening for additional cases for tomorrow.

9/30/2009: Today I tied up some loose ends prior to my trip to Philadelphia for the CABANA Investigator's Meeting. The day also consisted of 2 meetings. The first meeting pertained to our site initiation visit for another trial known as CABANA; however this one is a carotid stent registry. For the site initiation visit (SIV), a monitor from the sponsor comes to your site and trains the study staff accordingly. The second half of the day consisted of a meeting about FDA Inspections which was given by Lynn VanDermark of MedTrials.

10/01/2009 - 10/03/2009: CABANA Investigator's Meeting in Philadelphia, Pennsylvania. Training will take place to ensure that all investigators and coordinators are prepared to start the trial when the conference is over. There will be basic training on what to expect with enrollment, etc. Also, there will be training on EDC (Electronic Data Collection) for the study. Expect a full explanation in my thesis.

WEEK 19

10/05/2009 - 10/09/2009: Since our theses are due in 2 weeks, I am working from home this week to wrap things up with my paper and PowerPoint presentation. On Thursday, I completed the NIH Stroke Scale Certification in order to determine if individuals have had a stroke or not. I want to say for about 3 of our trials this certification is essential because of the nature of the trial. The trials are carotid stent trials and it is imperative to check if the patient has had a stroke because if plaque is present in the artery, placing a stent and moving a catheter around in it can easily break off a piece of the plaque and cause a stroke. Therefore, we check before surgery, after surgery, and 30 days after surgery to ensure that our subjects are stroke-free.

WEEK 20

10/12/2009: With today being my first day back in a week, I had some housekeeping items to take care of. I had to sort through some documents and establish what tasks have been accomplished that were left from last week and where I need to continue from. I had to make a call to a subject because they filled out a form incorrectly, and I also followed up on some CVs. It was perfect timing that I became certified to administer the NIHSS Exam because two subjects need a follow-up this week; one today and one Thursday. The exam went well; it was liberating to be able to do it on my own. The day ended with me screening for potential cases for tomorrow.

10/13/2009: The day started off with me relieving Ilene and taking over watching a superficial femoral artery (SFA) stenting procedure on one of our research subjects. After the proper data was collected and the procedure was complete, I returned to the office. Next I scheduled a couple of follow up appointments for two of our subjects in another stenting trial for diabetic patients. The rest of the day included me working on a couple of smaller projects dealing with improving our department. The day ended with me screening for potential cases for tomorrow.

10/14/2009: This morning I started off following up on some CV and license queries that were still unanswered. I also spent the bulk of the day completing the summaries of the TEG articles that I started a few weeks ago; that seemed to take up most of the day. The afternoon wrapped up with me screening for potential research subjects.

10/15/2009: When I arrived today I performed another Stroke Scale assessment on a patient for their 30 day follow up. The middle portion of the day included me sorting through documents for a meeting we plan to have with the PI of CABANA, Dr. DeVille. We are going to go over the CRFs so we have an idea of what to expect when we start enrolling patients. The last part of the day consisted of me watching a carotid stent placement on a research subject. I had to obtain certain data during the exam.

10/16/2009: When I arrived today, I had to perform another Stroke Scale assessment on the same patient that had the carotid stent surgery yesterday afternoon. As part of the protocol, we have to do the assessment prior to procedure, within 24 hours after the procedure, and 30 days after the procedure. I then noticed I received Dr. Gwartz's comments on the first portion of my thesis. I reviewed her comments so I have an idea of what and how to edit my paper over the weekend. I will also be sending her the rest of it sometime today. The second half of the day consisted of me picking up where I left off with sorting documents for our meeting with Dr. DeVille, organizing some patient data for CRFs, and then screening cases for the early part of next week.

WEEK 21

10/19/2009: Today the morning was spent organizing another office where 4 of our coordinators will be moving to. We ordered 4 desks and I helped make sure they were delivered to the right place. After lunch, I worked with Jennifer, one of our Research Nurses, to organize materials and brainstorm what we are going to talk about at our bi-weekly CABANA meeting Wednesday morning. The day ended with me screening for any add on cases.

10/20/2009: The morning was once again consumed by trying to put together a work order to add phone and data lines in our other office so the coordinators can have phones and use their computers. This time I brainstormed with Lisa and the Engineering Dept on what the best method would be to accomplish the task at hand. The rest of the day consisted of putting final touches on materials for our meeting with Dr. DeVille tomorrow morning and screening for any add on cases.

10/21/2009: The morning started with an early meeting with Dr. DeVille, Ilene, Jennifer, Lisa and I discussing our progress with CABANA. The rest of the morning consisted of me helping Sandi find patient documents needed by a sponsor of one of our studies, as well as following up on trying to get our hands on a few more physician licenses. After lunch, I helped Sandi find more documents, edited my thesis, and screened for additional cases for tomorrow.

10/22/2009: I had a leak in my apartment which was potentially leading up to becoming a severe electrical hazard so Lisa was nice enough to let me work from home today. I soon came to find out that the problem was more severe than initially anticipated and had to switch apartments immediately. However, I do plan on coming in tomorrow because there is an important GCP meeting scheduled.

10/23/2009: The morning started off with a Good Clinical Practices (GCP) Meeting with Sue Latham from MedTrials. It took up the bulk of the day. The rest of the day consisted of me doing some clerical duties and screening for next week's cases.

WEEK 22

10/26/2009: I will be working from home for the rest of the week since my Thesis is due this Wednesday. I did go in today for our office meeting, however, because we are rearranging the work load in our department and I think it is important for me to be there. I then returned home to continue working on my thesis.

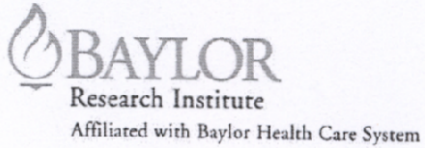
10/27/2009: Early this morning, I had a meeting with Dr. Gwartz in Fort Worth to discuss my internship and talk about my game plan for my defense which will take place on November 11th. Talking to Dr. Gwartz really helped ease my worries with such a momentous event. We talked through my thesis as well as my PowerPoint presentation. I look forward to defending in a few

weeks; there has been a lot of blood, sweat, and tears put into this program and I am excited that the culmination of everything has finally arrived.

10/28/2009: Thesis Due. My Defense date is Nov 11, 2009 at 9:30 a.m. in LIB 318. The zenith of all of my hard work has finally arrived and it is very bittersweet to be at this point. I turned in my final product today and will continue to edit my Power Point presentation.

APPENDIX E

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A handwritten signature in dark ink, consisting of a stylized, cursive script that appears to read "Bernard Brignonnet". The signature is written over a circular stamp or seal that is partially visible.

Bernard Brignonnet
Chief Operating Officer

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