

EVALUATION OF NEW OPERATING PROCEDURES FOR SUBMITTING
INVESTIGATOR-INITIATED
RESEARCH TO BAYLOR'S IRB

INTERNSHIP PRACTICUM REPORT

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CHAPTER 1

PROBLEM/ HYPOTHESIS

A toolkit (BRI Toolkit) for investigators interested in investigator-initiated research that outlines the steps to complete Baylor's Internal Review Board (IRB) submission process was created at Baylor Research Institute. The following hypothesis were tested:

- 1) Will the BRI Toolkit decrease the amount of time needed to obtain IRB approval?
- 2) Will investigator satisfaction with the BRI Toolkit be high?
- 3) Will investigators who used the BRI Toolkit recommend its use to others?

SIGNIFICANCE

The course through a successful clinical trial is not as concise and efficient as many investigators would imagine. In order to have a successful clinical trial, much consideration needs to go into the launch of it for approval from both the IRB and the U.S. Food and Drug Administration (FDA). An influential study requires forethought in not only the scientific realm but the logistical as well. This project streamlined the bureaucratic process by developing a step-by-step guide through the operational procedures, which is called the BRI Toolkit. A copy of this document is included as Appendix 2. The BRI Toolkit allows investigators to focus more on development of their research protocol and less on federal and institutional regulations. A step-by-step investigator guide like the BRI Toolkit increases the efficiency of the IRB approval process. This increased efficiency allows the trial “to maintain the validity and relevance of the questions addressed” (Baer, et al, 2010, p. 250). A decreased time frame can prevent investigators losing interest. This in turn increases the overall productivity and scientific contributions of the institution. It may also help encourage investigator-initiated trials, which may be preferable to industry-sponsored trials in terms of scientific rigor (Relman, 1990).

Over the past six decades the landscape of clinical trials has changed drastically. The rise of industry-sponsored clinical trials and Contract Research Organizations (CRO) has left individual investigators unprepared for the bureaucracy of the IRB submission process. The rigidity and number of rules that the investigator must follow and adhere to has also increased dramatically during these past few decades. Investigator-initiated research projects can become so engrossed in the process of getting the project approved by the IRB that the investigator can lose interest and the project fails to launch. In other instances the investigator can lose valuable

time by a delayed approval. This can happen when they fail to have something completed, forget a step, or the protocol needs to have several rounds of revisions (Baer, et al, 2010). The BRI Toolkit effectively guides an investigator through the development of a clinical trial through the IRB submission.

Grimshaw et al (2004) stressed the need for a coherent and simple instructional manual for investigators to follow, and that data on the use of such a manual should be collected to assess its efficacy on research (*Ibid.*). Collecting data would allow the Baylor Research Institute Toolkit to be further tailored to the investigators' needs.

After the BRI Toolkit was created, this project tested whether the BRI Toolkit 1) decreased the amount of time needed to obtain IRB approval 2) gauged the investigator satisfaction with the BRI Toolkit and 3) determined whether investigators would recommend the BRI Toolkit's use to other researchers.

BACKGROUND

SITE OF EXPERIMENT

Baylor Health Care System was founded in Dallas, TX as a Christian ministry of healing in 1903. They were founded with the mission to serve all people through exemplary health care, education, research, and community service (Baylor Health Care System, 2013). Their vision was to be trusted as one of the best places to give and receive safe, quality, compassionate health care. Baylor health care system prides themselves on their founding values of integrity, servanthood, quality, innovation, and stewardship. They strive to demonstrate the following values in every aspect of their care:

- Integrity through conducting themselves in an ethical and respectful manner.
- Servanthood through serving with an attitude of unselfish concern.
- Quality through meeting the needs and striving to exceed the expectations of those they serve through continuous improvement.
- Innovation by constantly exploring, studying, and researching new concepts and opportunities.
- Stewardship by managing the resources entrusted to them in a responsible manner.

The Baylor health care system has undergone many changes over the last century. They have grown from a fourteen room modified house to a health care system with over 300 access points that sees over 2.8 million patients annually.

They have received many awards and accolades over the past century as well. They have been recognized as one of America's best hospitals for the past twenty years with seven of their hospitals in the top 1% of the nation. They have been recognized as a top place to work both locally and nationally. In addition, Baylor is continuously recognized for their research and the translational medicine that this research creates.

Baylor Research Institute (BRI) oversees research within the Baylor health care system (Baylor Research Institute, 2013). Baylor Research Institute was founded in 1984 to help promote and support the translational medicine within the Baylor health care system. They oversee a wide spectrum of activities, from basic science up through its application in clinical trials. They also examine the effectiveness of their healthcare and conduct research on the quality of care patients receive at Baylor. They oversee and facilitate the meetings of the three separate Institutional Review Boards (IRBs) within the Baylor Health Care System.

BRI also houses nearly all of the departments that an investigator planning to submit an investigator-initiated study to the IRB would need to interact with. This creates the ideal setting for the creation of a toolkit for investigator-initiated research submission to an IRB, specifically Baylor's IRB. The BRI Toolkit explains each of these departments (*Table 1*) and how the investigator can use them to his/her advantage, as well as who specifically to contact and what forms to complete prior to contacting them.

Table 1. Baylor Research Institute Departments and Purposes

Department	Purpose
Accounting	Development of study budget
Clinical Research Associates	Monitor many trials to assure that activities are being recorded and reported to the IRB properly
Clinical Research Coordinators	Oversee individual trials and reports all study activities to the IRB
Grant Specialists	Locate and secure funds for study
IRB Coordinators	Aide study personnel in the submission of documents to the IRB and set IRB agenda
Legal	Negotiation of contracts with outside entity
Regulatory Affairs	Maintain IRB accreditation and oversee that studies follow FDA guidelines

THE FDA AND CLINICAL GUIDELINES

Clinical trials have only been required for new treatments and devices over the past century. For example, prior to 1906, new medicines could go straight to market without any oversight at all. Then, in 1906, the government passed the “Pure Food and Drug Act” which prohibited the sale of mislabeled or adulterated food or drugs across state lines. It was created due in part to the influence of Harvey Washington Wiley who was the chief chemist of the Bureau of Chemistry in the Department of Agriculture. Drugs and food were managed and overseen under this act until 1930, when the United States Food and Drug Administration was formally created (Swann, 2009).

The FDA’s oversight now extends to a wide variety of products, which account for 25% of what Americans spend. The FDA oversees the quality and safety of most food products (except for meat and poultry), human and animal drugs, therapeutic agents of biological origin, medical devices, radiation-emitting products for consumer, medical, and occupational use,

cosmetics, and animal feed. One of the departments under the FDA's authority is the Center for Drug Evaluation and Research (CDER). This department assures that all pharmaceuticals put on the market in the United States follow the same rigid guidelines in order to receive FDA approval. They must first be tested in the laboratory and on animals. If they are found suitable, safe, and effective they can then begin testing on humans, which is referred to as clinical research (FDA, 2012).

Clinical research happens in a series of four phases. Each phase tests a different aspect of the substance or device in question and increases the number of subjects in subsequent trials (Friedman, et al, 1998).

- Phase one trials are conducted on a small number of healthy individuals, typically less than fifty. The goal of this phase is to determine how well the substance can be tolerated. This determines the standard dosage and the maximum tolerated amounts.
- Phase two clinical trials have a slightly larger study population. This phase is conducted in people who are the target population; they have the ailment that the chemical or device is intended to treat. The focus of this trial is to determine if the drug creates any biological activity against the disease or sickness in question. The investigators will use the dosage determined from the phase one trial in this phase.
- The final phase before FDA approval, known as the pivotal phase, is phase three. In a phase three clinical trial, the pharmaceutical is given to a much larger study population, hundreds to thousands of patients, to determine the effectiveness of the new drug compared to the current treatment in the target population. After this trial is completed the substance is submitted to the FDA through an Investigational New Drug application (IND).

- The fourth phase in a clinical trial is a study that determines the long-term effects of the treatment within the entire target population after the FDA has approved it (Friedman, Furberg, & DeMets, 1998).

Baylor Research Institute may oversee any of the stages, but focuses mainly on the first three phases of clinical trials (Baylor Research Institute, 2013). By the time the trial is in stage four it has already been approved by the FDA and no longer requires an IND submission in most instances (Baylor Research Institute, 2013).

IRB approval is a pivotal step in the course of a clinical trial and is mandated by law. Under Title 45 Code of Federal Regulations Part 46, an IRB is overseen and governed by the Department of Health and Human Services (Code of Federal Regulations, 2009). An IRB's primary concern is the protection and rights of the patients in the clinical trial. They assure that the trial is performed ethically and that the patient will receive, at minimum, the standard of care. The IRB must approve the protocol of the trial prior to the collection of any data on a human subject involved in a study to ensure that the study adheres to ethical codes established for clinical research. (*Ibid.*).

CODES OF ETHICS

Protection of human research subjects has undergone a gradual evolution over the past eighty years. There have been a number of foundational documents whose requirements must be met in order to protect clinical trial participants. The Hippocratic Oath of “do no harm” predates the FDA and should have always applied to persons in a clinical trial. However, as history shows, this has not always been the case. Three documents have been created to protect human subjects, and were written in response to the abuse or disregard of subjects' rights by researchers.

The Nuremburg Code, The Declaration of Helsinki, and The Belmont Report all address the rights that humans have as participants in a clinical trial.

The first code put into place for the protection of human research subjects was the Guidelines for Human Experimentation of 1931 (Ghooi, 2011). This was not a very well known document and was later eclipsed and built upon by the Nuremburg Code. The Nuremburg Code was written in response to the war crimes committed by the Nazis during World War II. Written in 1947, this document discussed the fundamental rights of research subjects and the responsibility of the investigator to protect them. It is a list of ten directives that outline how subjects are to be protected. The most important contribution to medical ethics from this document is the idea of informed consent (Shuster, 1997). Although no nation or major medical association has put the document into law in its entirety, it has laid the foundation for all ethical guidelines written since.

In 1964 the World Medical Association wrote the Declaration of Helsinki, which became the guiding statement for physicians and others in the clinical research field (Carlson, et al, 2004). This document has been revised several times but is still regarded as “The most widely recognized source of ethical guidance for biomedical research,” according to a speech given to the World Medical Association General Assembly (Macklin, 2003).

In 1979 the Belmont Report was written by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Belmont Report was written in response to the atrocities of the Tuskegee Syphilis Trial and outlines principles that every clinical trial in the US must follow. The three principles of the Belmont Report are Beneficence, Justice, and Respect for Persons (Department of Health, 1979). The principle of Beneficence assures that all people in a clinical trial will not be intentionally put in danger or at risk. The principle of

Justice is exercised in clinical trials by the assurance that one group is not selectively treated better than another group in the trial. All participants must be treated according to the standard of care (at least) and have an equal chance of being in either the experimental or control group. The final fundamental precept from this report, Respect for Persons, has two parts. The first is that participants have the right to choose whether to participate in a trial, and that they can end their participation if they so choose. The other aspect of Respect for Persons is the protection of subjects with diminished autonomy or historically disadvantaged groups such as children, pregnant women, prisoners, mentally disabled persons, or economically or educationally disadvantaged persons. Not only do they have the same rights as previously discussed, autonomous persons, but they also require additional protection to assure that others do not influence them with regard to their participation in a trial.

Requirements for participant protection outlined by these reports must be included in clinical trials submitted to the FDA and an IRB. It can be difficult for an investigator to encompass all these required components in the clinical trial proposal. The dissemination of the BRI Toolkit guides researchers to fully explain participant protection plans in their proposals so that they are more likely to be approved by the IRB. The BRI Toolkit supports individual investigators, and it may also help promote investigator-initiated research in general, contributing to a counterbalance of the modern shift in the clinical research industry which is further discussed in the next section.

SHIFT IN THE INDUSTRY

How research is initiated has also changed drastically over the past five to six decades. There has been a shift in clinical trials from investigator-initiated trials to industry-sponsored trials. Pharmaceutical companies now sponsor most clinical trials and “there is mounting

evidence that they often skew the research they sponsor to make their drugs look better and safer” (Angell, 2008). Companies are now involved in every aspect of the trial, from the design of the trial, the analysis, the information put into the published papers, and the decision of the form that the publication should take, if the results are published at all.

Prior to pharmaceutical and device companies’ intense involvement in clinical trials, there were fewer guidelines and less oversight, and the system was more tailored to investigators. In the modern industry, the pharmaceutical and device companies often have a specialized department for the IRB approval process or they hire a Contract Research Organization (CRO), which specializes in IRB approval. The increase in guidelines and oversight is beneficial for patient protection but has decreased the number of investigator-initiated trials. The researchers do not want to navigate through the bureaucracy that this increased protection for patients has caused.

There are other sources of funding available to investigators to perform clinical trials. The National Institute of Health, other government entities, and some private non-profit organizations all support clinical trials (Reed, et al, 1999). In some instances a pharmaceutical company can sponsor a trial but it is still an investigator-initiated trial. The principle investigator is still responsible for the design and outcome of the trial. The substance or procedure is the intellectual property of the investigator, but the pharmaceutical company provides the funding and will have a stake in the outcome of the trial. This can be an advantageous relationship because these companies often have a designated person or department whose job it is to walk the investigator through the IRB submission process.

The percentage of funds that come from non-industry sources has been on the decline since the mid 1980’s (Reed, Phil, & Camargo, 1999). The rise of pharmaceutical and device

companies and CROs has left the independent researcher without much knowledge of how to navigate the IRB submission process. Investigators interested in independent research are hesitant to initiate their own study because of the increase in regulatory and bureaucratic hurdles that they must overcome before they even begin the trial (Bergmann, et al., 2010). Without investigator-initiated trials, translational medicine will suffer.

There has been some effort from academia in the past to suppress the trend toward industry-sponsored research and avoid the bias that industry funding can cause. In academe, peer reviewed journal publications are the benchmark of success and achievement. *The New England Journal of Medicine* is one of the leading peer reviewed journals in the medical field. They do not accept articles from researchers who have consulted or received funds from corporations in order to avoid potential biases in their results, whether overt or unconscious (Relman, 1990). The decline in investigator-initiated research must be addressed by increasing support for investigators. The dissemination of the BRI Toolkit to the investigators can serve as part of this support, as a way to navigate them through the bureaucracy and regulations that now exist in the clinical trials landscape. Assistance with initiating trials results in better science, translating to better medicine and a healthier world.

Investigator-initiated projects are empirically better and more accurate than those sponsored by pharmaceutical and device companies (*Ibid*), but researchers are often ill equipped to begin a clinical trial. The BRI Toolkit is designed to support IRB applications of investigator-initiated clinical trials. The project addresses the effectiveness of the BRI Toolkit in creating support for IRB submission by determining whether investigators were satisfied with the BRI Toolkit and whether its use resulted in faster approval from the Baylor IRB. Additional support

for clinical trial initiation, such as IRB approval application, may help better equip investigators to initiate clinical research, as discussed below.

LITERATURE REVIEW

The implementation of guidelines or instructions on how to complete a task is widely practiced because without them people do not know what to do (Guren, 2011). People work more effectively when told how to accomplish a task. They can focus on the completion of the task rather than trying to figure out what it is that they need to do. This is true for initiating clinical trials as well as other complicated tasks. Generally, investigators have a scientific background, not one in clinical research management. Their scientific knowledge is credible and advanced, but they can get lost in the bureaucracy and paperwork of submitting a proposed trial to an IRB and then the FDA. This has been observed at Baylor Research Institute numerous times; an investigator will submit a protocol to the IRB only to learn that they failed to complete a necessary portion of the submission packet. This costs both the investigator and the institution time, which is crucial for the relevance of the research and funding.

Farrell et al (2010) observed how the initiation and beginning of a clinical trial is similar to a business and should have a plan prior to its launch. They highlight some areas that need careful consideration and thought early in the development process such as recruitment, monitoring, data management, promotion, safety reporting, and distribution of the results (*Ibid*). They emphasize the need for guidelines and claim the lack of them can be “extremely challenging and at times very frustrating” (*Ibid*). The creation of the BRI Toolkit helps to prevent repetitive processes and avoid missteps by investigators, thereby reducing investigator frustration.

Francis et al (2007) examined how the treatment of a trial as a business and creation of a business model would greatly increase the likelihood of successful IRB approval. They stress this by proposing that a trial is only one fifth science and four-fifths management (*Ibid*). Frances et al have not published any results on the efficacy of their project. The advantage that the BRI Toolkit has over these aforementioned articles is that it has data to back its claims of shortening the amount of time needed for IRB approval. Chapter 2 presents data to support this project's claims of increased efficiency.

Many organizations, such as the National Cancer Institute, the John Hopkins Institute, and the Mayo Clinic, have also taken note of the inefficiency of trial development and have looked for ways to decrease the time needed for trial approval.

Recently the National Cancer Institute (NCI) Clinical Trials and Translational Research Advisory Committee established the Operational Efficiency Working Group to advise on strategies to become more efficient (Baer, et al, 2010). Baer et al (*Ibid*) proposed the establishment and enforcement of deadlines at key points in protocol development. They also suggest certain actions in the protocol development process that can occur at the same time, such as budget and contracts. No results on the effectiveness of their recommendations have yet been published, which situates this project on the cutting edge of CRM research, as it both establishes a set of guidelines for investigators to follow and gauges the effectiveness of them.

The standardizing process which the BRI Toolkit project implements is not a unique system. The Mayo Clinic also has a similar operational process to standardize and streamline the clinical trials process. Their Clinical Trials Management System (CTMS) is based on the same idea that a system such as the BRI Toolkit will decrease the administrative burden and increase

the overall efficiency (Mayo Foundation for Medical Education and Research, 2012). They have not, however, published any data related to the efficiency that they discuss.

John Hopkins Institute, another leading research institute in the US, also has a system to help investigators interested in clinical research. Much like Baylor has the Baylor Research Institute, The Johns Hopkins Institute for Clinical and Translational Research is designed to help the investigators with the management of their clinical trials. The studies are put into a Clinical Research Unit (CRU) where they have access to the Research Participant Advocacy Office (RPA) that provides consulting expertise on human subjects and regulatory issues, including IRB applications and the informed consent process (John Hopkins Clinical Research Units, 2012).

The project at Baylor Research Institute combines aspects of all of these previously discussed cases. The new investigator-initiated research Toolkit has incorporated numerous steps into the same time frame, a protocol formulated after Baer et al (Baer, et al, 2010). As Francis et al (Francis, et al., 2007) proposed, it acts as a business model for investigators to follow. The BRI Toolkit helps to create a structure for the business aspects of their research and allows them to focus on the scientific investigation for which they are trained. This new toolkit also incorporates a standard, systemic approach to investigator-initiated research similar to that implemented by the Mayo Clinic (Mayo Foundation for Medical Education and Research, 2012) and Johns Hopkins CRU (John Hopkins Clinical Research Units, 2012).

The aforementioned entities have noted the need for a solid foundation to a clinical trial. The approval from the IRB is one of the first steps taken in the process and requires the same level of attention and planning as the scientific investigation, if not more. The ethical codes and federal regulations that a trial must follow continue to be more numerous and rigid. Several

institutions have put into place guidelines and operational procedures to help investigators obtain IRB approval and get the strong start that a clinical trial needs. The BRI Toolkit developed as part of this project is helping Baylor investigators through the IRB submission process and is decreasing the time it takes to obtain IRB approval as well as increasing investigator satisfaction with the IRB submission process.

This project, unlike any of the previous published studies, also directly evaluates the effects that the BRI Toolkit has on efficiency and satisfaction. Efficiency was measured by the amount of time an investigator needed to submit their study to the IRB for approval compared to previous studies with investigators who did not have access to the BRI Toolkit. The satisfaction with the new operational process was measured by a survey document that was disseminated to the coordinators after their IRB submission. How the study was conducted and data was collected is discussed in the next section.

RESEARCH DESIGN AND METHODOLOGY

This trial was a prospective pilot study compared with a historical cohort of investigators. Two studies were observed as they completed the process of IRB submission. The goal was to decrease the amount of time that it took for a study protocol within the Baylor Healthcare System to be approved by the Baylor IRB. The experimental group was selected with the help of Baylor Research Institute's employees, research coordinators in the field, managers, and investigators. Phase one projects were targeted for this project to mitigate the challenges of the limited time frame and make the studied projects more comparable.

The control group in this project consists of previous investigator-initiated trials that obtained approval from the Baylor Research Institute's IRB prior to the creation of the BRI Toolkit. This project examines trials from years 2011-2013. Within this specific time frame, the control studies should have been subject to the same oversight, guidance, and regulations as the experimental studies that used the BRI Toolkit. The control studies were selected based on their similarities to the experimental group of trials. They are the same type of trial, either drug or device, and had a relatively similar goal for recruitment. The recruitment goals did not have to be an exact match because this study did not follow the groups through their recruitment process. The investigators were also matched on their relative degree of experience with the Baylor IRB. They also have a relatively similar degree of risk or invasiveness.

The data was collected via a survey that was distributed to three clinical research personnel following submission of their protocol to the Baylor IRB. The survey was brief and took the coordinators no more than 15 minutes to complete. It covered topics such as satisfaction

and time periods. It asked specific questions about the date which they began using the BRI Toolkit, the date which they submitted to the IRB, and the date which the IRB approved their protocol. This information provided the amount of time needed to obtain IRB approval as well as measured satisfaction with the BRI Toolkit (see Appendix 1 for the survey). The survey results were compared to data on the previous studies, whose time frame was measured from the first contact they had with BRI regarding their study until IRB approval. This study qualified for an exempt status from the UNTHSC IRB and was approved as protocol # 2012-194 on 11/26/12.

The BRI Toolkit was announced to Baylor research employees via an email on November 20th, 2012. Coordinators in labs were encouraged to use it by their managers. Studies assigned to the experimental group were chosen specifically because they were investigator-initiated and were not yet approved by the Baylor IRB.

TIME NEEDED FOR IRB APPROVAL

The time to IRB approval (hypothesis #1) was measured in weeks. A week in this study consists in the five working days. With this measurement system each day is 0.20 of a week. Each study was compared to a specific historical study similar to the control to measure the increased efficiency created by the BRI Toolkit. To determine if efficiency was increased, the amount of time needed for the experimental group to receive approval was subtracted from the amount of time that the control group needed to receive approval and then divided by the control time period. The project hypothesized that the BRI Toolkit would increase efficiency by a positive %.

$$(\text{Control time} - \text{experimental time}) / \text{control time} \times 100 = \% \text{ increased efficiency}$$

SATISFACTION WITH THE BRI TOOLKIT

Qualitative comparison was important for this project due to the limitations of sample size. The investigators' satisfaction with the BRI Toolkit was qualitatively measured on the survey on a scale of 1-9 (1 being unsatisfied, 5 being neutral, and 9 being the most satisfied). The project hypothesized that the BRI Toolkit would have a rating above a 5 (neutral) in terms of both satisfaction with the BRI Toolkit (hypothesis #2) and likelihood that they would recommend use of the BRI Toolkit to other investigators (hypothesis #3). This shows some level of positive satisfaction with the Toolkit. The survey also helped to guide what edits should be made for future investigators who will also follow the BRI Toolkit.

CHAPTER 2

RESULTS

The Toolkit used in this project was created for two reasons:

1. To decrease the time for IRB approval of a study (by at least 0.2 of a week).
2. For the research personnel to have a high degree of satisfaction with the BRI toolkit (satisfaction rating higher than 5).

This study followed two separate IRB submissions; they will be called Study #1 and Study #2. Three participants completed the survey for this pilot study. All three participants were clinical research coordinators or assistants on the studies included in the experimental group.

DECREASE IN TIME FOR IRB APPROVAL

Study #1 was a clinical trial that required a full board review. It has a goal of recruiting 35 subjects. It was submitted to the IRB on December 5, 2012 and was tabled after 4.4 weeks at the first full board review because some additional information was needed. The additional information was submitted and was approved as is by the full IRB board on March 7, 2013. This resulted in a total of 13.4 weeks needed for IRB approval

It was compared to another full board review study that attempted to recruit 50 research subjects. It was submitted on December 1, 2011 and approved on August 30, 2012. This study was tabled 7 times, taking 39.2 weeks for full IRB approval. This comparison indicates that the study that had access to the BRI Toolkit had an increased efficiency of 66% (Table 2).

Table 2: Increased Efficiency in Study #1

Study	Submitted	Approved	# of Weeks	Increase in Efficiency
Study #1	12/5/12	3/7/13	13.4	66%
Comparison Study	12/1/11	8/30/12	39.2	25.8 more weeks needed

Study #2 is a trauma clinical trial that qualified for an expedited review by the IRB. They had the goal to recruit 200 research subjects in the trial. It was submitted to the IRB on November 26, 2012 and approved by the IRB on December 10, 2012. Using the BRI Toolkit resulted in IRB approval in just 1.8 weeks.

This study was compared to another trauma clinical trial, which also qualified for an expedited review, with the goal of recruiting 106 subjects. This study was submitted on May 12, 2012 and was approved on June 15, 2012, taking 3.6 weeks for full approval. This comparison indicates that the study that had access to the investigator-initiated research BRI Toolkit had an increased efficiency of 50% (Table 3).

Table 3: Increased efficiency in study #2

Study	Submitted	Approved	# of Weeks	Increase in Efficiency
Study #2	11/26/12	12/10/12	1.8	50%
Comparison Study	5/12/12	6/15/12	3.6	1.8 more weeks needed

Both studies that had access to the BRI Toolkit show a dramatic decrease in the amount of time that they required for complete IRB approval compared to similar, previous studies. This

is valuable time that is vital to maintaining the validity of the trial and advancing medical knowledge to save human lives.

SATISFACTION WITH THE TOOLKIT

Data was collected from a total of three key research personnel who used the BRI Toolkit to submit to the IRB. They were asked three different questions which used a 1-9 scale as the response. The study hypothesizes that each question would receive a response greater than 5, indicating a positive response.

The first question: Was the toolkit provided useful in the navigation of the IRB approval process?

All survey participants responded “9” to this question, showing that the personnel who used it found the BRI Toolkit useful and effective in the IRB approval process (Table 4).

Table 4: Response rates for survey question #1

	Detrimental				No Effect				Very Useful
	1	2	3	4	5	6	7	8	9
% of Responses									100%

The second question: What effect do you feel this toolkit had on the time from protocol development until IRB submission?

Two participants indicated a “9” as the response and one indicated an “8” as the response (Table 5). This shows that the personnel believed that using the toolkit helped to shorten the time frame required for complete IRB approval.

Table 5: Response rates for survey question #2

	Lengthened Time Frame				No Effect				Shortened Time Frame
	1	2	3	4	5	6	7	8	9
% of Responses								34%	66%

The third question: Would you recommend other investigators follow similar guidelines when submitting to an IRB?

All participants responded “9” to this question, indicating that they would recommend the BRI Toolkit to future investigators and that the Toolkit helps to address the previous lack of instructions (Table 6).

Table 6: Response rates for survey question #3

	Would advise against it				Indifferent				Would definitely advise it
	1	2	3	4	5	6	7	8	9
% of Responses									100%

DISCUSSION

The control studies were chosen as the most similar, investigator-initiated studies available to the experimental studies. They were selected based on their expected sample size, relative level of invasiveness, and that they were submitted recently. It was important to have recently conducted control projects because this would limit other variables, such as different IRB members voting on the studies, different IRB coordinators, and different regulations and rules that had to be followed. They are also similar in their recruiting goals, studies hoping to recruit 35 to 50 subjects are a similar size as are studies hoping to recruit 100 to 200 people (FDA, 2012).

The results on effectiveness of the BRI Toolkit are preliminary but nevertheless have a strong impact. The effectiveness is most likely a conservative estimation because of the lack of detail from previous studies as to when investigators began working on their protocol. The time for the control group begins at the first contact with BRI but likely began many weeks before this time. If more detail were available for the control group, greater effects on efficiency created by the BRI Toolkit could likely be demonstrated. This can save time, energy, and money, contributing to the overall research output of individual investigators and Baylor Health Care System. The decrease in frustration may also increase the number of investigator-initiated trials relative to industry-sponsored trials, thus reducing potential biases in clinical research.

The BRI Toolkit had a very high level of satisfaction according to the survey. Personnel who used it included some very positive feedback. When asked if they would change anything in the Toolkit, they responded:

“I think having this packet available will make [IRB submission] a much easier process to navigate and I do not see the need for any changes at this time.”

“I think that this is a great resource for investigator-initiated research and I am so excited to integrate it into our department research. I hope to see this as a ‘standard issue’ to not only new researchers, but also to existing coordinators, assistants, and principle investigators.”

Data should continue to be collected on the BRI Toolkit to show a stronger effect on efficiency and to gather feedback on what should be added and edited. However, pilot data regarding satisfaction is fairly conclusive.

The BRI Toolkit disseminated at Baylor served as coherent instructions that investigators needed. The Toolkit helped to decrease the confusion of navigating the various departments of BRI and Baylor Healthcare System and shortened the time period required for IRB approval. The Toolkit proved, through survey responses indicating high satisfaction, to be the effective tool that investigators had been looking for.

LIMITATIONS

The greatest limitation of this project was the time frame in which it had to be completed. There was a limited window in which the BRI Toolkit could be distributed to investigators, they could use it, and the data could be collected from their surveys. A longer time period would have allowed more thorough observation of the benefits of the BRI Toolkit on more clinical cases and allowed for a better comparison to previous cases. There are far fewer investigator-initiated clinical trials than industry-sponsored clinical trials at Baylor because of the reasons mentioned in the section “Shift in the Industry”, specifically the lack of funding available and the

bureaucracy associated with a clinical trial. There were only a few of these studies attempting to get approval from the IRB within the time that this project was completed. Within the available time frame, it was possible to collect data on two studies.

A challenge with this and any study using a historical comparison is lack of detail in the control group data. This is a factor in this study because it is difficult to know the exact date that the investigator began the IRB submission process. For this project the period of time began at the first contact that the investigator had with BRI regarding their trial. This may be a shorter time frame than it actually took for the study to be developed. It is possible that the investigator could have worked on the development of the trial for a substantial amount of time before contacting BRI, but there is no way of being able to calculate or validate that. Because control group studies may have actually taken longer than calculated for the purposes of this study, efficiency improvement calculations are likely to be conservative.

Another limitation faced by this project was the limited ability to see how closely the investigator followed the BRI Toolkit. When asked, the investigator could claim to have followed the BRI Toolkit very closely yet could have only used it as an occasional recommendation. People tend to report a stricter adherence to a system or routine than they actually follow (Adams, et al, 1999).

An additional shortcoming of this data is the direct and continuous interaction that the study personnel who created the BRI Toolkit had with the coordinators in the experimental group. The coordinators were able to speak directly to someone who had extensive knowledge about the BRI Toolkit, which will not be the case in the future. When the Toolkit is disseminated to a greater number and variety of investigators, they will not have such direct and constant

interaction and attention from someone at BRI. This interaction most likely reduced the amount of time that it took for the application to be submitted to the IRB.

Despite the limitations and challenges that this project faced, it still proved to be a worthwhile endeavor. Guidelines that the BRI Toolkit provided through the IRB approval process at Baylor Health Care are essential; investigators and their research teams need help navigating through the bureaucracy of investigator-initiated clinical trials. The results from this study have universal application because they demonstrate for the first time investigator satisfaction with a resource such as the BRI Toolkit and the difference in time (days) needed for the investigator to submit to the IRB. This is a solid foundation for the new Toolkit, allowing for it to be further tailored according to the information gathered from this study. This research is on the forefront of clinical trial management and the vanguard for directly measuring the effect of guiding documents such as the BRI Toolkit on satisfaction and efficiency.

CONCLUSION

The BRI Toolkit, despite its limited use to date, clearly had a substantial impact on the two studies that are the subject of this project. Each study, when compared to a previous, similar study that did not have the BRI Toolkit available at its time of submission, had a decrease of at least 50% in the amount of time it required to obtain IRB approval.

Valuable time was being wasted prior to the distribution of the BRI Toolkit, with its simple, succinct instructions. Investigators and their study personnel were losing resources, time, and energy by having to resubmit to the IRB and wait for approval. Newer studies that have access to the Toolkit will be able to use their time more effectively to get their study approved faster and continue to focus on improving healthcare at BUMC. Every day is critical when the outcome of a study can have a substantial impact on the health and well being of a patient. The creation of this Toolkit allows the investigator and the research personnel to get the study approved in less time and continue to focus their resources on the health of their patients.

The high degree of satisfaction with this Toolkit is another positive aspect of its implementation. The response from the surveys indicates that the clinical coordinators who used it found it very useful in the application process. They also indicated that they felt it greatly shortened the time frame until IRB submission, and they would advise others to use it. Their satisfaction with the Toolkit was important to this project. If there was a negative response associated with the use of the Toolkit, the personnel would not use it in the future even if it decreased the time to IRB approval. High levels of satisfaction with the BRI Toolkit shows that it was put together effectively and was an anticipated addition to BRI's arsenal of resources.

Increased use of guiding documents such as the BRI Toolkit can translate into more investigator-initiated research proposals going before the IRB and becoming trials. This increase in sound scientific research and clinical trials contributes to an increase in medical knowledge and a healthier future for subjects and patients.

FUTURE DIRECTION

The greatest challenge faced by this project was the short time frame in which it had to be completed. The results show that the BRI Toolkit has a strong effect in reducing the amount of time that studies require to receive IRB approval. In the future, should more studies be followed, the data would show an even stronger correlation between using the Toolkit and a reduced period of time needed for IRB approval.

The future survey could ask investigators if they've previously submitted to Baylor IRB, if they used the BRI Toolkit when creating their proposal, and whether their experience with the BRI Toolkit was more satisfactory. This would show this strong correlation from a larger sample and more studies.

Several items should be added to the Toolkit to further increase satisfaction with it. Based on the survey feedback, the items which should be added include: a frequently asked question section, information about the Radiation Safety Committee, a BRI organization chart, a checklist on the regulatory binder required tabs, and information regarding technology safety and data transmission.

The Toolkit also contains information on how to submit an Investigational New Drug application (IND) to the FDA. The investigator should complete most of this submission concurrently while using the BRI Toolkit because this will allow the investigator to simultaneously complete this portion of pre-clinical research. The time in which this project needed to be completed did not allow for follow up through the IND submission process, but could be a fruitful direction for further research.

Similar packets should also be made for other situations faced by investigator-initiated research. In the future, Baylor Research Institute should use this format to create a similar toolkit for the annual IRB review each study must complete. In addition, a toolkit on how to report Adverse Events (AEs) and Serious Adverse Events (SAEs) and how to shut a study down properly should also be created using the format of the BRI Toolkit. The effectiveness of and satisfaction with these documents could also be measured and documented.

Baylor also needs to create a standard protocol template of its own. Many investigators and research personnel stated that this was a much needed and desired item. The BRI Toolkit contains two separate protocol templates, and the one that investigators preferred was not a Baylor standard template but was from another institution. Baylor should create their own standard protocol template following the format of the other institution's template.

The IRB bureaucracy and logistics intimidate most investigators and research personnel. Any toolkits or packets that outline a systematic approach and stepwise instructions for the investigators to follow will be an asset to the Baylor research community and translational medicine as a whole. Similar studies evaluating the increases in efficiency created by future toolkits, and investigators' satisfaction with them, can be conducted in the future.

SUMMARY

This research project showed how the implementation of a new operational process (BRI Toolkit) about how to begin the clinical trial process for investigators through Baylor Research Institute (BRI) decreased the amount of time that was needed to obtain IRB approval. This trial was a historical comparison, which used previous investigator-initiated clinical trials from Baylor University Medical Center as the control and investigator-initiated clinical research begun after the BRI Toolkit was disseminated as the experimental group. The BRI Toolkit was developed with the help of various members of the Baylor Research Institute. After investigators with projects in the study group obtained IRB approval, this study compared the time needed to get approval between studies that used the BRI Toolkit and previous, similar studies that did not have access to the BRI Toolkit.

A survey was disseminated to senior key research personnel following their IRB submission. The survey asked them questions about their satisfaction with the BRI Toolkit, if they felt it was an advantage to them, if they would recommend it, and if they had any suggestions for improvements. The answers to these questions were then incorporated into a list of suggested updates for revisions of the Toolkit to help future investigators obtain IRB approval.

Three surveys were distributed to two different studies that were submitting to the Baylor IRB. The results of these surveys show that the research personnel think that the BRI Toolkit helped to shorten the time frame, was very useful in the navigation of the IRB submission process, and that they would highly recommend that other investigators follow the same set of instructions.

The BRI Toolkit needs to be maintained and updated in order to retain its relevancy. It is of the utmost importance to have this resource available to the Baylor research community. All pertinent contacts, procedures, and forms should be reviewed periodically to ensure they are current. Additionally, studies that are using the BRI Toolkit should continue to be monitored to gauge its effect on efficiency more precisely.

CHAPTER 3

INTERNSHIP SITE

My internship took place at the Baylor Research Institute within Baylor University Medical Center. The Baylor Research Institute oversees and manages the Institutional Review Boards that approve and monitor all human research conducted at Baylor. They can also aid investigators in most steps of the IRB and IND submission process. They are equipped to help with contract negotiations with pharmaceutical or device companies, federal grants and foundation funding, and can help to develop a budget for the clinical research. After a study has been launched, BRI can help with monitoring, staffing, and the yearly review that all studies submit to the IRB. My mentor throughout the internship was Elizabeth Cothran who is the Director of Research Regulatory Affairs.

SUMMARY OF INTERNSHIP

During my time at BRI I was able to observe and participate in a number of different activities and meetings run by BRI. Not only did I sit in on a monthly IRB meeting, but I also got to observe an emergency meeting of the IRB, which is a very rare occurrence. The emergency meeting happened on my first day at BRI and was in response to the epidemic of West Nile Virus outbreak in the late summer of 2012. The board felt that it was too important of an issue to postpone the vote on a protocol for a new treatment that was not yet approved by the FDA. It was a very exciting start to my internship.

In addition to these large meetings, I also had the opportunity to sit in on some smaller meetings for various committees at BRI, including the education committee, the Regulatory Affairs Team, and a technology meeting with the people that built and manage the IRB software. I also had a weekly meeting with Elizabeth to update her on the status of my various projects and discuss my agenda and items to work on for the next week.

I also hosted a number of meetings with people that were involved in the creation and use of the investigator-initiated research packet (BRI Toolkit) which I put together during my internship. I held meetings at the beginning of my internship with various people who work at BRI. The purpose of these meetings was to get a better understanding of what the person does at BRI and what they would need from the investigator who was interested in doing a research study. I was able to incorporate this into the packet in order to make the IRB application more streamlined for all involved.

After the packet had been distributed to various managers, coordinators, and investigators, I was able to meet with people that had used the packet to discuss items that were missing, ways to improve the packet, a plan to distribute it to more people, and how to proceed with the packet after my internship was complete.

I was also able to accompany Mary deHaas on a monitoring visit she was conducting. Mary monitors many studies on the Baylor campus as a service that BRI offers. This particular study was being conducted at The Institute of Metabolic Disease. During the visit I got to look through the regulatory binder of the study and help Mary find source documents that had previously been noted as missing. I enjoyed the experience because I have taken several classes

which describe the monitoring position but actually being able to observe and see firsthand clarified what they really do.

My internship also consisted of a lot of writing on my part. During the six month time period I had to submit a thesis proposal to my committee and file it with the graduate office. The proposal and revisions took several weeks to complete and were my main focus for the first few weeks at BRI. After the proposal was complete, I began to work on the BRI Toolkit that I was to distribute to the investigators. Once the BRI Toolkit was mostly completed, I began to work on my IRB submission packet at UNTHSC. The IRB at UNTHSC wanted the complete BRI Toolkit in my application yet I could not start collecting data and feedback on it until after I was approved. After the research was IRB approved and the BRI Toolkit was distributed, I began to work on my final thesis during the data collection stage of my project.

When I was not writing or attending meetings, my main task at BRI was to help keep the workload for the IRBs from becoming overwhelming for the coordinators. I was responsible for completing the Event Reports for the three IRBs and making sure they were routed to the proper people for their sign off.

I was also fortunate that during my time at BRI I was able to participate in a special seminar that BRI employees had never previously attended. They held a special full day conference on the Enneagram, which is a model often, used in the work place to describe nine different personality types and the ways in which they are interconnected.

APPENDIX

DAILY JOURNAL

Week 1

8/20/2012- First day of work. This morning was my introduction to the office and the Baylor system as a whole. I set up my access to the computer system and email and received my badge for clearance into the building. Over lunch I attended the seminar which Elizabeth gave to the radiology residents covering IRB basics. In the afternoon I attended the Education Committee meeting. Here they focused on competencies and their timeline, the “Mentor Model”, and subject matter experts for specific areas. Later, I also got to sit in on an emergency IRB committee meeting to discuss a protocol involving the West Nile Virus. It was a proposed protocol from UT Southwestern and they hope to collaborate with Baylor since the virus has reached epidemic size. Overall the day went by quickly. Everyone in the office is extremely helpful, and I am so excited to be working here.

8/21/12- This morning began with a meeting with Dr. Schiller in the main hospital. Elizabeth and Dr. Schiller meet on a regular basis to discuss progress within the IRB. This morning was mainly focused on debriefing of the emergency meeting yesterday regarding the West Nile Virus protocol. After the meeting, Elizabeth gave me a copy of the MedTrials educational binder on “Managing Investigator Initiated Trials”. I spent the rest of the day reading through their information on the process of starting an investigation. My previous class of “Introduction to Clinical Research” was also taught by a MedTrials employee so it was a lot of fun to read through the much more industry focused information having the more historical and broad spectrum background from my previous class. I also spent a good deal of time on the FDA’s website becoming more familiar with the forms which are mentioned in the MedTrials educational information.

8/22/12- I spent the first part of this day continuing my research into Investigator Initiated Trials. I compiled a random list of elements that I think should be mentioned in a timeline fashion for PIs interested in doing a clinical trial. I also spent time searching the web to find if a timeline already existed for PIs to follow; not one was found. I also spent some time during the morning setting up the printers in the office to my computer. In the afternoon I sat in on two IT conference calls. The first was an internal call discussing the issues that have arisen with the iRIS system and COI. The second call was with the vendors to discuss if these issues were user error or a problem with the system. It was fun being on the consumer side of the call having been on the vendor side many times previous. Also, getting a better understanding of what the iRIS system actually is helps me to narrow the scope of the information that I have been looking at.

8/23/12- Today was a very different type of day in the office. I had a brief meeting with Elizabeth yesterday right before I went home and we discussed creating a document compiling what I had been researching previously and the steps that a full FDA IND submission requires. So I spent today creating a mock up binder of what I think would be good and useful for Investigators to have. I brought in my notes from Intro to Clinical Research which proved extremely useful combined with the FDA's website, the MedTrials binder Elizabeth let me borrow, and my own internet research. The mock up also helped me to narrow my focus on where I need to talk to other people about their fields, mainly legal, budgets, and grants.

8/24/12- Elizabeth and I had our first "weekly meeting" this morning. I feel that the meeting was a reassurance that the track that I have been working on is what she had in mind. We discussed certain elements of my packet that I thought would be useful, such as a timeline, checklist, and important contact numbers, all of which I will need to update and revise. I also mentioned areas that I would like to know more about before I work on them, such as legal, budget, grants, and statistics. She recommended that we have meetings with key people in these areas and suggested people for me to get in contact with. We set up a meeting for next week with Jennifer Fox who is head of clinical research operations. I am also hoping to set up a meeting with Maggie to better understand the budget process that these trials go through prior to FDA submission. I spent the rest of the afternoon going through other forms that I think could be useful such as contract approval form, intellectual property form, recruiting, marketing, and documents related to annual review. I have already learned so much this first week and am starting to get a concept of the expansive scope of work that they do here at Baylor Research Institute.

Week 2

8/27/12- The beginning of this morning was a typical Monday morning, checking emails, checking my calendar for the week and seeing how people's weekends were. I scheduled meeting for Elizabeth and I to have with Jennifer Fox and Maggie Hewitt on Thursday. I hope these meetings help to write a better section on planning and budgeting for investigators, and that parts of a timeline will begin to be filled in. I have been working almost exclusively on this project so far in my internship and have done nearly all I can do on it until my meeting, so I decided to focus on something else for the remainder of the day. My thesis proposal deadline is looming in the not-so-distant future (4-5 weeks) so I decided to begin working on that as well. I plan on focusing on it for the next two days. Today I spent looking up background articles and literature regarding implementation of guidelines and processes for investigators to follow. There were a few good articles that I discovered on the importance of having a plan at the initiation of a clinical trial but none of them had an actual plan. This is exciting news to me, it validates the importance and necessity of having a plan yet the work that I will be doing does appear to be work that has not been published anywhere that I can find. Tomorrow I plan on continuing with my research and beginning to work on the background portion of my proposal.

8/28/12- Today was a bit of a writing day for me, very slow writing. I spent the day looking up more articles and selecting certain pieces that I can either quote or reference. I also have begun the search for how to formulate my statistics. I am looking for any article that shows the effectiveness of instating a new protocol or technique. I have yet to find anything. At this point I think that the best way to do a historical comparison trial will be to set a specific time period (4-6 weeks, Sept 1- Oct1or15) when the trial began and get an average over the past 5 years to set the "standard" or be my control to which my experimental group, which will use my protocol, will be compared to. I am also having difficulty distinguishing between the Significance and the Background portion of my proposal. My plan is to think about the differences and how they will use different references over the evening and ask Elizabeth and Claire about it tomorrow if I still cannot see a clear difference.

8/29/12- This morning was a relief, Elizabeth told me that she had been working on a case that she thinks should be my historical perspective to my research project. She says it's a pretty average case that has been trying to get through to IRB approval since June. The reason that it has been taking so long is that the investigator did not know all of the steps that are usually required, reassuring that the work that Elizabeth and I will be doing will be of true value to researchers. The rest of the morning and some of the afternoon were spent working on my thesis proposal. I then had to switch my focus. I have morning meetings tomorrow with both Jennifer Fox and then with Maggie Hewlitt. I spent time researching what they do, specific questions I think I should ask them tomorrow, and forms that researchers should submit to them. I have realized that I have an advantageous point of view for the investigators at this point. Because I still do not know all of the steps that the investigators would need to take or what roles everyone

has here, I have the same perspective as a new investigator would have. If the information is not obvious to me, then I need to find it and make it more obvious for the investigators.

8/30/12- I had my first two meetings with Jennifer and Maggie this morning discussing my project and what they think needs to be included. They were both extremely helpful and will be great references throughout this project. Jennifer stressed the importance of the Confidential Disclosure Agreement, and Maggie stressed how an investigator should never discuss monetary amounts with a sponsor prior to talking with “Budgets”. Both of these suggestions need to be stressed in my packet; BRI should be the first people that investigators speak with. Jennifer, Elizabeth, and I also discussed the concept of having a committee composed of various disciplines review I.I.T.s early in the process in order to triage and categorize them based on what help they will need and Baylor’s desire to support them. I spent the rest of the afternoon reviewing my packet and incorporating the issues that we discussed with Maggie and Jennifer.

8/31/12- Elizabeth and I had our weekly meeting this morning. We spent some time debriefing from our meetings yesterday. We both feel that they were good meetings to have and decided that one with Deborah Price in Grants would also be advantageous. Elizabeth also added me on a few more meetings and discussed me working on iRIS in the next few weeks. I think this would be a great learning experience and help me to find common problems with IRB submissions. This knowledge can then be passed on to the investigators as well. I worked some more on the packet, tweaking parts that I have learned more about over the past few days. This late afternoon Elizabeth and I are going to the Cancer Center to watch a documentary in the new cancer hospital space.

Week 3

9/4/12- This morning began my process of creating the packet that I need to submit to UNTHSC and Baylor's IRB. My research proposal has to be approved by both committees. I must be the first of the CRM students that is starting this process because I ran into many issues with the forms and had many questions for Dr. Gwartz. I plan on submitting to UNTHSC's IRB as an expedited review because it will be a survey comparison and there is minimal-to-no risk for the participants. I completed this document, wrote my survey document, and began working on my informed consent document and my protocol synopsis. We also had our Regulatory Affairs Staff meeting this afternoon, discussing performance evaluations, goals, the Holiday Schedule, and the mandatory flu vaccine. I sent my preference of holidays to work to Latoysa, but I'm not sure that it applies to me. I also spent time looking at the grant process since I have a meeting with Deborah Price tomorrow morning. I could barely find anything, this seems like an area I will need to put a lot of work into.

9/5/12- Today I continued to work on the packet I need to submit to UNTHSC's IRB to get approval for my research project. I completed my informed consent, research protocol synopsis, and recruiting email. The only part I have left to do is to complete the COI, which has to be done on UNTHSC's network or a VPN, so I can't do it on Baylor's network, and to get the approved letter from Baylor's IRB to do the research here. I had a meeting with Deborah Price in grants this morning. She is going to send me a document that she used to use that should be helpful for the PIs to fill out before they get in contact with her regarding funding of I.I.R. I also set up a meeting with Nanette Myers in 2 weeks to discuss the statistician's part of my guidelines. Tomorrow I will begin to work on the Baylor IRB submission forms for my research.

9/6/12- Elizabeth and I had a meeting this morning. We went over the forms that I have been filling out for my UNTHSC IRB submission. She had several good recommendations for me to incorporate or change in my packet so far. She checked that I was on the right track as far as the bureaucratic forms and also changing the number of participants in my study. I also got clarification on the type of consent form that I needed. I notified Dr. Gwartz of documents that I will need from her before I submit my packet. I also got to go to my first full IRB meeting today. I enjoyed getting to watch the process and was surprised by how efficiently they worked through the reports. I hope to continue going to these IRB meetings so I can see how the suggested corrections are incorporated into the protocols.

9/7/12- I spent today working on my thesis proposal. I looked up several other studies to check that this form of prospective pilot studies with a historical cohort-matched design is valid. I found many others that have used this design so I am confident in it. I also spent time on the data section of my proposal. The only part that I have really left to address is the background/literature review section of it. At some point next week I will need to go to Fort Worth to have Dr. Gwartz sign some documents and complete my conflict of interest form. But I

did contact Dr. Gwirtz about the papers that she will have to submit and she said that hers are already on file, which is great news, helps to maintain the flow of progress.

Week 4

9/10/12- Today was a good combination of different projects that I got to work on. I spent part of the day working on my thesis proposal. It is coming along well, I think, but the part that I had been avoiding, the background, needed to be started. I had previously looked up a lot of literature on efficient clinical trials and how to implement guidelines into research. It was easier than I thought it would be to do an abbreviated literature review in this proposal. One thing that I would like to incorporate is an idea as to how long trials currently take before they receive FDA approval. The other part of the day was spent working on the IIR packet. We had a meeting on clinicaltrials.gov and I got better clarification on what goes on here at BRI for that process. Jennifer and I have scheduled a meeting for tomorrow to brainstorm on how to incorporate some of the work and how to make it more effective. Deborah and I also discussed some grant issues and we have a meeting for Wednesday to further discuss how to incorporate the grant process into my guidelines.

9/11/12- I focused on clinicaltrials.gov today. This morning I had a meeting with Jennifer Fox to discuss some of the issues that we discussed in the meeting yesterday. We also discussed the idea of a committee to review the trials before they go to the IRB to see how possible some of them even are. I got a copy of the questionnaire that's given to investigators. I spent the rest of the day on this portion of the IIR packet and reading clinicaltrials.gov.

9/12/12- This morning was focused on the grant process that investigators would go through. I had a meeting with Deborah to discuss this process and get a better idea of what it entails. She spent time walking me through the website that she uses and collectively we came up with a list of information that would be helpful for her to get from investigators. I then spent some time learning how to make a template and created one that fits what we need in regards to grants. In the afternoon I switched my focus onto my thesis. I spent a good amount of time looking up other people's proposals to get a better understanding of what the school is really looking for in them. I also spent some time coming up with possible chapters for my thesis. The proposal is more in depth than I had previously thought but I think the more I put into it the easier writing the actual thesis will be. I also am more confident now in what the expectations are for the proposal and that I can meet and hopefully exceed them.

9/13/12- I focused on the "Background" portion of my thesis proposal today. I also read through a few other proposals that people have submitted in the past. I have decided that in this section I should put a brief history of clinical research because that has shaped how it is done now, various elements that are required, and why there is so much bureaucracy involved in submitting to the FDA. We also had a brief celebration for the September birthdays.

9/14/12- Elizabeth and I had our weekly meeting this morning. We discussed the progress that has been made on the IIR packet. We discussed how we think that a "roll out" of this product should go, and we both agree that a presentation should be made to the directors and the

managers. I also talked about the need to incorporate the marketing and advertising strategies that need to be in here. She told me to contact Kristine Hughes. We will have a meeting with her next week. The rest of the day was spent on my thesis. I added in elements of the Belmont Report and the Helsinki report.

Week 5

9/17/12- I was out of the office the entire day for a family funeral.

9/18/12- This morning I began my research on how clinical trials have shifted away from investigator initiated research and towards industry sponsored research. I think that part of the background section of my thesis should cover this. It explains why research for investigators moves slower than research with an industry sponsor. I found a few articles, but I need more current statistics. This afternoon we had a meeting of all the clinical research coordinators. It was nice to see all of the different departments and what the people do in them. I also think that it was beneficial to be able to tell other people what I am working on and getting the news out there. Over the next week or so I think Elizabeth and I should discuss a plan for how we are going to roll out this packet.

9/19/12- Elizabeth and I had a meeting this morning with Nanette Myers and Elise Priest from Baylor's Institute for Health Care Research and Improvement. We need to incorporate them into our IIR packet. They talked with us about steps to incorporate early in the process. They also think there is a need for a small committee to review the study very early on to assess the feasibility and the interest Baylor will have with it. We came up with a series of questions that the investigator will need to answer prior to working with Nanette's group. Nanette's group can then help with the protocol development, the form development, and organizing the data and statistical analysis portion of the project. During the afternoon I worked on typing up the list of questions we developed. I also went through my thesis and looked at the scope that I was covering. Nanette and Elisa suggested only covering the project until IRB approval and not until IND submission. This is a question that I will need to bring up with Elizabeth as far as what is actually feasible to finish and collect data on in the time I have.

9/20/12- We were supposed to have our meeting with Kristine Hughes this morning, but she did not show up. I followed up with an email instead explaining the project and asked her the questions that I had. I found one form this morning that I think she might use, but I wanted to know if there are others that she prefers. During the afternoon I found a few more articles on the shift from investigator initiated trials to industry sponsored trials. I spent some time writing about these in my thesis. I then went through and worked on the suggested chapters of my thesis. I am starting to understand the direction and form it will take.

9/21/12- Elizabeth and I had our weekly meeting this morning. We discussed our plan for the next few weeks. My thesis is due next week so I am going to focus on that until it's done. We decided on an end point for the time frame of my experiment. Kristine Hughes got back to me this morning on the email I sent to her yesterday, I will go over it more after my thesis is in. I spent the afternoon finishing the background portion of my thesis. Then I printed it off and went through and tried to edit different portions of it. I had originally written the proposal with the

intention of taking a trial all the way through the IND submission to the FDA, so after changing this until IRB approval I need to make sure that is how the paper is written.

Week 6

9/24/12- I spent the first part of the day writing about IRBs in my thesis. I looked up articles describing them and the federal codes that discuss them. The end point of my project is at IRB approval so I thought a description of what an IRB is and why they are needed would be relevant. In the afternoon we had an education committee meeting. Then I continued on my thesis, finishing up the last few parts and making sure the references were cited correctly. I will edit it some tonight and make the corrections tomorrow.

9/25/12- First draft of thesis proposal in! I spent today going over the thesis proposal and making edits. I also checked out the school's website and found that my thesis proposal is not due to the graduate office until mid-October, so some of the pressure is off for the time being to get over to Fort Worth to have the other two members of my advisory committee sign the proposal. Tomorrow morning Elizabeth and I are having a meeting to discuss the proposal.

9/26/12- Elizabeth and I had our first meeting to discuss the first draft of my thesis proposal this morning. She had several suggestions on minor changes to the design of my study. We decided to broaden the group that we will survey to include other key senior research personnel. We also came up with how we are wording our endpoint. I think next we need to come up with a working title for the project. Over lunch I got to attend an IACUC meeting, which approves trials using animal models. After the meeting I also got to go and see where some of the animals are housed. In the afternoon I worked on the edits that we came up with in the morning.

9/27/12- I have been working on incorporating the changes we have made to the design of my study into the things I have written up for my IRB submission. Things such as not following the study through to the IND application but including other key personnel, besides the PI, in the survey process. In the afternoon I got Dr. Kirchhoff's edits back on my thesis proposal. She had a lot of good suggestions on the writing and tone of the document. She also let me know that the survey I have created needs to be included in my proposal. I worked on the edits some and will work on more tonight.

9/28/12- Elizabeth and I had our weekly meeting this morning, and we discussed the changes that Dr. Kirchhoff recommended I make to my thesis proposal. We discussed a name for the project, the survey document that I want to incorporate, better defined my control group, and discussed my plans here after my thesis proposal is submitted. I also worked on the changes to the survey I hope to use and finished most of the edits on my thesis proposal. I think next week I will get to go on a monitoring visit with Mary.

Week 7

10/1/12- This morning I finished incorporating the edits on my thesis proposal that I worked on over the weekend. I emailed the document to all members of my advisory committee and hope to have their signatures on the document by the end of this week to submit to the graduate school office. In the afternoon I had a meeting with Mary DeHaas. I will be going with her tomorrow on a monitoring visit. We discussed what a monitoring visit entails and went over a bit about the trial which we will be monitoring. I spent the rest of the afternoon reading over the protocol, the monitoring plan for the trial, her previous report from a monitoring visit, the summary, and their responses.

10/2/12- Today I got to go on a monitoring visit with Mary DeHaas. She is monitoring a study that is being done in the center for metabolic diseases and disorders. This was a great opportunity because that is the area that I would eventually like to move into. I also got to talk to Mary about CRC certification which I would like to get in the next few years. On the monitoring visit I got to look over the study binder, the subjects' binders, and the FDA binder. The experience helped me to understand what it takes and means to be a monitor and the level of detail that it requires. I can also incorporate some of the things I noticed, such as GDP, into the toolkit that Elizabeth and I are working on.

10/3/12- I shifted my focus today, I have sent off my latest version of my thesis to my committee members and have not gotten edits back so I worked on the investigator initiated research packet again. The meeting with Nanette from the institute for Health Care Research Improvement needed to be incorporated into the packet. I spent some time reviewing what we discussed and on their website to see their process of review. I worked this into the "Steps to Take" portion and need to make the sheet that Nanette and I discussed to have the investigators fill out prior to meeting with her and her team.

10/4/12- This morning Elizabeth and I had our weekly meeting. We discussed how the monitoring visit with Mary went and talked about what I will work on for the next 3 days while Elizabeth is out of the office. She showed me how to generate the event report letters on the iRIS system and I can work on these between working on my thesis proposal. I got edits back from Dr. Kirchhoff and worked on those for the majority of the day. BRI had a town hall meeting this afternoon which was a "state of the Union" type of discussion about the current status of BRI and the direction they hope to go in. Mary came in this afternoon and she had some other suggestions for places to look at that have institutional guidelines which I can incorporate into my thesis. She also invited me to listen to a webinar by ACRP next Wednesday which I feel will be very informative.

10/5/12- I still don't have access to the iRIS system so instead of working on event report forms I finished my third revision of my thesis today. I sent it out to my committee so they can have the

weekend to look over it and send edits back to me. I am really hoping to have it turned in to the graduate office at some point next week before I go out of town.

Week 8

10/8/12- This morning I read through some PowerPoints that Mary gave me about the quality control that the University of Miami uses and their systems. I am considering incorporating this into my thesis somehow and will look into it more tomorrow. This afternoon I went and got my flu shot from employee health. I also finally got access to iRIS, the intranet IRB submission site. I was able to create the acknowledgement letters for several event reports. I hope I'm doing it correctly and that it's helping Jan and Elizabeth out.

10/9/12- Elizabeth came back a day early today. This was really fortunate for me since I had been working on iRIS and, after asking a few questions, realized I had not submitted any of the documents I had worked on yesterday. Luckily it was an easy fit to submit them and get them to Elizabeth. I also got another edition of my thesis proposal back from Dr. Kirchhoff today. I spent a good amount of time editing that. It is really getting down to the mechanics of the writing, and I think the majority of the content is there now. I would really love to submit that document to the graduate school office soon. I did manage to get another version emailed out to everyone today. Now I will wait to hear back on their comments. The rest of the day I spent going through event reports on iRIS in IRB blue for Heather.

10/10/12- Good news, I got another edition of my thesis proposal back from Dr. Kirchhoff today and she said after these edits were addressed that she would be happy to sign the form and I could submit it to the graduate office. I spent the morning working on part of this. I also got to attend a webinar that Mary had ordered by ACRP about Quality control and management. This was a very informative one for me. I gave examples of the different aspects of quality control and gave good descriptions of the different terms, something I needed. The rest of the afternoon I spent finishing the edits to my thesis and working on iRIS. I am hoping to get signatures in Fort Worth either Friday or Monday since I will be going through there those days.

10/11/12- Finally got the email that my thesis proposal was ready to sign. I spent the day going over it and filling out the necessary paper work to file it with the graduate office. I also spent some time on iRIS doing event reports for Jan and Heather. I need to schedule a time to meet with Dr. Kirchhoff and Dr. Gwartz in Fort Worth to get their signatures on my thesis proposal and intent to graduate form.

10/12/12- Elizabeth and I had our weekly meeting this morning. She agreed that my thesis proposal was ready to sign. We discussed our plan for the roll out of our IIR packet. Next week we are going to finalize what we think is a good draft, then we will meet with various people to get some feedback, and then announce it to BRI. After our meeting I emailed with Dr. Gwartz and Dr. Kirchhoff about when to meet with them. We are meeting Monday at noon as I come back into town. I then continued with some event reports on iRIS. I'm leaving at noon today to go out of town for the weekend.

Week 9

10/15/12- I got back into town this morning so I did not get into the office until this afternoon. I met with Dr. Gwartz and Dr. Kirchhoff at noon in Fort Worth today. My thesis proposal and my intent to graduate form were both signed and filed. This afternoon at the office I worked on iRIS for a bit and worked a bit on a plan for finishing out my IIR packet. Tomorrow is the all day enneagram seminar, but after that I am going to be working really hard on getting the new operational process out to the investigators as soon as possible.

10/16/12- Today we got to attend an off-site work shop on “Enneagram in the work place”. It is about different personality types and how they respond to others, stress, excitement, and various other situations. I think I am a 1 “The Perfectionist” but I would also like to know more about it. Overall, I think that it was a helpful exercise and an interesting tool to be able to use in the workplace.

10/17/12- This morning I worked on IRB White event reports. Elizabeth and I also discussed the enneagram even that we had yesterday. Everyone in the office is “buzzing” about it today and I think it was a great opportunity for all us to be able to understand each other better. In the afternoon I worked on IRB Blue and the IIR packet. I need to email Nanette with a few follow up questions that I have.

10/18/12- I got some great information from Janet today. I reread my email from Kristine Hughes and asked Janet about the brochures that BRI has. They were very helpful in summarizing all of the different aspects that BRI covers. Elizabeth and I also had our weekly meeting this afternoon. We discussed some aspects of the IIR packet that I was unsure of, such as where the COI form will be and the trials listing form. I was unaware that the listing form the Kristine sent me was separate from clinicaltrials.gov. The form she sent me deals with putting the trials on the Baylor website.

10/19/12- Today I did some work on iRIS in the morning. After completing the event reports that were available, I read through the investigator’s guide that Elizabeth sent me yesterday. Some of the information is no longer relevant because of the digitalization of the documents on iRIS but some of the information was useful. In the afternoon I worked briefly on the IHCRI section of my notebook and emailed Nanette with some questions. She emailed me back at the end of the day and I will work on that on Monday.

Week 10

10/22/12- This morning I looked at Nanette's response email. She attached a copy of her department's brochure and I found it very helpful. I think that I have had a hard time conveying to people what this packet is intended for. This packet is not detailing every small detailed task that must be completed but rather a road map of the general steps to take and the resources available. It is to make the investigator aware of the steps. Then they must take the initiative to contact the person in each specific department. After looking over her email I continued working on event reports and checking emails. In the afternoon I worked on the section regarding qualitative analysis and Nanette's department. I also had a few "daily journal" logs to catch up on.

10/23/12- this morning I went through all of my IRB submission components for the UNTHSC IRB submission. Many of the forms had to be changed and tweaked due to the changes that we have made in our study design. However, overall doing the forms early seemed to be a great advantage because I think at this point they are complete. I will email Dr. Gwartz in the morning regarding when/how I should submit these forms. I also got to visit with Jan some after that. I have been working on her event reports and had a few questions. She also taught me how to complete the event reports that answer "no" on section 1.4 of the event reports, meaning they require more than just a simple acknowledgement and are reviewed by Dr. Schiller. In the afternoon I went through the rest of the event reports that she had. I really enjoy getting to meet the other people in the office and getting to know what their work involves. It gives me a better idea of what I will potentially be doing soon and the direction I would like to take my career.

10/24/12- Today was a fun day for all of us I think. We have a new manager in the office, William, and we all got to go out to lunch at Palomino. It's also nice to no longer be the "new one" in the office. I also worked on iRIS event reports for Jan and had a catch up meeting with Mary. She and I went over the report that she wrote up in response to the monitoring visit that I got to shadow on. We discussed the different issues that she found, but in addition, we discussed the aspects of the job that are not so obvious. She has been a good help in showing me how you have to treat the people working on the studies and the different dynamics and power struggles she encounters. She has taught me that the delivery of the information needs to be direct but you have to do it with a degree of finesse in order to not insult and offend the study personnel.

10/25/12- Today has been an IRB centered day. I have been in contact with Dr. Gwartz for most of the day regarding how/when/what to submit to the UNTHSC IRB. I have gone through these forms and made edits and corrections. I now have her signature on all of the forms I need signed and am hoping to go deliver the packets to the OPHS-IRB office tomorrow afternoon. Tonight I will see if I can complete my COI form away from Baylor's server. I am not able to do it here because I have to set it up through a proxy and that's not allowed at Baylor. So if all goes well tonight I may be able to submit my IRB packet tomorrow.

10/26/12- Elizabeth and I had our weekly meeting this morning. She wants me to push to have a meeting with her and Will next Friday to go over the completed IIR packet. I emailed the “Steps to Take” section to all of the people I had meetings with, Mary, Will, and Elizabeth. I hope to get some good feedback from these people. I also got an email back from the woman at UNTHSC who has agreed to look over my IRB submission packet as a pre-review. I will drop it by her office when I go to Fort Worth this afternoon to complete my conflict of interest form.

Week 11

10/29/12- This morning I had my mandatory TB testing done. Maggie had emailed me her edits for the financial portion of the packet with some small corrections. I also spent a good portion of time going over what I had sent and making sure the order of everything made sense. I spent the afternoon creating a workflow that the investigators can visualize (flowchart) for both the IRB and the FDA submissions. Friday afternoon I submitted my IRB packet for a pre-review and am still waiting to hear back on that. I am going on Friday to observe a thesis defense to get a better idea of what to expect, so hopefully I will also be able to submit my IRB packet at this time if it's cleared through the pre-review.

10/30/12- I still have not heard back from the woman who is pre-reviewing my IRB submission, so I worked on iRIS this morning. I had not worked on it in a few days and there were a lot of event reports to complete. After that I continued to work on the IIR packet. I updated the contact information for the people that I mention in the notebook and that I think could be a good resource for the investigators. I also got a response back from Debora. She said that it looked fine but that we might want to consider including a section about Mark, who works on industry sponsored trials. I think he should be in there too if the investigator wants to work with an industry sponsor. I will ask Elizabeth about that.

10/31/12- I had a good talk with Maggie this morning. She suggested looking at studies that failed to launch. I think this is beyond the scope of my research but could be interesting in the future to analyze the effects of the IIR packet on increasing the likelihood of a study being paid for by a sponsor. After that I worked on updating some of the parts of the IIR packet. Some of the ideas that I had early on have evolved (such as the purpose and what the main focus of my research will be) and needed to be reflected in the intro, the table of contents, and contact personnel. I also spent some time on iRIS doing event reports. Tomorrow I will put the whole packet together for Elizabeth and Will in preparation for our meeting on Friday morning.

11/1/12- Today was prep for my meeting with Elizabeth and Will tomorrow morning. I went over all of my documents, incorporated the edits that I have received and thought of myself, and got a copy to each of them. I also had a really great meeting with Mary over the suggestions that she had for my document. She had some good suggestions and she also showed me some parts of iRIS that I was unaware of. Some of these new "revelations" about iRIS will need to be incorporated and reflected in my document.

11/2/12- I had my meeting with Will and Elizabeth this morning. I think it went well and am hoping to have a more complete version by the middle of next week. I wrote up a summary of the suggestions that they had and will work on that for the beginning of next week. I also went over to Fort Worth for the afternoon. I went so that I could observe a thesis defense for a girl who is also in my Masters program. The research that she did was interesting; it was covering the motivation behind caregivers of dementia patients enrolling them in a clinical trial and whether

they felt that payment was appropriate. However, English was not her first language and it was very evident that she was very nervous for the defense and got confused and flustered during the questioning portion.

Week 12

11/5/12- This morning I worked on iRIS to complete event reports for IRB White. Then in the afternoon I began to work on incorporating the changes that were suggested from my meeting with Elizabeth and Will.

11/6/12- Today I worked on finishing the changes that were suggested from the meeting last Friday. I completed a definitions section, a quick reference section, a new “elements of the application” section, as well as incorporating additional “legal” information and references, and a section that discusses the use of radiation and radioisotopes. I have a few questions for Elizabeth and I will figure those out in our meeting with Will tomorrow morning. I also got my IRB submission back, and there are MANY more changes than I would have anticipated given Itzel’s initial email that everything looked fine. I went through her email and marked the specific issues that were brought up. I am worried that she said there was a document missing and I know I submitted it. I’m hoping that she just needs me to sign the document as well as Dr. Gwartz, who already signed it. We also had a staff meeting this afternoon to discuss holiday hours, benefits, flu shots, and COI forms.

11/7/12- Will, Elizabeth, and I had a meeting this morning regarding the IIR packet. I think they both liked the “Elements of the IRB” bullet points that I did and I made another today for the FDA submission. After the meeting Elizabeth showed me how to use Acrobat and suggested making the packet in PDF. I spent the rest of the afternoon importing most of the documents that I created into Acrobat.

11/8/12- Jennifer met with me, briefly, this morning to discuss the section of my packet on clinicaltrials.gov and the CDAs. She felt that everything was fine but suggested that I make Ashley the contact person for CDAs. I made those changes to the documents and then continued to work in Acrobat. I finished importing and converting the documents I created and all the forms and appendix material that I feel is needed. I spent the rest of the day creating links and references throughout the document. I emailed a copy to Elizabeth, Will, and Mary in hopes of getting some suggestions and feedback. I have run into the problem with opening the excel budget template and need to find a way to do that, but other than that I am pretty proud of the document so far.

11/9/12- I spent the day going through the corrections that I need to make to my IRB submission. I numbered her suggestions and put them specifically where she mentioned an edit. She also suggested that I use a different format for my protocol synopsis or use the “track changes” function if I used the same one. Unfortunately, the “track changes” function does not work with the form, which I downloaded from their website, so I have to use the new form. This new form for protocol synopsis does not match up with the old one, so I have to fill it out anew. Some of the information is still being used, and will copy and paste over, but other information is new. I

hope to have the new form completed in a day or two. I also spent a good amount of time completing event reports. I had not done them in a few days and there were a lot of them.

Week 13

11/12/12- Today I continued to work on the revisions of my “protocol synopsis” for my IRB submission. We also had the office’s “work Thanksgiving” for lunch today. It was a lot of fun, but I think it decreased everyone’s afternoon productivity significantly.

11/13/12- Today I finished the changes that were suggested to me by the UNTHSC IRB reviewer. I had to change some on the protocol synopsis, the informed consent cover letter, and parts of the recruiting email. I spoke with the women in Fort Worth and Dr. Gwartz and I can email the corrections in, now that the initial packet has been reviewed. Elizabeth also wrote to me and said that she thought the IIR packet was ready to be sent out, so I wrote a cover letter for it and will get her opinion of it tomorrow in our weekly meeting. I am also waiting for Mary’s suggestions on my IIR packet, she said she would look over it today and tomorrow.

11/14/12- This morning was spent on Event Reports in iRIS. This afternoon Elizabeth and I had our weekly meeting to discuss the email to investigators with the packet. She had a few edits to make to the cover letter and after these are made, the packet is going to be emailed out today or tomorrow! I also sent the revisions to my IRB submission in today. I need to find out what training Elizabeth has to have to validate that she can work with human subjects, but other than that, it’s done! So, just waiting on approval and an investigator to show interest.

11/15/12- This morning I helped Jan with IRB White and finding documents that Will wanted. I went through the folders from the last 11 IRB meetings. The folders have minutes, ballots, notes, and sign in sheets. I went through and found most of the documents, scanned them in, and emailed them to Jan. In the afternoon I completed some event reports. I began to feel like I was coming down with a cold and left work a little after 3.

11/16/12- Sick day.

Week 14

11/19/12-today I received another email from the UNTHSC IRB regarding my submission. I spent the day making changes and corrections which were suggested. I was able to complete all of them and sent the documents back to the IRB by the end of the day. I am hoping to hear from them before I leave for Thanksgiving. I also spent a good amount of time on iRIS on event reports.

11/20/12-Elizabeth and I had a weekly meeting this morning. She sent out the packet to all the coordinators today. I am hopeful that we will have a study begin to follow the toolkit within the next week or two. Our plan is to get someone started in the next week. If we haven't had any interest at that point, we are going to re-mention it to the coordinators. The worst case scenario is that we will not have a study go through and will resubmit to the IRB to create a survey on how helpful people think this tool kit will be. It is then an opinion survey rather than a quality control, but at least it will give me some data.

11/21/12- We are already receiving feedback from the toolkit. The nurse coordinator has already told us that she thinks this will be very helpful. I hope they have a study. I spent the morning making sure event reports were completed prior to the Thanksgiving break. I left at noon.

Week 15

11/26/12- I think I have a study to follow! The nurse coordinator emailed Elizabeth today that they have a study which they will be uploading onto iRIS by next week. This is such a relief. I sent her a follow up email with a few questions that I had for her. I also spoke with the IRB person at UNTHSC. I added one line to the consent cover letter which she requested and sent it back to her. She said that everything looked ready for approval after they get the new cover letter and Elizabeth's human research subject training. I also had to register for classes today and catch up on a few "Daily Journal" entries.

11/27/12- I officially have approval of my study from UNTHSC's IRB. This is perfect timing because Susan Houston, the research coordinator for nursing, called me today and she thinks that she has 2 studies that will be using my new process. We both have some questions for each other, so I set up a launch meeting for us to get together with Elizabeth on Thursday. I am hoping to discuss what the expectations are that we have for each other. I want to know how involved she would like me to be. I also would like to come up with some sort of oversight in the process, probably Elizabeth, to make sure that we haven't missed any critical steps.

11/28/12- This morning I worked on the event reports for IRB White in iRIS. This afternoon I spent some time prepping for the meeting with Susan tomorrow. I came up with a list of questions that I have for her relating to my involvement and to hopefully get some sort of game plan moving forward with collecting data from the 2 studies that will be using my new process.

11/29/12- We had our meeting with Susan and Morgan this morning. I think that the meeting went very well. Susan has actually identified three different studies that I can work on. She also told me that they already collect data regarding how long it typically takes their experiments to get approval. This is really great news. Morgan is going to send me that data on Monday. This was half of the data that I thought I had to collect, so I am really ahead of where I thought I would be in regards to that. iRIS is down with a virus so the rest of the afternoon was slow.

11/30/12- Out of the Office

Week 16

12/3/12- Morgan sent me that spreadsheet that tells the time which the nursing studies typically take. I looked over it some today, and will spend some more time analyzing it over the week. iRIS has also been cured of the virus so I had to spend a good amount of time completing event reports that I had been unable to access during the virus.

12/4/12- I spent some time looking over the spread sheet again today. There are some numbers that are obviously incorrect data, which Morgan is working on fixing, but other data that will be so helpful to me. This will literally save me weeks of going through file cabinets. I also worked on some iRIS work. In the afternoon I got in contact with two of the people who are going to use the toolkit. Beth Hudson, with the catheter study, is having a meeting next Tuesday to continue with their project, and Susan Squires, with the diversity study at UNT, and I are going to talk tomorrow. They both seem very happy with the packet.

12/5/12- I worked on event reports for both IRB Blue and White today. We had a virus last week and the system was down for a while and the event reports have been coming in steadily now that the system is back up. I also spoke on the phone with Susan Squire at UNT this afternoon. She agreed to be one of the studies that we could follow. She had a few issues that she needs to work through such as getting an iRIS ID, completing the BLN ethics modules, and revising her research to a stage II proposal. She said that she expects to begin working on it in about 2 weeks. I will check back with her then if she doesn't send me an email with an update.

12/6/12- Today is pretty slow; I worked on event reports for both IRBs in the morning. In the afternoon after asking Latoysa, Jan, and Heather if they had any additional work I could be working on, I went home around 3:30.

12/7/12- This morning I worked the event report forms on IRB White. Then in the afternoon I decided that I should start reading previous CRM student's thesis so I would have a better idea of how I should proceed with my own. I am finished with the beginning of it, but I would like to have a better idea of what the discussion section typically looks like. I spent the rest of the afternoon at home reading previous theses.

Week 17

12/10/12- This morning I worked on event reports. In the afternoon we had the monthly staff meeting. In the meeting we discussed the holiday schedule, PTO procedures, and the recent iRIS virus. I spent the rest of the day reading a CRM thesis and catching up on my journal entries.

12/11/12- I spent some time on event reports for Heather and Jan today. I also had a follow up email with Beth Hudson. Her group was having a meeting today about her study and I wanted an update. She said that they were working on the literature review and would revisit and get the study started after the New Year hit.

12/12/12- I spent some time this morning reading other theses for CRM students on the library's webpage. I did a few event reports, but there weren't many of them since I did so many yesterday. I also had an email from Susan Squires in regards to her iRIS account. I spent some time working that out and hopefully she will have access to iRIS in the next few days.

12/13/12- Elizabeth and I had our first weekly meeting this morning in several weeks. We discussed the progress with getting people to follow for the IIR packet. Elizabeth wants me to follow up with Claudia Mattil and Michelle Ackers so I sent them an email seeing if they had anyone in mind. She also gave me the protocol for another study in the nursing department with Jenny Reynolds so I also sent her an email to see if she was interested. I also spent the afternoon completing the event reports for IRB Red, and there were a lot.

12/14/12- Today I made sure that Susan Squires now has access to iRIS. Hopefully this will get her moving towards getting her protocol rewritten and uploaded on iRIS for approval. I also worked on some event reports for Jan and Heather. This afternoon was the BRI Christmas reception. The reception was fun and it was fun to see how many people BRI works with and how they appreciate what BRI does for them.

Week 18

12/17/12- I had a chat with Will this morning after he wanted to know more about how I was collecting data and feedback. He was unaware that I had a survey that I would be using and was approved by my IRB. He agreed that some of the comparative studies would be a little nebulous in the exact time which they began but thought that the satisfaction section would have good data. He had a few suggestions on how I should reword the survey but Elizabeth said we would discuss it when she got back.

12/18/12- I spent today working on event reports and reading other theses from past years. I also began thinking about my own thesis. I think that I should include a printed copy of the IIR packet as one of the appendices and combined with my thesis proposal and this journal my thesis is going to be well over 50-60 pages.

12/19/12- out sick

12/20/12- yesterday when I was sick, Claudia Mattil sent me an email regarding Libby Callender and how her group has been using the IIR packet. I sent an email to Libby today stating that I would be happy to be a resource for her and that I'm hoping to get some feedback about the packet. I spoke with Claudia in person today as well and she gave me the name of another woman, Megan Self, who is also in the very early stages of using the packet. I sent an email to her as well and hope to hear back from both of them by next week, as well as from Jenny Reynolds and Susan Squires.

12/21/12- Today has been a great day. I sent some emails to people as a follow up to discuss how their projects are coming along. Libby Callender and Megan Self have already submitted their studies to the IRB for approval. I will follow up with other investigators next week.

Week 19

12/26/12- Today is a very slow day. I spent most of the time catching up on event reports. There were a surprising number of them. I also tried to come up with a game plan for this week and I think I will begin to outline my thesis.

12/27/12- Today was a shift back to the UNTHSC student rather than the BRI intern. I spent today looking over what I needed to complete prior to my graduation. I also spent some time reading previous theses from people in this program. After I found a few that I liked I printed their Table of Contents so I can get some ideas for an outline of my own. I spent the rest of the afternoon working on an outline of my own. I typed up a brief one and sent it in an email to Dr. Kirchhoff. I am hoping that she gets back to me with some suggestions in the next week.

12/28/12- last day of the year. This week has been a slow week. I spent the day working on some event reports, but not many are coming in. I also began looking up some information on the Baylor healthcare system and BRI within it. I plan on incorporating this information into a section within my thesis.

Week 20

1/2/13- Today I spent some time doing a few event reports that came in over the New Year's holiday. I then sent out an email to each of the investigators I have previously made contact with. Libby's study is going before the IRB tomorrow and Megan should hear back from the IRB about hers soon as well. Susan Squires got back to me but I am not very confident that she will have hers submitted prior to my internship being over. I also spent some time on the Baylor website gathering information about BUMC and BRI.

1/3/13- I wrote part of my thesis today. I am adding a section which discusses BUMC and BRI specifically so it will emphasize the size of Baylor and how desperately they needed the packet I made especially since there was not a document of this kind prior to me working here.

1/4/13- Elizabeth and I had our weekly meeting this morning. We both agree that we do not think that Susan Squires is going to make the deadline for getting the study submitted before my internship ends. I heard back from Dr. K today as well and she thinks that the outline for my thesis looks good and that I should move ahead with it.

Week 21

1/7/13- I spent this morning sending out emails to catch up with the studies that I am following. Neither of the two studies that I am following have heard back yet regarding their approval. I also reached out to Jeff Ellison who Megan put me in contact with as he is also interested in doing some research. I also got Megan's IRB number and will look into what the status on her study is; it should have gone through by now. I spent the rest of the day catching up on event reports as I hadn't done them in several days. UPDATE: Megan's study is through and passed! Elizabeth found it in the disaster of IRB Red. Megan does not know yet, but I should have data soon.

1/8/13- I sent out an email to another person who is interested in investigator initiated research. It would be too late in the time period to collect data from them but I think it is still valuable to give them the resource. I also spent the day going through the thesis outline and selecting the sections that I can work on now, before I have any data in. I am hoping to have data very soon. I am getting nervous at this point that I don't have any yet.

1/9/13-today I went through this journal and made a list of all the activities that I have done and want to mention in the section of my thesis which describes my daily activities

1/10/13- The event reports needed attention so I spent my morning completing all of them in all three IRBs. Then Elizabeth and I had our weekly meeting this morning. She said that I should take Latoysa with me to the meeting with Megan and Libby. I also worked on scheduling a day for my thesis defense since that is in the next two months. My thesis committee and I came to the coconscious of March 13th. I spent the rest of the afternoon completing my "Intent to Defend" form and reserving the room.

1/11/13- I had my meeting with Megan, Libby, and Kenleigh this morning. I think the meeting went pretty well. They were very happy with the packet that I have put together, and they told me that they had been in the process of putting a similar one together when they got mine. I got lots of feedback from them regarding edits that I need to make to the existing packet and new sections and documents that they think should be included.

Week 22

1/14/13- I spent the majority of the day completing event reports. There were over 100 of them between all the IRBs. Will also put me in contact with Callenda Hacker at Children's who is looking to do a study there and here at Baylor. I have been emailing with her about how to begin the process of setting up her Baylor account and completing the BLN modules. All of the Regulatory Affairs team went out to eat lunch as a welcome to the new IRB coordinator, Christine.

1/15/13- This morning I sat in on and took the minutes for the RAT meeting. I really enjoyed hearing from the coordinators some of the issues that they have been facing dealing with the investigators. I have asked Will if I can attend these meetings in the future. I think it could provide good material for updates for my IIR packet. After the meeting I typed up the minutes and emailed them to Latoysa. In the afternoon I put together a spreadsheet of all the investigators and coordinators that I have sent the IIR packet out to. This was requested at the meeting this morning and will be good for BRI to have once I leave.

1/16/13- Megan and I scheduled a meeting for us to finally meet face to face and discuss our investigator initiated research packets that we have separately put together. We are meeting on Friday mid-morning with Latoysa, Libby, and Kenleigh. I put together a packet for everyone with a copy of the IIR packet and the survey document with cover letter. I hope to have them fill out the surveys at the meeting on Friday so I will have data to analyze. Elizabeth and I also had a brief meeting to go over what I have been working on. She seemed to like the organizational documents that I have created to help others pick up my project after I leave. After the January birthday party this afternoon, I worked on creating a Word document of the IIR packet (at Will's request). I previously had all the elements saved as individual documents and it makes more sense to have it as one unified document, I had just never done it.

1/17/13- This morning I worked on event reports. In the afternoon I worked on my thesis section about what I had done during my internship. I also put together a packet with the toolkit and my survey document for the meeting tomorrow. I am hopefully going to get the ladies to complete the survey while they are here.

1/18/13- This morning I had my meeting with Megan, Kenleigh, and Libby. I feel over all it went very well. They had a ton of positive feedback and some great suggestions for moving forward. Some of their suggestions were to update the contact lists, now that there has been some shuffling around of the IRB and BRI as a whole. We also need to incorporate a section on the radiation safety committee, the BRU flowchart, sections required in the regulatory binders, and technology safely. They also recommended putting it on the L drive so it would be accessible to everyone.

Week 23

1/21/13- I got 2 survey responses today! I finally have data that I can review and add into my thesis. Both Megan and Libby gave me “9”s across the board, so I feel like my research project was a success. In addition to looking at these, I worked on event reports.

1/22/13- This afternoon I went to my last staff meeting here at BRI. It did give me the opportunity to tell the team that I am moving to Austin and to let me know if they know of any job opportunities there. I hope this will be a valuable networking opportunity. I also spent some time updating my resume, as I will be applying for jobs soon. I also worked the event reports that needed completing.

1/23/13- This morning I completed the event reports that were posted in the IRBs. I spent the majority of the afternoon going through all of the papers that I have collected during my internship and made sure they were filed in the correct places in my binders. I also reviewed my IRB submission to make sure that I was only using the documents that were approved by my IRB.

1/24/13- Today I worked on event reports in the morning. In the afternoon, I spent some time looking over previous thesis from other people in my program.

1/25/13- At our weekly meeting this afternoon, Elizabeth and I decided that we should email the survey out to people that have had a chance to look over the packet but have not submitted a study within this time period. The people may not be able to complete the first page of the survey, but the second page, with the satisfaction questions, will still provide valuable information and data for me. I wrote an email to send out to the coordinators and the managers. I also emailed my other two committee members to see when I can meet up with them to sign my intent to defend form.

Week 24

1/28/13- This morning I received an email that Dr. Gwartz and Dr. Kirchhoff could meet with me this afternoon. I needed to get both of them to sign my “Intent to Defend” form that needed to be filed. I spent some time making sure I had all the necessary paper work, and compiling my questions that I had for Dr. Kirchhoff. I went over to Ft. Worth in the afternoon. I got to meet with both Dr. Kirchhoff and Dr. Gwartz and talk to them separately about how my thesis and internship were going. My main question for Dr. Kirchhoff was what tense the thesis should be written in. She explained it to me that this is like writing the text book on the subject and I think that will help me to reformat my proposal into my thesis.

1/29/13-This morning we had the Research Regulatory Affairs meeting. Jan gave her presentation for the “Tip of the Month” suggestion on informed consent documents. Mary also spent some time explaining to all of us the initiative that the Education committee had taken on creating a program that all researchers will go through when they are hired on and then every so often to keep them current. In the afternoon I began going through my thesis proposal and formatting it as Dr. Kirchhoff had suggested.

1/30/13- Today I worked on going through my thesis and picking out things that I needed to change based on how the study has changed as I’ve done it. I went through and reworded some things to change the emphasis of the study to the investigators’ satisfaction from the efficiency idea.

1/31/13- I spent this morning working on event reports in IRB blue. There were a considerable number of them. In the afternoon I worked on the rewording of my thesis proposal to past tense, finally getting that part finished. I also had a chat with Jan and Mary. I wanted their opinion on different career paths and companies down in Austin.

2/1/13- Elizabeth and I had our weekly meeting this morning. We were slightly rushed because she had another meeting to run to so we rescheduled for Monday morning. I spent the rest of the day completing event reports and working on my thesis. I put the other sections of my thesis that I have completed into the newly revised proposal. I think it’s coming along well.

Week 25

2/4/13- Elizabeth and I had a meeting this morning to talk about career paths and companies that she thought I could work for in Austin. It was a very helpful meeting for me. I wanted to know some positions that she felt I would be qualified for and the salary that I could expect from some of them. I also wanted to know her opinion on the differences between working for a CRO and a Hospital or University. She said that a CRO would probably pay more, not have as good of benefits, and require more travel. A hospital, IRB or University would probably not pay as well, but require less travel and have better benefits. I think I will focus more on applying to hospitals and the University system. I also worked on event reports and looked at different companies in Austin.

2/5/13- Today I worked on looking at what I needed to complete on my thesis. I spent some time looking at the outline that I have made. I need to really start focusing on wrapping it up. This includes the section on future direction and discussion. I spent some time coming up with several directions that I feel the packet can go from here. I also have some suggestions on other projects that can be done on it. I feel the most important aspect of my project is that someone needs to maintain the toolkit after I leave.

2/6/13- I was out today because I had to go to the doctor's office.

2/7/13- This morning I worked on event reports and answering some emails that I didn't get to yesterday. I also created an instructional packet on how to complete event reports. Latoysa had asked me on Tuesday if I would remind her how on Wednesday. We did not have a chance today and I was gone yesterday, so I went through and did screen shots and then wrote instructions on the steps to complete event reports. I think this packet can also be useful for Cristine and any other new employee or intern that is asked to complete event reports. I then spent the rest of the afternoon completing journal entries that I had missed.

2/8/13- today I worked on event reports and my thesis as well as come up with the list of things that I know I need to complete before my internship is over.

Week 26

2/11/13- This morning was spent completing event reports that were filed over the weekend. I also spent some time in the afternoon coming up with a schedule of the items that I need to finish and make sure BRI has before I leave here. Tomorrow I will work on typing up a list of suggestions for the packet that I wrote. On Wednesday I will type up a list of suggestions for Elizabeth if she ever has another intern from my program, and on Thursday I will make sure that all of my files have been transferred from this computer and that BRI has a copy of them. During this time I will also continue to work on my thesis and continue event reports. I'm sure that other issues will come up that I will need to address as well.

2/12/13- I stuck to my schedule today. I worked on event reports this morning and then typed up a list of suggestions on how to continue the work on the IIR packet that I put together. I also spoke to Mark about his connection at the Austin Heart hospital and spent some time working on an email to him about the position, my resume, and my cover letter for him to forward on. In the afternoon I worked on my thesis. I finished writing my abstract, formatted my thesis to be coherent, and worked on the acknowledgement section. I also briefly spoke to Elizabeth about the job interview I have next Monday at PPD.

2/13/13- This morning I worked on completing some event reports and then worked in iRIS to help Jan out. She needed a list of the revisions in her IRB white that were only denoting a change in study staff and PI so I spent some time getting a spreadsheet of this information. I then worked on typing up a list of suggestions for future interns, suggestions for the interns and suggestions for Elizabeth. I hope this is useful if BRI ever accepts another intern. In the afternoon I worked on finishing my acknowledgements, created a smart table of contents for my thesis and deciding the work that I needed to do next. I sent the current thesis to Dr. Kirchhoff and I hope she likes what I have worked on so far. Mark also worked on some edits on my cover letter and resume and I spoke with him about those for a bit.

2/14/13- This morning I worked on some event reports and continued to work on my thesis. I had a luncheon with some of the ladies from our team this afternoon. After lunch I had a quick meeting with Latoysa to show her what I have typed up for Elizabeth to have as far as suggestions for future interns and suggestions for the packet in the future. I then spent some time organizing my documents and emailing them to Latoysa. We also made sure that my thesis is on Elizabeth's calendar and made a map of where my actual thesis defense will be. I then shifted my focus back to my thesis. I have been looking at the survey responses that I have and I don't think I will have conclusive results about the effect on efficiency that my packet will have. I just did not have enough time. However, the results are very conclusive that this was a needed packet and was helpful to the investigators and their team. I hope that during my defense this will not pose too much of an issue. I have read some other previous studies and some did not have conclusive results either. We will see what Dr. Kirchhoff has to say about that.

2/15/13- I can't believe it's actually my last day here. Elizabeth and I had our last weekly meeting this morning. I spent the rest of the day making sure that all of my documents had been emailed to me and to the other people that might need them. I worked on some event reports briefly. I also spent some time contacting other people that I have worked with to be references for me. In the afternoon everyone at BRI had a party/reception for me to wish me well as I start the next part of my Masters. After the party I wrote this last journal entry, printed it out, packed my stuff and got out of here.

IIR PACKET



Investigator Initiated Research Operational Process:
How to submit to the IRB and the FDA

Introduction

This document outlines a suggested process for the submission of an Investigator Initiated Research Proposal to the Baylor's Institutional Review Board and an Investigational New Drug application to the FDA following Baylor Healthcare System regulations. It is designed to serve as a guide for the planning, preparation, format, and submission of these applications.

Following the process laid out in this document does not guarantee approval from the Baylor IRB or that it will not be returned with suggestions for change, nor does this document guarantee approval from the FDA.

Every clinical trial is different and certain aspects and steps laid out may not apply to all trials.

The responsibilities of the investigator are to (Title 21 section 312.53)

1. Protect the rights and safety of subjects to protect them from unreasonable harm
2. Receive IRB approval
3. Acquire informed consent to protect and educate the subject prior to beginning trial
4. Follow the protocol to ensure validity and that ethics are not violated
5. Control investigational product, since product is not yet approved by the FDA to prevent misuse and proper distribution and disposal
6. Report adverse events and problems that the subjects experience during the trial

Ultimately, the Principle Investigator is 100% responsible for the clinical trial.

In all cases a valid, successful trial is preferred but protection of human research subjects is mandatory.

Elements of the IRB Submission Process

1. Administrative
 - a. iRIS log in ID
 - b. Baylor Learning Network (BLN) modules complete
 - c. Conflict of Interest (COI) on file
2. Presubmission
 - a. Begin FDA presubmission process
 - b. Support Strongly Suggested
 - i. Protocol development [sample]
 - ii. Legal contracts discussed (CDA, MTA etc.)
 - iii. Funding search [form]
 - iv. Budget development [form]
 - v. Marketing and advertising development
 - c. No Support Required
 - i. Informed consent document [samples]
 - ii. Study application (iRIS web based form)
 - iii. Supplemental application [form]
 - iv. PI signature form [form]
 - v. Administrator signature [form]
 - vi. Scientific review signature [form]
3. Submitting to the IRB
 - a. IRB Submission Packet
 - i. Study Application
 - ii. Supplemental Application
 - iii. PI Signature Form (or PI may sign electronically)
 - iv. Administrator Signature Form
 - v. Scientific Review Signature Form
 - vi. Consent Form(s) or Survey Cover Letter (See BRI Template)
 - vii. Protocol
 - viii. Investigational Drug Brochure (if applicable)
 - ix. Advertisements (if applicable)
 - x. Any other supplemental documents that are used in execution of the study
 - xi. Any other written materials provided to the study subjects
 - xii. Documentation of FDA submission
4. Post IRB Submission
 - a. Clinical Trials Listing Form [form]

Elements of the FDA Submission Process

1. Presubmission
 - a. Begin IRB Presubmission Process
 - i. Letter from IRB indicating their review
 - b. Support Strongly Suggested
 - i. Protocol development
 - c. No Support Required
 - i. Informed consent
 - ii. IND/IDE form [Form 1571 or equivalent]
 - iii. Statement of investigator [Form 1572]
 - iv. Financial disclosure [Form 3454] or [Form 3455]
 - v. Certification of compliance [Form 3674]
2. Submitting to the FDA
 - a. FDA Submission Packet (in triplicate)
 - i. Protocol and standard operating procedures
 - ii. Letter of IRB review
 - iii. IND/IDE form
 - iv. Statement of investigator
 - v. Financial disclosure
 - vi. Certification of compliance
3. Post FDA Submission
 - a. Notify IRB of FDA's decision
 - b. Clinical Trials Listing Form [form]

Investigator-initiated Research

Important Phone Numbers

Baylor Research Institute Main Number 214/820-2687

IHCRI

214/265-3654

QS@BaylorHealth.edu

Nanette Myers 214/818-1616

NanetteM@BaylorHealth.edu

Grants and Contracts

Helena Jackson 214/820-9904

Helena.Jackson@BaylorHealth.edu

Ashley Dowell 214/820-7531

Ashley.Dowell@BaylorHealth.edu

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Financial Services

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iRIS Support

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MaryDeH@BaylorHealth.edu

IRB Specialists

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214/820-9989

CherylEd@BaylorHealth.edu

Jan Harrell IRB White

214/820-9625

JanHar@BaylorHealth.edu

Heather Whitacre IRB Blue

214/820-9692

Heather.Whitacre@BaylorHealth.edu

Quick Reference for Elements of IRB Submission which Require Support

- **Protocol Development**
 - Who: IHCRI (Nanette Myers)
 - What is needed: short description of the study and the type of services that may be needed
 - When: 1st, before other documents are created
 - Where: 8080 N. Central Expressway, Suite 500, Dallas, TX 75206
 - How: QS@BaylorHealth.edu 214-265-3654 or [NanetteM @BaylorHealth.edu](mailto:NanetteM@BaylorHealth.edu) 214-818-1616
- **Confidential Disclosure Agreement**
 - Who: Ashley Dowell
 - What is needed: Protocol for trial
 - When: Prior to speaking with any party outside of Baylor
 - Where: BRI, 3310 Live Oak, Suite 500, Dallas, TX 75204
 - How: Ashley.Dowell@BaylorHealth.edu
- **Material Transfer Agreement**
 - Who: Helena Jackson
 - What: Protocol for trial
 - When: If seeking outside (industry) funding after protocol development
 - Where: BRI, 3310 Live Oak, Suite 500, Dallas, TX 75204
 - How: Helena.Jackson@BaylorHealth.edu
- **Grant Applications**
 - Who: Deborah Price
 - What: Funding Opportunities Search form
 - When: After protocol development and concurrently with Budget and Legal
 - Where: BRI, 3310 Live Oak, Suite 500, Dallas, TX 75204
 - How: DeboraPr@BaylorHealth.edu
- **Budget Development**
 - Who: Margaret Hewlitt
 - What: Protocol and completed study budget template
 - When: After protocol development and concurrently with Funding and Legal
 - Where: BRI, 3310 Live Oak, Suite 500, Dallas, TX 75204
 - How: Margaret.Hewlitt@BaylorHealth.edu
- **Marketing and Recruiting**
 - Who: Kristine Hughes
 - What: Synopsis of Trial
 - When: After Grants, Budget, and Legal process is underway
 - Where: Bryan Tower, 7th floor
 - How: Kristine.Hughes@BaylorHealth.edu

Definitions

- **1571-** See IND
- **1572-** Statement of Investigator, federal form where the investigator agrees to abide by the federal guidelines set forth in the Code of Federal Regulations for the use of drugs in an investigational setting.
- **3454-** Financial Disclosure with no interest, certification to the FDA that no financial arrangements with an investigator have been made where study outcome could affect compensation; that the investigator has no proprietary interest in the tested product; that the investigator does not have a significant equity interest in the sponsor of the covered study; and that the investigator has not received significant payments of other sorts.
- **3455-** Financial Disclosure with interest, Disclosure of specified financial arrangements between the investigator and the sponsoring company of the trial to the FDA and any steps taken to minimize the potential for bias.
- **3674-** Certification of Compliance, contract between the investigator and the FDA that the clinical trial will be registered and maintained in the databank ClinicalTrials.gov.
- **AE-** Adverse Event, any unfavorable and unintended sign, symptom, or disease temporally associated with the use of an investigational product, whether or not related to the product.
- **BLN-** Baylor Learning Network, Baylor's learning management system. This tool allows employees to enroll for instructor-led courses, webinars and e-Learning lessons. It's also a mechanism for assigning required training, delivering e-Learning lessons, administering tests, and tracking courses you've completed.
- **BRI-** Baylor Research Institute, The governing body that oversees all research in the Baylor Healthcare System and the administration behind the IRBs at Baylor.
- **CDA or NDA-** Confidential Disclosure Agreement (non-disclosure agreement), a contract between two or more parties that discusses confidential material, intellectual property, or information that the parties wish to share with one another for research purposes, but wish to keep private from third parties.

- **CRSR-** Baylor Committee on Radiation Safety and Radioisotopes, the Radiation Safety Committee for Baylor University Medical Center (BUMC) but serves to review all BHCS IRB protocols using radiation (standard of care and research if the radiation procedure is in the IRB research consent document).
- **CV-** Curriculum Vitae, written description of work experience, research experience, educational background and skills. Includes any published work.
- **FDA-** Food and Drug Administration, the department of the government responsible for monitoring prescription and over-the-counter pharmaceutical drugs (medications), vaccines, biopharmaceuticals, blood transfusions, medical devices, electromagnetic radiation emitting devices (ERED), and veterinary products as well as food, tobacco products, and dietary supplements.
- **IBC-** Institutional Biosafety Committee, the governing board which oversees all recombinant DNA research.
- **IDB-** Investigational Drug Brochure, a document given to investigational sites summarizing the information relevant to studies with human subjects about an investigational new product.
- **IDE-** Investigational Device Exemption, allows an investigational device to be used in a clinical study in order to collect safety and effectiveness data required to support a Premarket Approval (PMA) application or a Premarket Notification [510(k)] submission to the FDA.
- **IHCRI-** Institute for Health Care Research and Improvement (8080), they conduct research and supports operational goals related to clinical effectiveness, patient safety, and health care quality improvement. The Department of Quantitative Sciences is within this department and consults on the design of clinical research.
- **IND-** Investigational New Drug (FDA 1571), The FDAs application by which they grant permission to ship an experimental drug across state lines (usually to clinical investigators) before a marketing application for the drug has been approved. One is needed for a:
 - New indication
 - Change in the approved patient population (e.g. pediatric) or a population at greater or increase of risk (elderly, HIV positive, immunocompromised)
 - Change in the approved route of administration or dosage level
 - Significant change in the promotion of an approved drug
- **IP-** Intellectual Property, property that derives from the work of an individual's mind or intellect and is recognizes by law.

- **IRB-** Institutional Review Board, an ethical review board that approves, monitors, and reviews research involving human subjects.
- **iRIS-** Baylor Healthcare System's online IRB submission site. All IRB forms must be submitted through this site.
- **MTA-** Material Transfer Agreement, a contract that negotiates the transfer of tangible research materials between two organizations, usually Baylor and a pharmaceutical company
- **PI-** Principal Investigator, the lead scientist for a clinical trial, the person who takes direct responsibility for completion of a funded project, directing the research and reporting directly to the funding agency.
- **RFA-** Request for Application, A type of solicitation notice in which an organization announces that grant funding is available, and allows researchers and other organizations to present bids on how the funding could be used. It usually defines the type of studies that are eligible for funding.
- **SAE-** Serious Adverse Event, untoward medical occurrence that at any dose
 - Results in death
 - Is life-threatening
 - Requires inpatient hospitalization
 - Prolongation of existing hospitalization
 - Results in persistent or significant disability/incapacity
 - Congenital anomaly/birth defect
 - Requires intervention to prevent permanent impairment or damage

Steps to Take

The following is a suggested order of steps to take to submit a clinical trial proposal to the Baylor University Medical Center IRB and the FDA. Not every step will apply to all clinical studies. Every clinical trial is unique and will need different actions taken to complete the IRB and FDA submission. If at any point during the trial development there is a question, please contact **Baylor Research Institute** at **(214) 820-2687**.

Additionally, if the investigator is going to be submitting an IND or IDE to the FDA, this process should occur concurrently with the IRB submission process. The application should be sent out to the FDA in the same time period.

ADMINISTRATIVE PROCESS

All IRB forms are submitted electronically through the iRIS system. A valid Baylor ID is needed to log-in and submit forms; if you do not have a valid Baylor ID contact Gail Colbert at ArrieMo@BaylorHealth.edu. Most forms can be accessed on the MyBaylor.com page under “Baylor Research Institute” or in iRIS under “Help”

Prior to undertaking a clinical trial, a current “Conflict of Interest” form must be on file with the Corporate Compliance Office.

In addition, the Baylor Learning Network modules covering clinical research and human subjects must be completed. The modules will be emailed to you.

SUBMITTING TO THE IRB

All IRB required documents are submitted electronically through the iRIS system and a list of them can be found [here](#).

Approval of the trial by the Baylor IRB is required by the FDA as outlined in Title 21 Part 56. The proposal is submitted to the Baylor Research Institute digitally through the iRIS system. Much more detailed information on the IRB submission process can be found on the MyBaylor.com website under the Baylor Research Institute page. The IRB requires a copy of the protocol that is to be followed, the informed consent document that is to be used, the Investigators C.V., and all additional material that will be used regarding the trial, including, but not limited to: the Investigational Drug Brochure, advertisements, supplemental documents used in the execution of the study, and any written materials provided to the subjects.

The IRB also requires documentation of correspondence with the FDA if applicable.

Protocol Development

The first step is to create the trial protocol. The development of a protocol is required by the IRB and the FDA and helps to create a more valid and scientifically sound trial.

The design of the study should help to identify and control confounding, eliminate bias, ensure protocol and treatment compliance, eliminate treatment failures and unforeseen events, and provide assurance of the validity of the research. As well, the protocol should demonstrate the methodology for safeguarding the health of the participants as well as answer specific research questions. Creating a data managing plans is strongly encouraged at this point. Begin working with a statistician early in the protocol development

The Guidance Document (Title 21 Section 312.145) clearly states that deviation from the protocol exposes the subjects to unreasonable risks and fails to protect them. They are bound to following the protocol by signing the “Investigator Agreement”. Not following the protocol is unethical and compromises the validity of the experiment.

A protocol template can be found at http://www.med.upenn.edu/ohr/docs/ProtocolTemp_guidelines.doc or [here](#).

The Institute for Health Care Research and Improvement (8080)

The Institute for Health Care Research and Improvement (IHCRI) at Baylor is a department that specializes in the design and development of protocols, data management plans, survey development, statistical analysis, and case report forms, among other study related documents and management tools. IHCRI staff can be consulted for many aspects of the study design and format. There is a charge for their time, but a development fund has been allocated in the budget of all departments for this purpose. ICHRI costs can be worked into the study budget during the budget development process. Funds can also be recuperated after receiving a grant or industry funds.

The IHCRI has a specific department for the handling and development of data plans. The Department of Quantitative Sciences specializes in biostatistical planning and analysis, survey design and analysis, clinical trial study design, and data management and coordination. An initial consultation is free of charge and can be set up by phone at 214-265-3654 or emailed to QS@BaylorHealth.edu . Nanette Myers can also be contacted for questions and scheduling at 214-818-1616 or at [NanetteM @BaylorHealth.edu](mailto:NanetteM@BaylorHealth.edu) . Please include a short description of the study and the type of services that may be needed.

Informed Consent

IRB submission requires the consent form that will be used in the trial. The BRI Informed Consent templates can be found on the website at www.mybaylor.com > Tools and Resources> Baylor Research Institute> Forms> IRB Sample Consent or [here](#). There are different consent documents based on the type of trial that will be done. All informed consent documents must contain the following information according to Title 21 Part 50.25:

- research- purpose of the research, duration of participation, description of procedures, and if experiments
- reasonably foreseeable risks or discomforts
- any benefits
- alternative procedures
- confidentiality
- compensation
- contacts

- that participation is voluntary
- unforeseeable risks
- termination circumstances
- additional costs
- withdrawal consequences
- new findings
- number of subjects

All informed consent documents must also contain the phrase:

“A description of this clinical trial will be available on www.clinicaltrials.gov , as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at anytime”

Confidential Disclosure Agreement

A confidential disclosure agreement needs to be written up immediately during protocol development. Contact Ashley Dowell at Ashley.Dowell@BaylorHealth.edu to get this process started. There is no template for this step because each trial requires different negotiations. Do NOT speak with anyone outside of Baylor Healthcare about the research/trial before they sign this paper. If you do, the outside party is not under any legal obligation to give you any credit or acknowledgement. CDA should be one of the first steps that Investigators should go through if they are going to be working with any other agency/organization outside the Baylor Healthcare System.

Additional Legal Support

If the investigator will be working with a party outside of the Baylor Healthcare System, additional legal support will be needed. Contracts such as a Material Transfer Agreement (MTA) will need to be drawn up during the planning process. This process can be started by contacting Helena Jackson at Helena.Jackson@BaylorHealth.edu.

Budget Development

Budget development should also begin to occur during this time. The templates are online at www.mybaylor.com page under BRI> Forms and Templates> Study Budget Templates or [here](#). The investigators need to take time to fill this form out to the best of their ability. Then present it, along with a completed protocol, to the budgets department at BRI. It has proven beneficial to mark the protocol at every step that will affect the budget and take note of the expense, and be sure to include addition costs such as IRB and Monitoring fees. This will assure that every procedure is accounted for and will help the Budget Analysis capture all anticipated expenses for the study. If the investigator has any questions along the way, they can contact Maggie Hewlitt at Margaret.hewlitt@BaylorHealth.edu. Know the cost of the study and formulate a complete budget in partnership with the BRI Finance Department before you speak with a sponsor about funding.

Grant Applications

If the Investigator is planning on or would like to use federal grants or foundation funds to finance their research, they should begin to find an appropriate grant. Deborah Price is the grants specialist at BRI. If no funding has been secured, the investigator needs to contact her and

present to her the form found [here](#) and a copy of their C.V. If a grant has already been selected, then the investigator should send her the R.F.A and the grant application. Any of these forms can be sent to her at deborapr@BaylorHealth.edu . She can help in searching, applying, and maintaining grants and outside funding sources.

If the Investigator is planning on or would like to seek funding from a pharmaceutical company, there are grants specialists available to negotiate the agreement on behalf of the Investigator.

A critical point in the process of legal, budget, and grants is to have a negotiator and a budget representative go with the investigator to the sponsor, if there is one, after the budget has been worked out to discuss funding. This combination of people at this point in the trial development seems to be a very effective combination.

Marketing and Recruitment

This is a step that few investigators think about during the protocol development, yet without subjects enrolled there is no trial. The marketing department may charge a fee for their services but this can be worked into the study budget. A meeting with the marketing department can be arranged through BRI or by contacting Kristine Hughes at kristine.hughes@BaylorHealth.edu . All materials that will be used for marketing need to be submitting in the IRB submission packet.

Additional Forms to Complete

Several forms need to be filled out and submitted during the IRB submission process that can be completed without the assistance of a specific department. The complete list of IRB submission material can be found at <https://BRIOPS.BaylorHealth.edu> under Help> IRB Forms. The forms that can be completed at anytime during the process prior to submitting to the IRB are:

- Study application (iRIS web based form)
- Supplemental application (form 1- word document)
- PI signature form
- Administrator signature form
- Scientific Review Signature form

Or at www.mybaylor.com under Tools and Resources> Baylor Research Institute> Forms

SUBMITTING TO THE FDA

A checklist of all forms that must be submitted to the FDA can be found here and a copy of them can be found at [fda.gov](http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/InvestigationalNewDrugINDorDeviceExemptionIDEProcess/default.htm). Further instructions for submission can be found at <http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/InvestigationalNewDrugINDorDeviceExemptionIDEProcess/default.htm>

Clinical Trials Listing

All trials at Baylor University Medical Center are posted on the Baylor webpage, allowing potential subjects to search for the clinical trial. The form that facilitates the online posting is found here or at www.mybaylor.com > BRI> Forms> Clinical Trials Listing Form. This form needs to be completed and returned to Kristine Hughes at 214-820-4952 or kristine.hughes@baylorhealth.edu . <https://www.mybaylor.com/BRI/Pages/Forms-Index.aspx>

Investigational New Drug (IND) (FDA 1571) or Investigational Device Exemption (IDE)

Prior to receiving notification of approval from the IRB, you should begin filling out the Investigational New Drug Application as required by Title 21 Part 312 or an Investigational Device Exemption as required by Title 21 Part 812 depending on the type of trial. The IND form can be found here or at

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083533.pdf>

There is no set form for an IDE but a list of required elements in the order they must be presented in is as followed:

1. Name and address of sponsor
2. Report of prior investigations (§ 812.27). A report of prior investigations must include reports of all prior clinical, animal, and laboratory testing of the device. It should be comprehensive and adequate to justify the proposed investigation. Specific contents of the report must include:
 - a bibliography of all publications, whether adverse or supportive, that are relevant to an evaluation of the safety and effectiveness of the device
 - copies of all published and unpublished adverse information
 - copies of other significant publications if requested by an IRB or FDA
 - a summary of all other unpublished information (whether adverse or supportive) that is relevant to an evaluation of the safety and effectiveness of the device
 - if nonclinical laboratory data are provided, a statement that such studies have been conducted in compliance with the Good Laboratory Practice (GLP) regulation in 21 CFR Part 58. If the study was not conducted in compliance with the GLP regulation, include a brief statement of the reason for noncompliance.
3. Investigational plan (§812.25)

The investigational plan shall include the following items in the following order:

 - purpose (the name and intended use of the device and the objectives and duration of the investigation)
 - protocol (a written protocol describing the methodology to be used and an analysis of the protocol demonstrating its scientific soundness)
 - risk analysis (a description and analysis of all increased risks to the research subjects and how these risks will be minimized; a justification for the investigation; and a description of the patient population including the number, age, sex, and condition)
 - description of this device (a description of each important component, ingredient, property, and principle of operation of the device and any anticipated changes in the device during the investigation)
 - monitoring procedures (the sponsor's written procedures for monitoring the investigation and the name and address of each monitor.
 - additional records and reports (a description of any records or reports of the investigation other than those required in Subpart G of the IDE regulation).
4. A description of the methods, facilities, and controls used for the manufacture, processing, packing, storage, and installation of the device
5. An example of the agreement to be signed by the investigators and a list of the names and addresses of all investigators. Information that must be included in the written agreement are found in § 812.43

6. Certification that all investigators have signed the agreement, that the list of investigators includes all investigators participating in the study, and that new investigators will sign the agreement before being added to the study
7. A list of the names, addresses, and chairpersons of all IRBs that have or will be asked to review the investigation and a certification of IRB action concerning the investigation (when available)
8. The name and address of any institution (other than those above) where a part of the investigation may be conducted
9. The amount, if any, charged for the device and an explanation of why sale does not constitute commercialization
10. Please note that an environmental assessment as required under 21 CFR 25.40 or a claim for categorical exclusion under 21 CFR 25.30 or 25.34 is no longer required. [§25.34(g)]
11. Copies of all labeling for the device
12. Copies of all informed consent forms and all related information materials to be provided to subjects as required by 21 CFR 50, Protection of Human Subjects
13. Any other relevant information that FDA requests for review of the IDE application. Information previously submitted to FDA in accordance with Part 812 may be incorporated by reference.

This covers the same information that is asked for in form 1571.

Certification of Compliance (ClinicalTrials.gov) (FDA 3674)

All clinical trials under the FDA's supervision will be uploaded onto the ClinicalTrials.gov website under Title 21 Part 42. There are a few steps that need to be taken in order to have the trial posted. The first step in this process is to set up an ID and password to register the trial on the website by contacting Sherece Beasley-Ray at shereceb@BaylorHealth.edu. In addition to registering the trial, FDA form 3674 should be filled out to submit in the IND application. Certain details of the trial will be made available to the public on this website. The form can be found here or on the FDA's website at

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM048364.pdf>

In addition, there is another form titled "ClinicalTrials.gov Submission Form", which can be found on www.mybaylor.com page at Baylor Research Institute > Clinical Trials > Baylor Research Institute Clinical Trials Forms and here. This also needs to be completed and turned in to Sherece Beasley-Ray at BRI. The information will be entered into the clinicaltrials.gov website and checked by the investigator prior to becoming available to the public. The clinicaltrials.gov entry needs to be kept up to date as the trial occurs. It is suggested to update every six months. In addition to the updates, all final data must be entered to the website as part of the close out of the trial.

The International Committee of Medical Journal Editors (ICMJE) requires trial registration as a condition for publication of research results generated by a clinical trial. <http://www.icmje.org>. Trials initiated after 9/27/2007, or trials that are ongoing as of 12/26/2007 must be registered.

Statement of Investigator (FDA 1572)

Form 1572 is a legally binding contract between you, the principle investigator, and the FDA as required by Title 21 Part 312.53 for investigational drug studies. By signing you agree to adhere to the protocol described for the study. The form can be found here or on the FDA's website at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM074728.pdf>

There is no equivalent form for device trials. However, the sponsor or investigator is strongly encouraged to create a similar document to form 1572, containing the same information required in Title 21 Part 812

Financial Disclosure (FDA 3454 or 3455)

The FDA requires the principle investigator to fully disclose all financial interest (personal, spouse, and all dependent children) in the outcome of the study as described in Title 21 Part 54. There are two different forms, 3454 and 3455. Form 3454 is used when there is no financial interest in the outcome of the trial. Form 3455 is used when the outcome of the trial could financially benefit the investigator, the sponsor company has made payments to the investigator, or a proprietary or equity interest is held by the investigator. Both forms can be found on the FDA's website. Form 3454 can be found here or at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM048304.pdf> and form 3455 can be found here or at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM048310.pdf>

FDA Receipt of the IND

According to the FDA

“Upon receipt of the IND by FDA, an IND number will be assigned, and the application will be forwarded to the appropriate reviewing division. The reviewing division will send a letter to the Sponsor-Investigator providing notification of the IND number assigned, date of receipt of the original application, address where future submissions to the IND should be sent, and the name and telephone number of the FDA person to whom questions about the application should be directed. Studies shall not be initiated until 30 days after the date of receipt of the IND by FDA unless you receive earlier notification by FDA that studies may begin”



IRB Submission Checklist

New Study – Interaction with Subjects (submit via iRIS):

- Study Application (iRIS Web Based Form)
- Supplemental Application (Form 1 – Word Document)
- PI Signature Form (or PI may sign electronically)
- Administrator Signature Form
- Scientific Review Signature Form
- Consent Form(s) or Survey Cover Letter (See BRI Template)
- Protocol
- Investigational Drug Brochure (if applicable)
- Advertisements (if applicable)
- Any other supplemental documents that are used in execution of the study
- Any other written materials provided to the study subjects

In addition to the above documents, gather signed copies of IRB Form 14's for all members of the research team, scan and email to Cheryl.d@baylorhealth.edu. Make sure you include the IRB number on the forms (it is provided to you when you hit the submit button on the form).

In addition to the above documents, you are also responsible for submitting all funding paperwork to the Office of Sponsored Research. This includes not only grants and contracts, but the BHCS Foundation Funding or Departmental Support Forms. These forms can be found on the BRI website under Finance Forms and once completed must be submitted to Helena Jackson at BRI. She can be reached at 214-820-9904 or Helena.jackson@baylorhealth.edu.

New Study – Chart Review/Existing Specimens (submit via iRIS):

- Study Application (iRIS Form)
- Supplemental Application (Form 15 – Word Document)
- PI Signature Form (or PI may sign electronically)
- Administrator Signature Form
- Scientific Review Signature Form
- Protocol
- Any other supplemental documents that are used in execution of the study

In addition to the above documents, gather signed copies of IRB Form 14's for all members of the research team, scan and email to Cheryl.d@baylorhealth.edu. Make sure you include the IRB number on the forms (it is provided to you when you hit the submit button on the form).

Version 10/2011



FDA Submission Checklist

- ☐ Protocol and Standard Operating Procedures
- ☐ Letter of Approval from IRB
- ☐ IND/IDE form (Form 1571 or equivalent)
- ☐ Statement of Investigator (Form 1572)
- ☐ Financial Disclosure (Form 3454 or 3455)
- ☐ Certification of Compliance (Form 3674)



Appendix Contents

1. Protocol Templates
 - a. Simple
 - b. Detailed
2. Funding Search Form
3. Consent Forms
 - a. Survey Cover Letter
 - b. Short Form
 - c. Non-clinical
 - d. Clinical Trials
4. IRB Supplemental Application
5. PI Signature Form
6. Administrator Signature Form
7. Scientific Review Signature Form
8. Clinical Trials Listing Form
9. ClinicalTrials.gov Submission Form

SURVEY DOCUMENT

2012-194

IRB #:

Survey to Evaluate the New Operational Procedures for Submitting Investigator Initiated Research to an IRB

Name of Participant:

Date (MM/DD/YY):

Role in Study:

Phone # and/or email address:

Did you voluntarily follow the new operational procedures?

Approximate date you began using the toolkit:

Date your protocol was submitted to the IRB:

Date your protocol was reviewed by the IRB:

Date the IRB met:

Was it approved? (If “No” please write the reason and date of resubmission):

Was it tabled? (If “Yes” please indicate the number of times):

Date of final approval:

Was this your first Investigator Initiated Research proposal submitted to an IRB?

Was this your first Investigator Initiated Research proposal submitted to Baylor's IRB?

Was the toolkit provided useful in the navigation of the IRB approval process?

Detrimental				No Effect				Very Useful
1	2	3	4	5	6	7	8	9

What effect do you feel this toolkit had on the time from protocol development until IRB submission?

Lengthened Time Frame				No Effect				Shortened Time Frame
1	2	3	4	5	6	7	8	9

Would you recommend other investigator follow similar guidelines when submitting to an IRB?

Would advise against it				Indifferent				Would definitely advise it
1	2	3	4	5	6	7	8	9

Is there any additional information that should have been included in the guideline?

Is there anything that you would like to see changed in the guidelines for investigator initiated research?

UNTHSC OHRP-IRB DOCUMENTS



Office for the Protection of Human Subjects

DATE: 26 November 2012
TO: Patricia Gwirtz, PhD
(with CRM student Taylor Rutter)
Department of Clinical Research Management
Graduate School of Biomedical Sciences

PROTOCOL: #2012-194

"Evaluation of New Operational Procedures for Submitting Investigator Initiated Research to an IRB"

IRB BOARD ACTION AND NOTICE OF APPROVAL

The Institutional Review Board (IRB) of the University of North Texas Health Science Center (UNTHSC) has reviewed your protocol and has granted approval for **EXEMPT** status as specified in Federal Regulations 45 CFR 46.101 (b) category (2).

*** Please see attached for additional OPHS/IRB determinations ***

Note that you are responsible for complying with all UNTHSC IRB and OPHS policies, decisions, conditions and requirements regarding projects involving human subjects. You are responsible for insuring that the research is implemented as specified in the approved protocol. Unless otherwise authorized by the UNTHSC-IRB, you are responsible for notifying subjects that their participation and information will be used for research purposes. In addition, you are required to use **ONLY** the IRB approved documents, materials and/or process designated for this protocol.

You must report to the Chair of the IRB any changes affecting the protocol upon which this certification is based. **No changes may be made without prior approval by the IRB** except those necessary to eliminate immediate hazards.

If you have any questions, please contact Ms. Itzel Paola Pérez, Human Subject Protection Coordinator, at phone (817) 735-0673 in the Office for the Protection of Human Subjects, or send email to her at

Sincerely,

A handwritten signature in black ink, appearing to read "Brian Gladue".

Brian Gladue, PhD
Chair, UNTHSC Institutional Review Board

cc: I. Paola Pérez, OPHS

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