

OVERVIEW OF STUDY START UP ACTIVITIES FOR A CLINICAL TRIAL
AT AN INVESTIGATIVE SITE

INTERNSHIP PRACTICUM REPORT

Presented to the Graduate Council of the
Graduate School of Biomedical Sciences

University of North Texas

Health Science Centre at Fort Worth

in Partial Fulfillment of the Requirements

For the Degree of

MASTER OF SCIENCE

By

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Fort Worth, Texas

November, 2012

ACKNOWLEDGEMENT

I would like to express my cordial and humble thanks to Dr. Gwartz for her valuable guidance and support in completing this internship practicum. Solving the problems of the students has always been her priority. I would like to thank her for taking time out of her busy schedule to review my thesis. I am indebted to my on-site mentor Ms. Heema Marwah for giving me the training opportunity and introducing me to the various aspects of the clinical trials. She helped me in understanding the study start up process for a clinical trial and gave her inputs in completing this practicum research report. I am also grateful to my committee member, Dr. Robert Barber for his valued opinions and advice in completing this report.

I take this opportunity to express my sincere thanks to all the staff members of the ACRC Trials, Shirisha Chiluka (CRC), Raquel Layton (CRC), Raj Bhatia (Regulatory Specialist), Hardeep Marwah (Administrative Head), Aarti Gupta (Assistant CRC) for making my internship valuable and enjoyable. They have always helped me learning new things and solved my doubts whenever needed.

Heartfelt thanks to my friends Sushma, Rutika, Sahitya and Nikhil for their support and making this journey memorable.

I would like to thank my husband Amit whose unconditional love, support and encouragement have made this project possible. I remain indebt to my parents and in-laws for being my strength and source of inspiration. Last but not least I bow before Almighty for showering his blessings on me.

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CHAPTER 1

INTRODUCTION

Clinical trials are biomedical or health-related research studies using human subjects that investigate how well new medical approaches work in people. Each study answers specific scientific questions and attempts to discover better ways to prevent, diagnose or treat a disease.¹ Clinical trials are extremely important to the pharmaceutical industry for the development of new drugs or therapies. Every clinical trial has a protocol or action plan, for conducting the trial. The plan describes what will be done in the study, how it will be conducted and why each part of the study is necessary. The study start up phase of clinical trials is a very crucial and time-consuming component of the clinical study process.² A key challenge in conducting the clinical trials is that it spans so many different parties, including study sponsors, contract research organizations (CROs), site management organizations (SMOs), patient recruiters, investigators and patients. It is critical that sponsors, CROs and SMOs bring the right resources, tools and techniques to the clinical trial start up process to meet study start up timelines. It is important to streamline the start up from the beginning because it sets the pace for the study. Study start up activities includes assessment of site feasibility, negotiation of contract and budgets, planning for patient recruitment, legal reviews and approvals by Institutional Review Board (IRB) and/or ethics committee.³

The pharmaceutical industry is bestowed with an impressive history of blockbuster drugs, lifesaving medicines and new therapies that have enhanced our lives. But today pharmaceutical companies are facing intense financial pressure due to patent expiration on blockbuster drugs.

This has led the drug development costs and timelines to increase at alarming rates⁴. As a point of comparison, a new drug in 1960 could be developed in 8.1 years versus 15 years in 1990's.

Over the past 40 years, the cost of developing one drug development has escalated from a mere \$4 million in 1962 to an astounding \$800 million or more in today's market. Drug industry is facing challenges which include satisfying ever increasing consumer demands, following stringent rules and regulations in drug development and conducting clinical trials. These challenges are contributing to the delay in the process of bringing the drug to the market. On an industry-wide basis, clinical trials often fall behind their timelines due to delay in study start up.⁵ Thus, there is greater opportunity for an investigative sites and sponsors to evaluate better ways to optimize productivity by expediting the clinical trial start up process.

The internship practicum site, Advanced Care Research Center (ACRC) Trials, is a Site Management Organization (SMO) which provides services to the Contract Research Organization (CROs) and pharmaceutical companies in conducting successful phase II, III and IV drug trials. ACRC Trials has its own Standard Operating Procedures (SOPs) and checklists to expedite the study start up process. The general study start up activities at ACRC Trials include maintaining regulatory documentation, obtaining IRB approval for the study, negotiating budget and contract and preparing for the first patient first visit. The study start up activities also includes recruitment task like chart review of in-house patients, creation of recruitment materials like advertisements for local newspaper and radio, pocket inclusion and exclusion cards for PIs, study synopsis, phone screen synopsis, etc.

It is challenging on part of the investigative sites to meet the timelines of the study start up process because of the following factors:

- Communicating with sponsors, principal investigators (PIs), Institutional Review Boards (IRBs),
- Obtaining IRB approval,
- Maintaining regulatory documentation,
- Patient recruitment.

Each investigative site has its own SOPs for study start up. These SOPs ensures that the conduct of clinical trials is in compliance with Good Clinical Practice (GCP) and helps in adhering to the timelines of the study start up process. Hence, the aim of the internship practicum was to comprehend, describe and analyze the crucial study start up activities at the practicum site (ACRC Trials).

LITERATURE REVIEW

Success of the clinical trials irrespective of their size and complexity depends on efficient management. Efficient management warrants qualified personnel and business-like approach to the trial management. The conduct of a clinical trial involves huge investment of time and money and hence it should be managed from inception like any other business. The key challenges for pharmaceutical industries and CROs in conducting clinical trials are patient recruitment and retention, conducting trials as per International Conference on Harmonization (ICH) Good Clinical Practices (GCP) guidelines, finding GCP trained investigators, handling regulatory issues with specific country requirements, providing high quality data and meeting enrollment timelines, etc. There are limitations for patient and physician participation in the trial. The limitations to patient participation includes issues such as additional demands of the trial and concerns about information and consent while the limitations to the physician participation includes time constraints and concern about the impact on doctor-patient relationships. It is essential to establish and implement management systems and techniques that are effective in overcoming these challenges. Clinical trials require the coordinated processes and systems regardless of the size, scope, cost or duration of the study.⁶ Hence, numbers of pharmaceutical companies and CROs now choose to outsource their clinical trials to a more professional clinical research organization like SMOs.

A SMO is an organization that provides clinical trial related services to a CRO, pharmaceutical company, biotechnology company, medical device company and clinical sites. SMOs are emerging as the number of clinical research sites are increasing. The site is usually a hospital or a

similar health care institution that has adequate infrastructure and staff to meet the requirements of the clinical trial protocol. SMOs, in the traditional sense, were established to offer the sponsor consolidated services at the site level. SMOs have established themselves as a professional organization providing essential services to the sponsor or the CRO. SMOs offer PI recruitment, patient recruitment, regulatory, contract management for multiple sites and data management. SMOs can also provide the sponsor/CRO with multiple PIs and centralized contract and regulatory services. SMOs thus help in expediting the study initiation.⁸

SMO models vary widely in the industry. Some SMOs hire physician investigators as employees of the company. Others simply subcontract for the investigator services. SMOs that sub-contract investigators have the luxury of selecting the most appropriate investigators on a study-by-study basis. For example, if the study is for diabetes, the SMO is free to approach a diabetologist about the study. In addition, SMOs that retain coordinators that are strong clinically are the most equipped to be successful with this model. SMOs have made enormous contributions in overcoming several clinical hurdles that may be encountered throughout the conduct of the study⁸. The pharmaceutical industry and CRO's would greatly benefit working with SMO's for more productive research. The much apprehension regarding quality of data that is collected and time factor involved in the conduct of clinical trial can be reassured by working with a SMO. In summary, SMO plays a key role in bridging the gap between a research site and a sponsor/CRO and accelerating patient enrollment and taking trials to next phase faster.⁷

Clinical research sites execute trial protocols while providing the best patient care and experience, ensuring patient safety and gathering and providing accurate clinical data. Typically

research sites conduct multiple concurrent trials, in various stages from recruitment to trial close out. Simultaneous recruitment of patients meeting different criteria is necessary. Patients visits must be scheduled and take place within time window. Such ongoing activities at an investigative site may slow down the new study start up.⁹ It is well recognized by the investigative sites that the study start-up activities take more time and resources than should be required, and there are opportunities to gain efficiency while maintaining or increasing quality.¹⁰ The only way for investigative sites to achieve the objective of expediting the study start up process is by establishing and managing robust quality system with their integral quality documents including SOP.¹¹

The ICH GCP guideline defines a SOP as “detailed, written instructions to achieve uniformity of the performance of a specific function.”¹² SOPs specify in writing, who does what and when, or the way to carry out an activity or a process. SOPs establish a systematic way of doing work and ensure that work is done consistently by all persons who are required to do the same task. To be user friendly, they should be clear, unambiguous and must be written in plain language.¹¹ SOPs can improve communication among staff, reduce dependence on individuals with institutional knowledge and improve efficiency of staff training. The clinical research site that maintains and operates under SOPs demonstrates that it has a commitment to the research. For the sponsors who view SOPs as necessary administrative support, the efficient SOPs of the site may be the favorable attribute that gets the site through the selection process successfully.¹³

The SOPs embeds GCP in the conduct of the research activities and prevent errors from occurring, thereby minimizing wastage of time and resources. Well written SOPs can ensure

quality of the clinical data.¹¹ It is essential for sponsors of clinical trials, CROs and investigative sites to establish, manage and monitor their quality control and quality assurance systems through SOPs to provide high-quality services to the customers. Quality relates to the end products and services a company provides and the way the company employees do their job and the work processes they follow to produce products or services. SOPs ensure that the quality control and quality assurance system are regulated at an investigative site. A SOP establishes delegation of the responsibilities to the personnel involved in the research activity.^{11, 14} Top management of a pharmaceutical company, CRO and SMO should provide the training and an appropriate motivating environment to foster teamwork both within and across organizational units for employees to improve processes. ICH GCP guideline states that “ The sponsor is responsible for implementing and maintaining quality assurance and quality control systems with written SOPs to ensure that trials are conducted and data are generated, documented (recorded) and reported in compliance with protocol, GCP and the applicable regulatory requirement(s). Quality control should be applied to each stage of data handling to ensure all data reliable and have been processed correctly”. Investigative sites should have the arrangements to continually monitor and improve their quality management system to conduct successful clinical trials.^{12, 14}

CHAPTER 2

SPECIFIC AIMS AND SIGNIFICANCE

Specific Aim 1: To describe and analyze the regulatory documentation for clinical study start up at an investigative site.

Significance

Essential documents for a clinical trial are those documents that individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. These documents serve to demonstrate the compliance of the investigator, sponsor and monitor with the standards of GCP and with all applicable regulatory requirements. Filling out the essential documents at the investigator/institution and sponsor sites in a timely manner can greatly assist in the successful management of a trial by the investigator, sponsor and monitor. These documents are usually audited by the sponsor's independent audit function and inspected by the regulatory authorities as a part of the process to confirm the validity of the trial conduct and the integrity of data collected. This policy is based on the U.S Code of Federal Regulation (CFR), and the Standards for GCP, ICH E6.¹²

The importance of good documentation practice needs to be emphasized to investigator sites to ensure that the study results are built on the foundation of credible and valid data. One of the most common inspection findings in investigator site inspections is lack of reliable, accurate and adequate source documentation. This also happens to be the most common pitfall identified during sponsor audits. Clinical trial monitors and auditors also report documentation issues as a frequent area of GCP concern. Accurate documentation supports the fundamental principle of

protecting rights, safety and well-being of research subjects. Basic training in clinical research will definitely include these phrases:

1. “What is not documented is not done”; and
2. “Document what is done”
3. “Document what is not done.”¹⁵ Just as the data validates and or invalidates the study hypothesis; the documentation validates or invalidates the data. The only way for an outside person (such as sponsor, monitor or FDA inspector) to assess the quality of the study and its results is through the documentation.¹⁵

Specific aim 2: To describe and analyze the creation of recruitment material for the study start up.

Significance

Recruitment of research subjects to a study has almost always been a much greater problem than was anticipated by the investigator. Delays in recruitment have an impact on the cost and workload throughout the trial. Failure to recruit a sufficient number of participants could result in termination of a trial and loss of funding. One major problem in recruitment efforts is related to the lack of published information regarding recruitment. The type of recruitment source that is used may dramatically influence the response by potential subjects.¹⁶ Many studies have relied primarily or exclusively on physicians, hospital records or clinical laboratories for the recruitment of participants. But this approach has generally been unsuccessful if used alone. Two factors appear to be important in recruitment of subjects: increased community awareness (both physician and public) and active participation of the investigators or staff.

Identification, initial contact, screening and recruitment of potential human subjects form the foundation of the informed consent process. The research team, the study sponsor, and the IRB share the responsibility for making the recruitment process compliant with ethical and federal regulations. The recruitment material for study start up includes advertisements, flyers, telephone script, web postings, etc. Appropriate recruitment material can help make the recruitment process more efficient and ethically appropriate.

Specific aim 3: To describe the Clinical Research Coordinator (CRC) responsibilities during the study start up.

Significance

The CRC, regardless of their job title (study or site coordinator, data manager, research nurse, etc.), plays a key role in the clinical trial process. A well trained CRC can contribute significantly to the quality of the data collected. In fact, the two major advantages described in the literature of having a CRC involved in clinical trials are: (a) to increase recruitment rate and (b) to have good data quality. According to the Association of Clinical Research Professionals, the CRC works at a clinical research site under the immediate direction of a principal investigator, whose research activities are conducted under GCP.¹⁹ Among other tasks, CRC's perform site preparation, patient screening and recruitment, patient enrollment, conduct and ensure the quality of case report forms, maintain source documents, and ensure site quality. The main tasks of the CRC seem to be monitoring activities. In the implementation of clinical trials, the importance of the contribution of CRCs is now widely recognized.²⁰

CHAPTER 3

METHODOLOGY AND DESIGN

The main goal of this practicum internship was to provide a detailed summary of the start up process for a newly granted study. The following start up activities were analyzed in detail:

1. Regulatory documentation
2. Preparation of recruitment materials
3. Role of CRC in study start up

The above activities are explained within this practicum report with reference to migraine study start up at ACRC Trials.

The specific aims of this practicum project were focused towards answering the following research questions:

4. How do the SOPs help the investigative site to adhere to their timelines of the study start up?
5. How the GCP are followed during study start up?
6. What are the challenges faced by the site during the start up of a study?
7. What are the precautionary and corrective steps taken to overcome these challenges?
8. What is the online document management and exchange system used?
9. What is the procedure for Electronic Data Capture (EDC)?
10. How is communication with IRB, sponsors, CRO, PIs and staff maintained?
11. How are staff members trained?

The goal of the internship practicum was accomplished by reading SOPs, checklists and regulatory binders. The methodology also included developing and conducting a survey

questionnaire which was administered to ACRC Trials staff members. This survey gathered information regarding the duties and responsibilities of the ACRC Trials staff members during the study start up phase of a study. It also summarized the regulatory procedure each staff member has to follow during the clinical study start up. Thus, the survey questionnaire focused particularly on understanding the study start up activities at the ACRC Trials. The questions asked in the survey are shown below.

Questionnaire for ACRC Trials staff members

How do you initiate a new study start up task?

How do you plan and distribute the study start up task to staff members?

Does your site have SOPs for each study start up task?

Does your site have study start up checklist?

What is the online document management and document system used?

How do you communicate with PI for a new study?

How long does the site take to initiate the new study?

Questionnaire for regulatory personnel

What are your roles and responsibilities during a new study start up phase?

What are the initial regulatory documents sent by the sponsor to the site?

How are the regulatory documents submitted?

How is the initial regulatory binder prepared for study start up?

How is the process for obtaining IRB approval for a new study?

What is the method of document exchange between sponsor, site and IRB?

Questionnaire for CRC

What are your roles and responsibilities during a new study start up phase?

How do you prepare for pre study site visit and site initiation visits?

How are source documents created?

How do sponsor discusses the study procedures and requirements?

What training is required to be completed by the sponsor before starting a new study?

How do you plan to prepare for First Patient First Visit?

How are recruitment materials created?

How is study drug received and stored?

How is study material stored and labeled?

The Questionnaire was reviewed and approved by the IRB at University of North Texas Health Science Center. The approval by the IRB is shown in appendix D.

CHAPTER 4

RESULTS

The purpose of this chapter is to give an overview of the study start up SOPs followed at practicum site, ACRC Trials and discuss the specific aims of the practicum project. SOPs were studied with an aim to understand the working process of the site and role of the staff members in the study start up process. Survey questionnaire was prepared for ACRC Trials staff members to gather information needed to analyze and discuss the three specific aims of the practicum report. ACRC Trials staff member included two CRCs, one regulatory personnel and one Research Director. The responses of these staff members to the survey questionnaire was noted and information was gathered based on these responses to discuss the regulatory documentation for a study start up, recruitment material creation for a study start up and role of CRC in a study start up.

OVERVIEW OF STUDY START UP SOPs

These SOPs applies to all clinical research trials conducted at the ACRC Trials and all site personnel responsible for the conduct of clinical research trials. These SOPs are reviewed annually by ACRC Trials but may be reviewed more frequently if the site staff reported that it does not reflect the current operations.

SOP # 1 Title: Opportunity

Definition of study status “Opportunity” is initial study status prior to selection and submission.

Following a Confidentiality Agreement (CDA), the sponsor requests that the site complete a site questionnaire pertaining to specific study of interest. The final decision of site selection is still pending.

Procedures

1. Noting study status as “opportunity”

The study status is noted as “opportunity” on Clinical Trial Management System (CTMS).

CTMS is a web-based technology designed to manage the flow of activities starting with initial trial planning, study start up activities such as site selection, followed by study initiation once regulatory approvals are obtained, regulatory affairs, patient recruitment, scheduling visits and study close out activities etc. Minimum information of the study is updated on CC CTMS system.

The opportunity list is reviewed once a month to update the study statuses. Follow up information is requested from the Research Director to determine current status of the study. If the site is selected and the site decides to proceed with the study, the study status changes to “Submission”. A series of tasks is required to be completed to change the study status. If the site does not move forward with the study, the reason is noted on CTMS as follows:

- Cancelled: Study is no longer being pursued.
- Lost: Opportunity was not awarded. Study will not progress.
- Not selected: Opportunity was not chosen as a study to pursue
- On hold: Study progress has been suspended.

- Opportunity on hold: Opportunity has been placed on hold prior to the commencement of patient enrollment or visit scheduling
- PI declined: PI has declined to move forward with opportunity

2. Filing of CDA and site questionnaire

A. CDA

A yellow file folder is created using naming convention as “Sponsor name_Study Indication_Date”. This file folder is provided to the Research Director for filing.

B. Site questionnaire

- Server

Site questionnaire pertaining to a specific study of interest is saved on the server under the section labeled “Potential study Questionnaire”

- Folder

A manila file folder is created using the same naming convention as for CDA folder and the site questionnaire is stored in it. The folder is filed in filing cabinet for Potential Site Questionnaire and is filed by PI name.

Upon internal review, if the sponsor feels that the site may be suitable for the study, a Pre-Study Site Visit (PSSV) may be performed. The PSSV may be waived if the sponsor has recently conducted a study with the site.

SOP # 2 Title: Pre-study Site Visit

Procedures

Prior to selecting the site, the sponsor or CRO will conduct a PSSV. The PSSV may be via teleconference upon the Sponsor or CRO's discretion. Prior to the visit, the sponsor or CRO representative schedules an appointment with the site and confirms the appointment in writing. During the visit, the sponsor or CRO meets with the PI, the designated CRC and other study related personnel to briefly review the protocol/investigational plan, investigational product and plans for patient enrollment.

Prior to the sponsor or CRO visit, study related personnel should have an understanding of the protocol/investigational plan, investigational product and plans for patient enrollment. Study related personnel must make certain that they are available for the PSSV.

ACRC Trials site personnel ensure that the facility has adequate:

- Storage with documentation of the temperature logs,
- Appropriate equipment,
- Space and number of exam rooms,
- Access to emergency equipment,
- Monitoring space,
- Laboratory facilities (if applicable),
- If needed, equipment issues are discussed with the sponsor or CRO representative.

ACRC Trials site personnel ensure that the following tasks are completed prior to the study visit:

- Setting up an appointment time for the PI and the clinical research associate to meet and discuss the protocol and recruitment timelines,

- Reminding the PI the day before the appointment,
- Providing PI with the protocol summary, copy of Investigator Brochure and any other documents that have been provided by the sponsor,
- Setting up a brief meeting with the PI, if new to research, to review the documents and go over the PSSV process with him/her.

The following documents are to be provided via electronic or hard copy to the staff member responsible for the PSSV:

- Signed/dated, current curriculum vitae of PI,
- PIs license,
- Folder containing the study summary and study questionnaire that was completed during the initial study discussion.

The designated site representative accompanies the sponsor or CRO representative on a tour of the facilities. Site's method for collecting source data, informed consent procedures along with other SOPs as requested are reviewed with the sponsor or CRO representative. If the source data is collected electronically, the monitor's access to these records is discussed and documented.

The sponsor or CRO representative also meets with the PI at some point during the visit. The decision is made within specific time frame on whether the site has been selected for the study.

SOP # 3 Title: Study Initiation Procedures

Procedures

This SOP outlines the procedure for preparing for study initiation. The study initiation visit is a meeting conducted by the sponsor study monitor to inform the investigator(s) and study staff

about the details of study procedures. This meeting occurs after the pre-study site visit and selection of the investigator. A multitude of study start up tasks has to be completed prior to study initiation visit. These study start up task includes the following:

- Regulatory study submission and IRB submission task
- CRC tasks
- Advertisement/Recruitment tasks

Regulatory study submission and IRB submission task are discussed under SOP # 4: Regulatory Documents – Preparation and Maintenance. Sometimes pre-study visit and study initiation visit can be combined.

According to ICH GCP 8.2.20, the sponsor of a clinical study must carry out and document a trial initiation visit.¹² Following this visit and upon sponsor approval, the site can then begin to recruit subjects into the study. There may be delay in First Patient First Visit (FPFV) because of late arrival of study supplies, mainly lab supplies and study drugs.

Major activities that are discussed during the study-initiation visit are as follows:

- Study protocol (Study objectives, purpose, endpoints),
- Procedures,
- Reporting Adverse Events (AEs) and Serious Adverse Events (SAE),
- Investigational drugs (storage, dispensing, destruction, accountability),
- Inclusion/Exclusion criteria of protocol,
- Patient enrollment/ Recruitment and retention,
- CRF completion and error correction,

- Randomization procedures,
- Protocol compliance and deviation issues.

Study initiation visit

- The lead CRC or site manager schedule and arrange the initiation visit as requested by the sponsor representative at a mutually agreeable time. The site personnel is excused from other duties during the time of a site initiation visit. The PI is reminded one day prior to the meeting.
- Site initiation visit occurs in a conference or other private room to maintain confidentiality of materials provided.
- Participants include sponsor representative(s), PI, sub-investigator (SI), regulatory personnel, other clinical site research personnel, pharmacy and other institutional staff as indicated. Other staff may include the pharmacy, lab personnel, X-ray lab personnel, nursing staff, etc.
- The lead CRC or site manager arranges for appropriate audiovisual equipment necessary to complete the training (if applicable).
- If requested by the sponsor, the lead CRC or site manager schedules a tour of the facilities to be conducted during the initiation visit. The purpose of the tour is to confirm the availability of necessary equipment, adequate space to conduct the study, secure and limited access area for the study supplies and clinical trial material storage.
- If not provided by the sponsor, the lead CRC or site manager prepares an agenda to be distributed to all attendees that includes the date, time and location of the initiation visit.

- The lead CRC or site manager provides the copies of appropriate study-related materials to all meeting attendees.
- Each site participant prepares for the meeting by reviewing the protocol and noting areas of discussion or any questions.
- Each site participant is required to arrive, if possible, at least ten minutes prior to the scheduled start time of initiation visit.
- If possible, subject screening, randomization and enrollment procedures are reviewed in detail with sponsor representative(s).
- If possible, initial investigational product inventory will be reviewed with the sponsor representative(s). Investigational product storage, preparation, dispensation and accountability are reviewed with individual(s) who prepare and dispense clinical trial material.
- If possible and applicable, laboratory specimen collection, processing and shipping procedures are reviewed with individual(s) who process laboratory specimens and the sponsor representative(s).
- The lead CRC reviews the case report form completion guideline, monitoring procedures and expectations with the sponsor representative(s).
- The lead CRC confirms the following:
 - Who will submit the IND safety Reports? Sponsor or Site,
 - Query turnaround time,
 - Source to CRF transcription timeframe.

SOP # 4: Regulatory Documents – Preparation and Maintenance

4.1 Roles and responsibilities of the IRB

The IRB is a committee designated by an institution to review and approve biomedical research studies involving human subjects. The role of the IRB is to ensure that the rights safety and well-being of all study subjects are protected.¹² A committee comprised of individuals with varying backgrounds accomplishes this through a rigorous research review and approval process.

IRB membership

Collectively this group has the qualifications and experience to review and evaluate both the medical and scientific aspects of the protocol along with the ethical implications associated with the study.¹² Specifically the IRB membership includes the following:

- At least five members with varying backgrounds,
- At least one member whose primary area of interest is in a non-scientific area, usually a lay person or a member of the clergy to represent research subject's rights,
- At least one member who is independent of the institution/trial site and who is not part of the immediate family of a person who is affiliated with institution,
- A diversity of race and gender among its member,
- At least one member from the scientific community.

In the event an IRB member has a conflict-of-interest then that member may participate in discussion but cannot vote. A list of IRB members and their qualifications is maintained in the administrative study file.

Investigators as members of the IRB

The investigator or other key study personnel may serve as members of the IRB but they are not allowed to vote on the approval for a study in which they have a vested interest. Thus, the investigator or other study personnel may provide information on any aspect of the trial but they cannot participate in the deliberations of the IRB or in the voting process.

IRB review

An IRB has the authority to approve research, modify the research, and disapprove the research.¹² The IRB requires and ensures that all elements of informed consent be provided to research subjects. The IRB requires documentations of informed consent process.

The IRB is also responsible for periodically reviewing the study progress. This is done at least annually but may be done more frequently depending on the degree of risk associated with any given study. While the IRB meets formally during these periods to review the study, they are also updated throughout the course of the study. Such updates include the following:

1. New safety information, e.g., SAE reports,
2. Protocol changes or amendments,
3. Amendments to the consent form,
4. Amendments to the Investigator's Brochure,
5. Number of subjects entered,
6. Number of withdrawals and reasons for withdrawals,

It is important to consider that according to the regulations, the site may not change or deviate from the protocol without first obtaining written approval of the sponsor and IRB except when

the change is necessary to eliminate any immediate hazard to the subject or the change involve only logistical or administrative aspects of the study.

Expedited review procedures

Expedited review is a procedure through which certain kinds of research may be reviewed and approved without convening a meeting of the IRB. Expedited review may occur in the following circumstances:

- Research involving no more than minimal risk,
- The probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological exams,
- Minor changes in approved research.

This review may be carried out by the IRB chairperson or by one or more experienced members as designated by the chairperson.

IRB records and reports

ACRC Trials prepares and maintains adequate documentation of the following IRB activities:

- Copies of all research proposal reviewed, approved sample consent documents, progress reports submitted by investigators and reports of injuries to subjects,
- Minutes of IRB meetings in sufficient detail to show attendance at the meetings, action taken, the voting record and a written summary of the discussion of controversial issues and their resolution,
- Records of continuing review,

- A list of IRB members identified by name, degrees, experience and licenses, etc.
- Written procedures for IRB,
- Statement of significant new findings provided to subjects.

These records are retained as required after completion of the research. IRB committee have written procedures (SOPs) specifying how all of the required procedures will be executed and followed.

IRB-Sponsor-Investigator relationships

The regulations do not prohibit direct Sponsor–IRB contacts, although this interaction customarily occurs through the investigator. At times, direct communication between the IRB and the sponsor may facilitate resolution of concerns about study procedures or specific wording in an informed consent document. An investigator is apprised of this discussion. The regulatory personnel and CRC are integrally involved in managing and documenting correspondence with IRB and thus play a critical role in assuring both IRB and investigator complies with the regulations.

4.2 IRB protocol review and approval process

Evaluation of the protocol

When evaluating a given protocol, the IRB considers the following points

- What measures are in place to assure that risk to the research subjects are minimized?
- Are the risks reasonable in relation to the anticipated benefits?
- Will selection of subjects be equitable?

- Are the vulnerable populations (e.g. children, minorities, physically or mentally disabled, prisoners) not being coerced into participating?
- Have all subjects who could potentially benefit from the study have been given an equal opportunity to participate? For example, the IRB would want to make sure that non-English speaking subjects are not arbitrarily excluded because of perceived inconvenience in preparing translated documents or securing a translator.
- Has the investigator provided assurance that informed consent will be sought from each prospective subject or their legally authorized representative?
- Has the investigator provided assurance that informed consent will be obtained and documented appropriately?
- Are adequate measures in place to closely monitor the data collected, to ensure the overall safety of the research subjects?
- Are adequate measures in place to protect the privacy of the research subjects and maintain the confidentiality of the data?

Document review and approval

The following documents must be approved by the IRB:

- Protocol,
- Protocol amendments,
- Consent form(s),
- Advertisements used to recruit research subjects,
- Educational materials,
- Subject payments (amount and payout schedule).

Additionally the following documents are reviewed by the IRB but are not approved per se:

- Investigator's Qualification, e.g., curriculum vitae (CV)
- Investigator's Brochure,
- Sample of case report forms to assess extent of data collected and amount of effort required of subjects,
- Study grant to assess whether the investigator's financial stake may impact his/her ability to influence a subject participation,
- Annual reports describing the status of the investigation,
- Copies of safety reports for serious, related and unexpected adverse events occurring during the course of the study,
- Waivers.

Written notification and decision

An IRB notifies investigators in writing of its decision. If an IRB disapproves a research activity, it includes a statement of the reason for its decision and gives the investigator an opportunity to respond in person or in writing. The approval letter contains the following:

- The sponsor's protocol identification (title, number etc.),
- Which documents are being approved (e.g. protocol and consent, advertisements),
- Date the documents are approved,
- Approval or disapproval of the protocol and/or documents,
- Any modifications required prior to formally approving the protocol.

4.3 Regulatory documents and the regulatory binder

4.3.A The regulatory binder (Investigator's Study File)

The Investigator and sponsor are required to keep a complete set of study records (patient specific as well as general study records).¹² This allows all the data and the events of the trial to be re-created at a later point in time such as during a regulatory audit or when analyzing the data. The regulatory binder contains the entire general (non-patient specific) information relevant to the investigation. The regulatory binder is developed in conjunction with the monitor to ensure that both the site and sponsor have a complete set of study records. The regulatory binder may take the form of file folders, a 3-ring binder or some other type of filing system. It is imperative that the regulatory binder be set up in an organized fashion to allow rapid filing and retrieval of critical study documents. An additional regulatory binder is created with the discretion of the CRC. All original documents are kept in the investigator's regulatory binder and a copy is submitted to the sponsor. In this way both the sponsor's files and the investigators files are a mirror image of each other. If a section of the regulatory binder does not contain any information, then a note is placed under this section. If the regulatory binder is divided into several binders, then a note is kept in the original binder indicating where to find the other sections (e.g., section X can be found in volume II). If a document is too large for the binder then it is filed using another filing system and a note is written indicating the location of the document.

4.3.B Study Submission-Initial IRB Submission

Once the site has been selected to conduct a study, the sponsor or CRO forwards an initial regulatory documents packet for the site to review, complete and sign accordingly. This packet of documents normally consists of the following:

1. Cover letter and instruction sheet,
2. Protocol (with signature sheet),
3. Pre-completed or blank 1572,
4. Financial disclosure forms,
5. Investigator Brochure ,
6. Package inserts,
7. Proposed patient informed consent,
8. Central IRB justification letter.

Upon receipt of this packet, the protocol and necessary information is noted on an Initial Submission Regulatory Tracker. All the documents are reviewed and completed and if they are accurate, the PI signs the documents. The documents that require the PIs signature are as follows:

1. Form FDA 1572,
2. Protocol signature page,
3. IRB site questionnaire,
4. IRB additional site questionnaire,
5. Financial Disclosure Form,
6. Central IRB justification letter.

The documents are completed by the site and returned to the sponsor or CRO so that they may be submitted to the designated central IRB and/or local IRB for approval. At times the packet is submitted directly to the central IRB. Instructions for submission are outlines in the cover letter/Instruction sheet.

4.3.C Creating the regulatory binder

The regulatory binder is organized with all documents and approvals filed in the correct tabs.

Two regulatory binders are created for longer trials. The PI name and site numbers are noted on the outside of the binder.

The following tabs are included in the regulatory binder for filing initial study start up documents:

- **Form FDA 1572**

Most recent signed and dated Form FDA 1572 is kept in a sheet protector. Older versions are filed underneath (not in sheet protectors), with the most recent on top.

- **Investigator Brochure**

If it is the site's responsibility to print out the Investigator Brochure, upon sponsor approval, the the Investigator Brochure is downloaded to a disc and stored in the regulatory binder. The disc/CD is labeled with the version of the Investigator Brochure.

The CD label contains the following:

1. Version of Investigator Brochure,
2. Date CD was created,
3. Initials of who created the CD.

A new CD is generated for each Investigator Brochure, containing the updated version.

- **Protocol and amendments**

The Protocol with current version is kept on top of the older ones. Every new amendment to protocol is filed under this section.

- **Financial Disclosure Forms and CVs and licenses**

Signed and dated financial disclosure forms for all PIs, SIs and site related personnel listed on Form FDA 1572 are filed in regulatory binder. The CVs and licenses of all PIs, Sub-investigator (SIs), and CRCs are filed in regulatory binder. Upon Sponsor approval, the CVs and licenses may be downloaded to a CD.

The CD label contains the following:

1. Date CD was created,
2. Initials of who created the CD.

The Memo is filed alongside the CD. It includes the following:

- Name of all staff,
- Version dated of the CVs,
- Expiration dates of the licenses.

Any updates are added to a new CD/disc. A new memo to file will include all applicable information.

- **Site signature log**

Everyone listed on Form FDA 1572 is added to the site signature log and the CRC or regulatory personnel obtain the required signatures.

- **Informed Consent Form**

The current consent form is always placed in sheet protector. Upon receipt of a new consent form, the study staff is notified immediately. All outdated consent forms are removed from sheet

protector. The top middle section of the informed consent is stapled so that entire consent may not be copied. On the upper right hand corner of the first page, a note saying “DO Not Use” is written. A current copy of informed consent form is provided to the study coordinator for inclusion in the vertical file cabinet for specific study. No documents from the regulatory binder are shredded or thrown away. The documents always remain in the same tab even if it is not valid anymore.

4.3. D. Storing and retaining study documents

All essential study documents are maintained in a dedicated and secure area throughout the duration of the trial. This ensures that only authorized site personnel or the sponsor/CRO representative have access to the data and protects both the confidentiality of the subjects and proprietary information of the sponsor. Some sponsors require the documents to be kept in locked file cabinets while other sponsors may only require to be stored on a bookshelf on a locked office. All clinical research documents are available on a long term basis for review by sponsor representative, quality assurance auditors or regulatory authorities who may need to verify the data being used to support a New Drug Application (NDA). Essential documents should be retained until at least two years after the last approval of a marketing application according to ICH GCP guidelines. The documents are retained for a longer period if required by the applicable regulatory requirements or by an agreement with the sponsor. It is the responsibility of the sponsor to inform the investigator in writing as to when these documents are no longer needed to be retained

DISCUSSION

The first aim of this practicum project was to describe and analyze the regulatory documentation for clinical study start up at an investigative site. This goal was accomplished by reviewing SOPs, checklists and regulatory binders at the internship site, ACRC Trials. The study start up regulatory documentation is focused on migraine clinical trial conducted at ACRC Trials. A review of the regulatory documentation required an understanding of the regulatory process from the initial stage. Information regarding the regulatory documentation was gathered through observation and analysis of results from a survey questionnaire administered to the regulatory personnel, CRC and Research Director at ACRC Trials. The SOPs for regulatory documentation further helped in analyzing the process.

The initial contact for the study was through the Clinical Research Associate (CRA). The CRA provided the information regarding the study design and requirements. After reviewing the information provided, the site decided to participate in the study. Usually, the sponsor wants a Confidentiality Agreement (CDA) to be completed and signed by the investigator prior disclosing confidential information about the study. The CDA is a legal contract between investigator and sponsor to maintain the confidentiality of the study information. CDA is a precursor for any clinical trial. Without signing the CDA no sponsor will disclose the information included in the study protocol to an investigative site. Execution of CDA ensures the protection of confidential information of the study. However, ACRC Trials has a master CDA since it has conducted many studies with the same sponsor. Thus, it was not necessary in this case to sign a new CDA.

Based on the interest shown by the site, the sponsor sent a letter confirming the selection of the site for further screening process in the form of a site validation visit. Site validation is the next step taken by some sponsors to confirm the ability of the site to enroll the potential patients in the study. The following documents were enclosed with the confirmation letter:

- Site Validation Questionnaire,
- Medical Review Form,
- Site Validation Verification Form,
- Protocol Core & Summary,
- Confidentiality Investigator Brochure (CIB).

The confirmation letter stated that the final selection of the site would be based upon the ability of the site to access the appropriate patient population and willingness to work within the designated study timelines. Study timelines were included in the letter for site reference. The site was compensated for the time spent during the site validation visit.

After the site validation visit, the site was notified of their final selection by the sponsor through the site selection letter. The site selection letter included the randomization goal for the site i.e. the number of the patients needed to be randomized by the site. In addition the letter stated the projected timelines of the study, sponsor contact information and arrangements for site initiation visit and investigator meeting.

The projected timelines of the study stated the deadlines for first patient enrollment and last patient enrollment. Sponsor contact information included the name, telephone number and email address of the responsible personnel for various activities, such as general study execution,

urgent medical or patient consultation, non-urgent medical or patient consultation, budget/contract, consent form and IRB submission. The letter stated that the sponsor will be contacting the site to schedule the site initiation visit and gave the proposed date for investigator meeting. The enclosed documents included the following:

- Approved protocol,
- Investigator Site Information Form,
- Patient Consent Form.

Before scheduling the site initiation visit, the sponsor wanted the IRB submission task to be completed by the site. Thus, the letter was sent by the sponsor through Clinical Portal and Collaboration (CPAC), which included information about regulatory documents, study budget and the IRB submission process. CPAC is a sponsor portal that allows access to study documents, important announcements, surveys and exchange of study documents between the sponsor and an investigative site.

The Regulatory binder was sent to the site for maintaining the study documents. The Regulatory binder had the PI name and protocol number on it. All the original documents have to be maintained in the regulatory binder and copies are sent to be stored in the sponsor binder. The Regulatory binder serves as a tracker of the study activities and helps with monitoring the research. There were two regulatory binders with different sections. The first regulatory binder included the following sections:

- Financial Disclosure Forms,
- Form FDA 1572,

- CVs and Licenses,
- Sponsor contact Information,
- Protocol and Amendments,
- Regulatory authority/authorization/approval,
- IRB,
- Monitoring report,
- ICFs,
- Subject participation log and subject recruitment,
- Clinical supplies.

The sections included in the second binder were as follows:

- Correspondence,
- Data management,
- Serious Adverse Event,
- Training and certificate.

The following documents were required to be submitted to the sponsor as a part of study start up regulatory documentation:

- Partially completed FDA Form 1572,
- Protocol Signature Page,
- CVs of PI and SIs,
- Clinical Trial Research Agreement,
- Financial Disclosure Forms.

The letter from the sponsor gave detailed instructions for completing and submitting the above documents. IRB submission instructions included the name of the central IRB used by the sponsor and the contact information of the Patient Informed Consent Specialist. The site was asked to access the site submission requirements from the central IRB website and submit the site specific materials directly to the IRB. The protocol, investigator brochure, ICFs, study specific patient diaries were submitted by the sponsor for IRB approval. The site was asked to receive the IRB approval before using any advertisement or recruitment materials for the study.

Detailed description of the study start up regulatory documents

1. Site Validation questionnaire

The main purpose of this questionnaire was to evaluate the site based on the infrastructure, facilities, previous experience and potential patient database. It included four sections namely site assessment, protocol synopsis assessment, site expertise and infrastructure, and patient recruitment. The site assessment section gathered information regarding the equipment availability and the refrigerated storage facility at the site. The protocol synopsis assessment section asked the site to anticipate any challenges with the study performance pertaining to enrollment and retaining patients, budget and contract, approval from IRB and to provide solutions for the challenges. The site expertise and infrastructure sections included questions regarding involvement of the site in any other migraine studies or special programs which might affect the patient enrollment. The patient recruitment section was aimed at estimating the number of patients the site can enroll in the study based on inclusion and exclusion criteria. It included questions regarding patient chart review and number of patients who participated in previous migraine studies.

2. Medical Review Form

The Medical Review Form was a document used to perform a chart review of the patient against the key inclusion and exclusion criteria of the study. The inclusion and exclusion criteria was based on the age group, migraine onset age, number of migraine attacks, patient medical history, and medication and lab reports. On the basis of this Medical Review Form, the sponsor was able to get the documented estimate of the number of potential patients in the database of the site.

3. Site Validation Verification Form

The purpose of the Site Validation Verification Form was to document the time spent by site personnel for gathering information necessary to complete the Site Validation Questionnaire and Medical Review Forms. This form ensured fair reimbursement of the site for its time and effort to complete site validation activities. It required information such as investigator name, payee name of the site, contact name for payments, payment mailing address, telephone number, email address and estimated time spent by CRC/Research Director for completing site validation questionnaire and Medical Review Forms. This form required the signature of investigator and Clinical Research Associate (CRA) and was faxed to the sponsor after its completion.

4. Protocol core and summary

The Core Protocol described the objective, hypothesis, study design, duration, patient inclusion and exclusion criteria and statistical analysis plan. Summary of the protocol presented details of the rationale for the study design, sample dosage, route and dose regimen and study flow chart. Information included in the protocol helped investigators to understand the critical requirements of the study and estimate the number of potential patients in the database.

5. Confidentiality Investigator Brochure

The Investigator Brochure is a compilation of the clinical and nonclinical information related to the study medication. The Investigator Brochure provides an insight for the design of the protocol. The main purpose of this document was to provide confidential information of the investigational product to the investigator.

6. Investigative Site Information Form

The Investigative Site Information form was aimed at documenting the participation of the site in the migraine clinical trial. The first section of the form gathered the information of all the different addresses, such as 1572 address, patient treatment address, additional patient treatment address, correspondence address, drug shipment address, laboratory supplies shipment address and ancillary supplies/CRF shipment address. The 1572 address was for Box 1 of FDA Form 1572. This address corresponded to the investigator office location and was used to send IND safety reports and confidential information. Patient treatment address and additional patient treatment address corresponded to box 3 of the FDA Form 1572. The second section was “Study Site Personnel”. This section required the information of name, telephone number, fax number, email address of the primary study coordinator, backup study coordinator, SI, additional SI, regulatory contact personnel, financial contact personnel and drug supplies contact personnel. Completed Investigative Site Information Form was emailed to the responsible sponsor representative.

7. Patient Consent Form

The goal of the patient consent form was to provide every possible information regarding the study protocol to the patient so that he/she can decide whether to participate in a trial or not. The consent form contained the study title, sponsor name, protocol number, PI name and protocol version number on the first page. This was followed by the introduction, background, description and purpose, and detailed procedure of the study. This form also included the risk and benefit information of the study. Compensation for participation was clearly mentioned in the form. The form ended with a certificate of consent from the patient. This certificate was aimed at documenting that the patient understood the study details and is willing to voluntarily participate in the trial. End of the form included column for patient and PI signature.

8. FDA Form 1572

Form FDA 1572, also known as Statement of Investigator, is an agreement signed by the investigator to provide information about the clinical site and his/her qualifications to the sponsor. According to 21 CFR 312.53(c), an investigator cannot participate in clinical trial until he/she provides the sponsor with a completed, signed Form FDA 1572.²¹ The form was partially filled by the sponsor. This form contains nine blocks. Block 1 included the name and address of the investigator. Block 2 required the site to attach a CV or other statement of qualifications, showing the education, training and experience that qualifies the investigator as an expert in the clinical investigation of the drug. Block 3 was intended to identify the research facility where the study activities will be conducted. The name and address of clinical laboratory facilities used in the study was written in block 4, while central IRB information was included in block 5. The name and address of the central IRB responsible for the study was pre-filled by the sponsor.

Block 6 captured the information of the SIs who assisted the PI in conduct of the study. Block 7, which included name and code number of the protocol, was pre-filled by the sponsor. Block 8 included the requirements for phase I, phase II and phase III of the clinical trial. Block 9 included the commitments of the investigator. According to the commitments, it was mandatory for the investigator to comply with the requirements of informed consent form in 21 CFR Part 50 and IRB review in 21 CFR PART 56. It was the responsibility of the investigator to maintain adequate and accurate records in accordance with 21 CFR 312.62 and to make those records available for inspection in accordance with 21 CFR 312.68. At the end of the form dated signature of the investigator was required. FDA Form 1572 was emailed to the sponsor representative after completion.

9. Protocol Signature Page

The Protocol Signature Page was the certification by the investigator of compliance with the study protocol and standards of GCP. It gave the assurance that PI is responsible for reporting serious adverse events and maintaining the confidentiality of the Investigator Brochure.

10. CurriculumVitae (CV) of the PI and SI

The CVs of PI and SI were created as per the requirements of the sponsor. Each CV included the following information:

- Name,
- Education,
- Internship and residency, if applicable,
- Clinical research experience,

- Employment.

The CVs of PI and SI were uploaded through CPAC system used by the sponsor.

11. Clinical Trial Research Agreement (CTRA)

A Clinical Trial Research Agreement was sent to the site via email by the Global Agreement Specialist. The Clinical Trial Research Agreement is a budget contract agreement for a clinical trial. This document was signed by the head of the administrative office and sent to the sponsor for execution.

12. Research Site Submission Form

The Research Site Submission Form is a central IRB document which was mandatory for the site to complete and submit. The aim of this form was to document and gather information regarding the site, the qualifications of PI and SIs, the study execution plan, and the resources and infrastructure for the research. Questions in the first four sections of the form were related to the protocol number, sponsor name and address and correspondence address for the study. Section 5 pertained to previous clinical experience of the site, provision for maintaining confidentiality and privacy of the patient, document management system and resources for emergency care of the patients. Section 6 collected information regarding the research experience, education and training of the PI and SIs. Questions in Section 7 were constructed to compile and document the informed consent process and the payment schedule of the study. Section 7 was followed by subject recruitment and vulnerable group questions. Sections 10 and 11 gathered information regarding the financial interest and regulatory history of the site. The last section of the Research

Site Submission Form dealt with investigator certification and signature. The completed form was directly submitted to the central IRB.

13. Financial Disclosure Form

In accordance with U.S. Food and Drug Administration (FDA) regulation titled Financial Disclosure by Clinical Investigator (21 CFR Part 54), clinical investigators are required to provide information regarding financial interest and arrangements with the sponsor of clinical studies. The Financial Disclosure Form provided by the sponsor included five questions. These questions were framed to know whether the investigator had any equity, proprietary or financial interest with the sponsor or received any compensation. The form included certification of the investigator. The signed and dated form was scanned and faxed to the CRA.

The second aim of the practicum project was to describe and analyze the creation of the recruitment materials for the study start up. Survey questionnaire on creation of recruitment materials for a study start up were administered to the CRCs and Research Director. This questionnaire helped to understand the content, purpose and type of the recruitment material. The recruitment materials for the migraine clinical trial at an internship practicum site were examined. The study protocol was reviewed in detailed to get insight of the information incorporated in the recruitment materials. Assisting the CRC and recruiter in developing the recruitment materials helped to gain the knowledge of the rules and regulations governing the process. Recruitment materials which are created for a clinical trial serve the purpose of reaching the potential patients and helps in efficient recruitment. The recruitment materials created for the migraine clinical trial included the following:

- Advertisement for local newspaper
- Phone screen synopsis
- Phone study synopsis
- Pocket inclusion and exclusion cards

According to FDA regulations, direct advertisement for potential study subjects is the beginning of the informed consent and subject selection process.²³ It is the responsibility of the IRB to protect the rights and welfare of the research subjects. The IRB reviews the advertisement necessary to assure that the advertisement is not unduly coercive and does not give assurance of a cure beyond what is stated in the informed consent and the study protocol. IRB review of the information contained in the advertisement and the mode of its communication is also necessary to assure that the recruitment procedure is justified and does not claim favorable outcomes or other benefits not mentioned in the protocol. The IRB reviews the final copy of the printed advertisement in order to evaluate the relative size of the type used, visual effects and wording. Advertisement for recruiting patients in a drug, device or biologic trial should not include the following²³:

- Claim that the drug, biologic or device is safe or effective for the specified indication and/or equivalent or superior to any drug, biologic or device,
- Use terms such as “new treatment”, “new medication” or “new drug” without explaining that the test article is investigational,
- Promise to give free medical treatment when the intent is only to say that subjects will not be charged for taking part in the investigation. The advertisement may state that subjects will be paid for their time and travel but should not emphasize the payment or the amount to be paid by means such as larger or bold type.

According to the FDA, any advertisement to recruit subjects should only contain the information necessary to confirm the eligibility of the patients and can include the following information if precisely worded²³:

- The name and address of the clinical investigator and/or research facility,
- The conditions under study and/or the purpose of the research,
- The criteria that will be used to determine eligibility for the study,
- A brief list of participation benefits, if any (e.g. no cost health examination),
- The time and other commitment required by the subjects,
- The location of the research and the person or office to contact for further information.

The advertisement for migraine clinical trial was created for a local newspaper. The three essential inclusion criteria emphasized in the advertisement were as follows:

- Migraine onset age,
- Number of migraine attacks,
- Migraine history.

The lower portion of the advertisement contained the financial compensation for the time and effort of the participants, name of the investigative site, contact phone number and name of the website. The advertisement was used for recruiting the subjects only after the central IRB approval.

Pre-screening of the potential subjects through telephone contact to determine eligibility and interest in participating in a study is a common strategy for recruiting the patients. The telephone script aimed at collecting data directly from the subjects through the oral responses to questionnaire constitutes a part of the research activity and, therefore, requires IRB approval.

The purpose of the phone screen synopsis developed for the migraine trial was to determine the eligibility of the interested subjects for participating in the study. The phone screen synopsis included the opening comments for the recruiter to read followed by the prescreen questions. Prescreen questions were based on the specific inclusion and exclusion criteria of the study. Other questions included were related to the issues such as ability of the subjects to visit the site multiple times and the availability of transportation. If the eligibility of the patient was confirmed based on the prescreen questions, then the patient was scheduled for the screening visit at the site. If the patient did not qualify for the study based on the phone screen synopsis, then the personal information of the subject was retained only if the subject gave their permission.

The phone study synopsis was prepared with the objective to provide the study specific information in lay terms to the subjects. The following information was included in the study synopsis:

- Purpose of the study,
- Study duration,
- Procedures of the study visits,
- Requirements of the study,
- Details of the first visit/screening visit,
- Follow-up visits,
- Compensation for the time and effort of the participants.

The study synopsis included the information given to the subjects and, hence, required the IRB approval.

Pocket inclusion and exclusion cards were distributed to physicians to serve as a quick reference guide. Physician used these cards to identify potential in-house patient. Pocket inclusion and exclusion cards included the following information:

- Indication name,
- Drug name and category,
- Rescue medication,
- Duration of the study,
- Compensation given to the subjects for their time and effort,
- Specific inclusion and exclusion criteria,
- Name of the investigative site,
- Contact phone number,
- Name of the responsible personnel for contact,

The last aim of the practicum report was designed to describe the CRC responsibilities during the study start up. This aim was fulfilled by observing and assisting the CRC in a study start up of the migraine clinical trial at an internship site, ACRC Trials. Responsibilities of the CRC in a study start up were studied by examining the responses to the survey questionnaire prepared for the CRC and the Research Director. The survey method was used to obtain a complete overview of the role of CRC in a study start up. The CRC played a crucial role in study start up and served as a backbone for the success of the trial. The CRC was involved in managing and execution of the trial from its inception to the end.

After the site was selected for the migraine clinical trial, the CRC updated the basic information of the study, such as protocol name, number, PI name, and the IRB approval document onto the CTMS system. The study start up task was aimed at preparing the site for the site initiation visit by the sponsor. The CRC started the study start up task by reviewing the protocol in detail. It was necessary to understand the various aspects of the study such as rationale for the study, number of visits involved and procedures for each visit. The number of visits involved in the study was identified. The time interval for reminder calls and phone call visits was calculated and finally, a visit calculator was prepared for patient visits. This information was updated on the CTMS system.

The next important task of the CRC was to create source documents for the study. Source documents are created to capture the patient medical data during the study visits. The ICH E6 document, section 1.52, defines source documents as "Original documents, data and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects diaries of evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the clinical trial.¹²" The source documents were created from the electronic Case Report Forms (eCRFs) provided by the sponsor. ICH E6 1.11 defines CRF as "A printed, optical, or electronic document designed to record all of the protocol-required information to be reported to the sponsor on each trial subject.¹²" Source documents were designed to capture the patient data according to the visit procedures given in the protocol. The patient data included information

such as demographic information, family ethnicity history, medical records, migraine history, vital signs, concomitant medication and physical examination. Source documents served as a main source of the data to be reviewed by the study monitor. Arrangements were made to store patient source documents and all the other study related documents.

It was the duty of the CRC to create patient payment forms to make payments to the patients for their visits. IND Safety Reports submission process to the central IRB was confirmed from the sponsor and necessary action was taken. The trial site signature and responsibility log was completed. This log included the names of all the CRCs, PI, SIs and other personnel involved in the study along with their task responsibilities. The signatures of all the responsible personnel were taken on this log. Regulatory binder set up was checked with the help of regulatory personnel. Arrangements were made to store laboratory supplies, such as lab resupply order forms, visit requisition forms, study kits, patient diaries, study brochures, study equipment and patient handout items. Temperature controlled storage space was made available for storing the study medication. It was the responsibility of the CRC to gain access to the sponsor EDC system. It was mandatory for the CRC and PI to complete the training and certification for performing data entry, reporting serious adverse events and implementation of Future Biomedical Research (FBR). The central laboratory required the CRC to complete Electrocardiograph (ECG) training.

Another study startup task for the CRC included running a chart review for in-house patients (i.e., clinic patients) and making a list of potential patients for the study. A chart review was done based on inclusion and exclusion criteria of the protocol. A newspaper advertisement was also drafted for recruiting the patients. A study synopsis was created in lay terms to provide

necessary information about the study to the patients. The ICFs were reviewed and the consent process was discussed with the trial study team. A call list for potential patients was generated and kept ready.

The job responsibilities of the CRC in the study start up included preparing for the Investigator meeting. The Investigator meeting was a web based conference meeting where the sponsor explained study protocol requirements to the CRCs, PI and SIs. The objectives of the Investigator Meeting included the following:

- To review the scientific rationale and protocol overview,
- To review patient diary,
- To discuss statistical overview,
- To review the process for pharmacogenomics sample,
- To discuss patient recruitment and retention,
- To discuss protocol specific eCRF,
- To discuss ECG procedure,
- To discuss adverse events reporting procedure,
- To discuss laboratory specimen collection and handling,
- To discuss the packaging and shipping procedures for laboratory specimens.

The lead CRC conducted the meeting for all clinical trial team members of the site to discuss the timelines of the study, visits requirements, source documents, patient recruitment, inclusion and exclusion criteria. The study management plan was prepared and tasks were delegated to each personnel involved in the study.

The CRC made additional arrangements for the study initiation visit. The study initiation visit was scheduled with the sponsor representative. The PI was informed of the meeting schedule. The CRC was responsible for assuring that all the study starts up tasks were completed before the study initiation and that the site was ready for First Patient First Visit (FPFV). The agenda for the meeting was prepared and major areas of discussion were listed and provided to the meeting attendees. The study initiation visit occurred in conference room with sponsor representative. All the topics included in Investigator Meeting were reviewed. Areas of concern were discussed with the sponsor representative. The sponsor representative inspected the site facilities and arrangements for study initiation. Regulatory documents and IRB approvals were verified for the site. A tour of the facility was arranged for the sponsor representative. The sponsor representative discussed the protocol with the PI. After the study initiation visit, the site was ready to start scheduling patients and conduct FPFV.

CONCLUSION

The main goal of the practicum project was to describe and analyze the study start up activities for a clinical trial at an investigative site such as ACRC Trials. This goal was accomplished by analyzing the regulatory documentation, recruitment material and role of the CRC in study start up. The Research Director, regulatory personnel and CRC at ACRC Trials have significant roles in the study start up. Efficient study start up is a combined effort of the entire study team.

ACRC Trials is a SMO which provides services to sponsors and CROs. During the study start up the main objective of ACRC Trials is to adhere to the study timelines of the sponsor and follow GCP at each step of the study start up. These objectives are met through well-developed SOPs and a checklist for the study start up task, effective communication with the sponsor and within the staff members and an efficient management system. SOPs are must for an investigative site to meet the study timelines and provide quality service to the sponsor. SOPs serve as a guide map for a study team to work in a coordinated manner. ACRC Trials has its own SOPs and checklist for study start up tasks. These SOPs and checklist ensured the delegation of the study start up tasks to the responsible personnel. The checklist also helps the Research Director to keep a track of study start up activities completed.

The site has to overcome number of challenges and limitations in the study start up. The study start up task imparts an extra workload on the personnel who are involved in multiple ongoing studies. Any management system needs to balance the workload and workflow of the site during the study start up. Delays in the arrival of the study medication or study supplies, budget contract

approval, or IRB approval can be a limiting factor in the study start up. PIs are usually physicians and, hence, have a busy schedule. Thus, obtaining the PI signatures on the study start up documents can be another limiting factor for the study start up.

The study start up is a crucial part of any clinical trial. An efficient study start up can enhance the chances of a trial being successful and reduce the chance of a clinical trial failure. It can make the drug development process more cost effective and reduce the length of time required for drug development. Basic study starts up activities are common to all the clinical trials. If an investigative site optimizes and develops the SOPs for a clinical trial, irrespective of type and length of the study, then significant time and money can be saved. Saved resources can be used to make an investigative site more efficient in conducting and managing multiple trials.

Appendix A
Internship Experience

INTERNSHIP EXPERIENCE

As a part of the Clinical Research Management Program I completed my internship practicum at ACRC Trials. ACRC Trials is a SMO which provides services to the pharmaceutical companies and CROs in conducting successful phase II, III and IV drug trials. ACRC Trials has its office located at Legacy Medical Village in Plano, TX, which is a master-planned facility offering primary care with open-access to specialty practices and convenient services.

I was fortunate to work with experienced staff dedicated to quality research. My daily duties at practicum site included arranging source documents for patient visits, creating patient charts and updating it on CTMS system, maintaining temperature and enrollment logs, requesting patient medical records, handling and shipping the laboratory samples and assisting CRCs in their day-to-day tasks. I got opportunity to observe the clinical trials in various stages such as start up phase, enrolling active and close out phase. I was actively involved in study start up and close out phase of the study. I was able to analyze challenges and limitations in the start up phase of the clinical trial. Getting hands on filling out site questionnaires, IRB and FDA forms helped me to understand the regulatory documentation process for the study start up. I also assisted regulatory personnel in setting up and maintaining regulatory binders for various studies. As a part of recruitment process I drafted phone screen synopsis, advertisements, pocket inclusion and exclusion cards, study synopsis and preformed chart review to identify potential patients.

I got to see the practical application of the knowledge gained through the course curriculum. This helped me to develop an insight for the clinical research. I realized the importance of

management in conducting successful clinical trials in the true sense. My internship experience has given me a confidence to work professionally in the field of clinical research.

Appendix B
Daily Internship Journal

DAILY INTERNSHIP JOURNAL

Week 1

Monday 4 June, 2012

Introduction to staff members by Heema

Signed the confidentiality agreement

Scheduled the Advisory Committee meeting at the site

Reported the patient's messages in patient message booklet

Completed IATA (International Air Transport Association) training on shipping Hazardous materials. This included the following topics:

1. Overview
2. Classifying specimens
3. Packing and labeling specimens
4. Transporting and documenting Specimens
5. Training employees

Lab processing: Observed the handling and processing of blood and urine samples tubes.

Shipment of the samples: Observed the packaging of the specimen samples and shipment to respective labs through FedEx courier pick up or the lab courier pick up facility. Shipping confirmation was then reported on Shipping Confirmation Log.

Shipment receiving and confirmation: Received the trial drug shipment from the sponsor and cross checked the number of samples with their component ID. This was given to the responsible CRC. Drug shipment confirmation was sent to the sponsor.

Drug storage: Observed drug storage facility. Study medications are stored according to the study protocol number in cabinets with controlled temperature. Drug temperature log is maintained every day

Observed scheduling meeting on CTMS system

Creating patient chart: Observed making patient chart. It included patient's medical record release form, Driver's license and new patient information form

Observed faxing enrollment log to the sponsor

Tuesday June 5, 2012

Scanned the study documents

Completed the OSHA (Occupational Safety and Health Administration) training for healthcare.

It included the following topics:

- General safety
- Blood borne exposure
- Hazard communication
- TB infection control
- Biomedical waste

Read ICF for the various protocol

Processed the lab urine and blood samples, packed in the box and sent the samples to the laboratory. Reported the Fedex confirmation number on Shipment Confirmation Log

Collected information sponsor, CRO, SMO responsibilities

Introduced to the following regulatory documents:

- IRB approval documentation

- Site questionnaire
- Regulatory binder sent by the sponsor
- Investigator Regulatory Document checklist
- Form FDA 157
- Investigator Protocol Agreement
- CV of the PI
- Investigator Brochure form
- Introduced to the terms “randomized” and “screen failed”

Wednesday June 6, 2012

Kept ready the source documents for the next day’s patient visits

Observed the process for ambient and frozen shipping of the specimens

Scheduled a pickup with FedEx for the shipment

Read Informed consent form

Thursday, June 7, 2012

Prepared the patient chart

Prescreening call to a patient with Diabetic Neuropathy study: Observed calling to the patient from the recruiter company data and gathering information like patient name, email ID, phone no., date of birth, race, condition suffering from, medications, allergies etc.

Observed the following regulatory document processing:

- Received the modified ICD (Informed Consent Document) for extension study and approval letter for the over reactive bladder study

- Modified ICD scanned and saved in CTMS system so that can be accessed by the CRC
- Modified ICD kept in sheet protector in the regulatory binder and labeled
- Filled memorandum in response to the email from the study monitor

Friday June 8, 2012

Reviewed the Regulatory binder

Study start up activity: Helped in setting up the labeled folders for the study

Prepared and kept the patients charts ready for Monday to Wednesday visits.

Scheduled a FedEx courier pick up and reported in Shipment confirmation log

Week 2

Monday 11 June, 2012

Reported patient messages in patient booklet

Entered new patient form information in CTMS system and observed uploading of the forms to patient documents.

Faxed the enrollment log of the study to the sponsor

Observed the answering and submission of study start up questionnaire to the sponsor for the diabetes study

Tuesday 12 June, 2012

Reported patient messages in patient booklet

Entered patient information in CTMS system

Completed CTMS training session 3

Observed filling of the site questionnaire

Observed regulatory submission process

Kept ready the source documents for the next day's patient visits

Wednesday 13 June, 2012

Prepared new patient chart

Entered new patient form information in CTMS system

Discussed research proposal writing with on-site mentor

Observed lab processing of the specimens

Arranged the hanging folder for diabetic neuropathy study in the drawer

Thursday 14 June, 2012

Reported patient messages in patient booklet

Called FedEx and scheduled a courier pick up for lab specimens

Received study drug and inventoried it

Attended a meeting with on-site mentor regarding advertisements and regulatory documentation

Completed CTMS training session 4

Friday 15 June, 2012

Entered new patient information in CTMS system

Scanned new patient form and uploaded to patients documents in CTMS system

Processed the lab specimens and shipped to the laboratory

Week 3

Monday 18 June, 2012

Prepared patient charts for next day visits

Converted the CVs of the PIs and SIs to be sent to the sponsor

Faxed the enrollment logs to the sponsor

Observed the phone screen synopsis preparation

Tuesday 19 June, 2012

Prepared patient chart and entered the new patient form in CTMS system

Read phone screen synopsis and pocket inclusion and exclusion criteria for constipation study

Seen the procedure for patient chart review

Read medical review form to find the potential patients for the study based on their medical records.

Processed the lab specimen

Made copies of lab accreditations and kept in lab manual

Worked on CVs of the PI and SI

Wednesday 20 June, 2012

Worked on CVs of PI and SI

Confirmed the IRB approval for advertisements of the different studies

Shipped the laboratory specimen

Arranged the IRB approved and not approved advertisement on the server

Observed and helped in the following study start up task: Patient visit Instructions, label making, drawer set up and visit calculator

Observed and helped in the following study close out task: Archiving, retrieving ICF etc.

Thursday 21 June, 2012

Observed the entering of screening criteria into CTMS system for new diarrhea study

Received the temperature controlled shipment

Arranged the confidentiality agreement (CDA) and questionnaire in different folders and prepared labels for them

Friday 22 June, 2012

Helped in making phone screen synopsis

Shipped the laboratory specimens

Pulled out ICF and arranged them in numerical order (patient no.) for study close out

Kept ready patient chart for visits on Monday

Week 4

Monday June 25, 2012

Faxed the enrollment log of the study to the sponsor

Prepared the patient chart

Arranged the patient chart and ICFs for the study close out

Uploaded new patient form in CTMS system

Worked on thesis

Processed the visit 1 lab specimens for the allergy study and shipped the specimen

Kept ready patient charts for the next day visits

Tuesday June 26, 2012

Reported the patient messages in patient message booklet

Requested the medical records of a patient from the doctor

Pulled the patient's consent ICFs and arranged them in file folder for study close out. Kept the patient charts separately in baker box

Received the temperature controlled shipment and inventoried it.

Confirmed the request of patient medical record

Wednesday June 27, 2012

Reported the patient messages in patient message booklet

Requested the medical records of a patient from the doctor

Created the phone screen synopsis for constipation study

Faxed the medical record request form of the patient to the physician

Observed the phone screen synopsis preparation for irritable bowel syndrome study

Thursday June 28, 2012

Observed the study synopsis preparation for Diarrhea study

Discussed the research proposal with on-site mentor Heema

Arranged the study material like diaries, training confirmation for migraine study in drawer

Separated the ICFs from the source documents of the patients and filed them in new ICF binder as a part of study close out task for hypertension and diabetes study

Kept the source documents ready for next day patients visits

Friday June 29, 2012

Filled the regulatory documents in regulatory binder

Processed the laboratory sample for visit 1 of over reactive bladder study and shipped the laboratory sample

Created the study synopsis of migraine study for IRB submission

Kept the source documents ready for patients visits on Monday

Week 5

Monday July 2, 2012

Prepared the patient chart

Created textual advertisement for Migraine study

Faxed the enrollment logs of allergy study to the sponsor

Worked on research proposal

Kept patients charts and source documents ready for the next day's visit

Worked on obtaining IRB approval for practicum project

Tuesday July 3, 2012

Reported patient messages in message booklet

Arranged the ICFs of all the patients for the ragweed allergy close out study

Processed and shipped the ambient and frozen specimen for diabetes study to
Inventoried the allergy study kits for different visits

Wednesday July 4, 2012

Independence Day

Thursday July 5, 2012

Reported patient message in patient message booklet

Processed the lab samples of visit 1 for diabetes study which included ambient and frozen
sample shipment

Processed the ambient lab sample of visit 3 for diabetes study and shipped through FedEx

Entered the new patient form information in CTMS system

Friday July 6, 2012

Processed the visit 1 lab sample for hypertension study and shipped

Worked on research proposal and IRB submission form

Week 6

Monday, July 09, 2012

Reported patient messages in patient message booklet

Prepared the patient chart

Processed the laboratory specimen of visit 6 for diabetes study and shipped

Faxed the enrollment logs to the sponsor

Tuesday, July 10, 2012

Went to the University to submit IRB exempt category form

Wednesday, July 11, 2012

Reported patient message in patient message booklet

Processed the laboratory sample of visit 6 for diabetes type 2 study and shipped the specimen

Helped in arranging the study kit boxes according to vendor

Prepared the patient chart

Faxed the request for medical records of the patients to the clinics

Thursday, July 12, 2012

Reported patient messages in patient message booklet

Received and inventoried temperature controlled shipment of study medications for diabetes study

Processed the laboratory sample for visit 6 of diabetes study and shipped through FedEx

Went to Medical Centre of Plano for study close out task of the ragweed allergy study with the CRC

Prepared the patient chart and entered the new patient form information in CTMS system

Made corrections to the migraine study synopsis

Created pocket inclusion and exclusion card for migraine study

Friday, July 13, 2012

Reported patient messages in the patient message booklet

Discarded the laboratory specimen tubes from old kits for hypertension study

Prepared the patient chart for two patients and entered the new patient form information in CTMS system

Inventoried the study drug for asthma study

Processed the lab specimen for visit 1 of hypertension study

Scanned the patient payment forms for different studies and saved according to the protocol numbers and PI name

Week 7**Monday July 16, 2012**

Reported the patient messages in the patient message booklet

Faxed the enrollment logs to the sponsor

Scanned the patient payment forms for the different studies and saved according to the protocol number and PI number

Processed the laboratory specimen of visit 1 for diabetes type 2 study which included ambient and frozen shipment

Kept the source documents ready for the next day's patient visits

Tuesday July 17, 2012

Saved the scanned patient payment forms of various closeout studies on the server

Prepared the labels for document folders

Observed arranging of the flyers for the various studies

Worked on research proposal

Kept the source documents ready for the next day's patient visits

Wednesday July 18, 2012

Entered new patient form information in CTMS system

Inventoried study drug for hypertension study and checked the allergy study kits for expiry date

Inventoried the temperature controlled study drug for diabetes study

Observed the maintenance of temperature logs for the freezers

Processed the laboratory sample of visit 7 for the over reactive bladder study which included ambient and frozen shipment

Arranged the migraine study material like kits, shipment boxes, investigator manual in cupboard labels

Confirmed the inventory checklist for various close out studies and made the list of close out studies which did not have inventory checklist

Checked the allergy study kits for expiry date

Kept the source documents ready for the next day's patient visits

Thursday July 19, 2012

Prepared the patient chart and entered the new patient form information in CTMS system

Updated the temperature logs for the freezers

Filled the inventory checklist in the regulatory binders for various studies as a part of study close out task

Separated and stored the migraine study kits according to visit numbers.

Kept the source documents ready for the next day's patient visits

Filed the documents like Form FDA 1572, Investigator Brochure Confidentiality Agreement, Financial Disclosure Forms, IRB approval letters, new version of Informed Consent, packing content list and packing slips in the regulatory binder for migraine study

Friday July 20, 2012

Updated the temperature logs for the freezers

Processed the laboratory specimen of visit 2 for diabetes type 2 study which included ambient and frozen shipment

Processed the laboratory specimen of visit 11 for hypertension study and shipped through FedEx

Made the changes to phone screen synopsis and study synopsis for migraine study as per the IRB requirement

Filled the IRB approval letters and recruitment materials for migraine study

Week 8

Monday, July 23, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Faxed the enrollment logs for allergy study to the sponsor

Saved the IRB approved phone screen synopsis with approval letter on the server

Arranged and separated the recruitment material for the migraine study as IRB approved and non-IRB approved on the server

Added the names of PI, SIs and myself with responsibility codes on the responsibility log for migraine study

Kept the source documents ready for the next day patient visits

Tuesday, July 24, 2012

Updated the temperature logs for the freezers

Saved the IRB approved print advertisement, phone screen and study synopsis for the migraine study on the server

Started the CPAC training data entry and eSignature

Processed the laboratory specimen of visit 6 for diabetes study and shipped the specimen

Filed the translated ICF for the irritable bowel syndrome (Diarrhea) study in the regulatory binder

Filed the IRB approval letters for recruitment materials of migraine study in the regulatory binder

Wednesday, July 25, 2012

Processed the laboratory specimen of visit 4 for the diabetes study which also included frozen sample

Updated the temperature logs for the freezers

Kept ready the source documents for the next day patient visits

Continued with the CPAC data entry training

Week 9

Monday, July 30, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Faxed the enrollment logs for allergy study to the sponsor

Processed the laboratory specimen of visit 9 for hypertension study and shipped the specimen

Scanned patient payment forms for the archived trials and saved on the server

Pulled out and uploaded the study close out documents like site status report. Close out confirmation visit letter and enrollment logs on the CTMS system

Confirmed the IRB approved advertisements for various studies and named accordingly

Tuesday, July 31, 2012

Went to the University

Wednesday, Aug 1, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Filled the new informed consent form for the diabetes study in the regulatory binder and also saved on the server

Made patient chart and updated the information on CTMS system

Performed study close out task for allergy study

Processed the laboratory specimen of visit 7 for over reactive bladder study

Read investigator visit report for the migraine study

Thursday, Aug 2, 2012

Did not go to internship site due to health issue

Friday, Aug 3, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Created login account for completing sponsor data entry training for migraine study

Arranged the IRB advertisement according to their approval dates

Filed the regulatory documents in regulatory binder

Kept ready the documents for study start up submission task

Thursday, July 26, 2012

Reported the patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept the source documents ready for the next day patient visits

Kept the Investigator Brochure CD in regulatory binder as per the sponsor requirement for the migraine study

Saved the study close out documents like site signature & responsibility logs, principal investigator site closeout report, subject participation log for the ragweed allergy study in CTMS system

Friday, July 27, 2012

Kept the source documents ready for the next day patient visits

Updated the temperature logs for the freezers

Pulled out close out documents like subject participation log, final enrollment status alert,

Principal Investigator site closeout report, IRB approval notice for protocol from ragweed allergy study regulatory binder and scanned and saved on the server

Filled the IRB documents in irritable bowel syndrome study regulatory binder

Processed the laboratory specimen of visit 12 for the cholesterol study which included ambient and dry ice shipment

Week 10

Monday, Aug 6, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Faxed the enrollment logs for allergy study to the sponsor

Processed the laboratory specimen of prescreen visit for diabetes study and shipped the specimen

Filled in IRB site information questionnaire and additional site questionnaire

Uploaded the patient payment forms on CTMS system

Tuesday, Aug 7, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Uploaded the patient payment forms on CTMS system

Added the new patients in database according to their indications

Completed the sponsor data entry training and filled the completion certificate in regulatory binder of migraine study

Wednesday, Aug 8, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Processed the laboratory specimen of visit 5 for diabetes study and shipped the specimen

Filed the dear doctor letter in regulatory binder and saved on server

Helped CRC in compiling the dates on patient visits

Read the study start up SOPs for writing the practicum report

Thursday, Aug 9, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Created CV for SI in the required format

Uploaded the Patient payment forms on the CTMS system

Friday, Aug 10, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Worked on thesis writing

Processed the laboratory specimen of visit 2 for diabetes study and shipped the specimen

Filed the new Form FDA 1572 for the study since the CRC left the study

Week 11

Monday, Aug 13, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Faxed the enrollment logs for allergy study to the sponsor

Compiled the ICFs of the patients for the study close out of diabetes study

Processed the laboratory specimen of visit1 for hypertension study and shipped the specimen

Read study start up SOPs and investigator visit report

Filed the inventory checklist, ICF location memo and long term storage contact person memo

Tuesday, Aug 14, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Filed the dear doctor letter in the regulatory binder

Created the CV for PI in required format

Performed study close out task for allergy study

Read study start up SOPs

Wednesday, Aug 15, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Filed the subject diary confirmation of migraine study in regulatory binder

Arranged the IRB approved advertisement on the server

Performed the study close out task

Thursday, Aug 16, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Filed the migraine study documents in regulatory binder

Performed study close out task

Assisted CRC in arranging the study medication

Worked on thesis writing

Friday, Aug 17, 2012

Went to the University to fill Curricular Practical Training (CPT)

Week 12

Monday, Aug 20, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Faxed the enrollment logs for allergy study to the sponsor

Filed the IRB approved advertisement and protocol clarification letter for the migraine study in regulatory binder

Made patient chart and updated the information on CTMS system

Tuesday, Aug 21, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Saved the current license of the PI on the server

Helped the CRC in shipping back the study supplies for a close out study

Made patient chart and updated the information on CTMS system

Scanned the various training certification for old and new employees and saved on the server

Filed the new version of ICF for migraine study in the binder and provided the copy to the CRC

Wednesday, Aug 22, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Filed new ICF for allergy study and provided the copy to the CRC

Scanned the remaining training certification for old employees and saved on the server

Created folder for arranging CDA and site questionnaire

Made patient chart and updated the information on CTMS system

Thursday, Aug 23, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Filed new ICK for allergy study in the binder and kept the copy in source documents

Attended the meeting conducted by CRC to discuss the migraine study visits requirements

CRC discussed the migraine study protocol and assigned the task of arranging source documents and patient diaries and questionnaires

Friday, Aug 23, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Processed the laboratory specimen

Week 13

Monday, Aug 27, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Faxed the enrollment logs for allergy study to the sponsor

Performed chart review for identifying potential in-house patients for children allergy study

Arranged the CDA and site questionnaire and submitted to the CRC

Tuesday, Aug 28, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Observed data entry on eCRFs for migraine study

Ordered the genetic kit sample for migraine study

Completed the site questionnaire for gout study

Processed the laboratory specimen for diabetic neuropathy study and arranged for dry ice from the courier service to ship frozen sample

Wednesday, Aug 29, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Filed the study documents in the binder

Thursday, Aug 30, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Performed chart review for identifying potential in-house patients for children allergy study

Friday, Aug 31, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Processed the laboratory specimen of visit 1 for hypertension study and shipped the specimen

Made the patient chart and updated the information on CTMS system

Created CDA file folder and provided to the CRC

Completed the site questionnaire for asthma study

Week 14

Monday, Sep 3, 2012

Labor Day Holiday

Tuesday, Sep 4, 2012

Went to the University for Literature Review of the thesis topic and for paper work of F1 visa

Wednesday, Sep 5, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Completed the additional facility site information questionnaire for allergy study

Made patient charts and updated the information on CTMS system

Filed the regulatory documents in the binder

Thursday, Sep 6, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Completed site information form the upcoming study and submitted to the Research Director

Arranged the patient charts with proper labels

Performed study close out task

Filed print advertisement approval in the binder and saved the new Spanish consent for the diabetes study on the server

Friday, Sep 7, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Assisted CRC in laboratory specimen handling and arranging source documents for migraine study

Week 15**Monday, Sep 10, 2012**

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Arranged the study kits in the laboratory

Filed new ICF for allergy study

Worked on thesis writing

Observed the informed consent process for migraine patient and noted the study information given to the patient

Tuesday, Sep 11, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Wednesday, Sep 12, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Filed the regulatory documents in the binder

Assisted CRC in discarding expired kits for heart attack study and arranged the new study kits

Completed the subject identification log with patient phone number, initials, birth date and randomization number and submitted to the study monitor

Thursday, Sep 13, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Arranged the study material for constipation study

Processed the laboratory specimen of visit 6 for heart attack study and shipped the specimen

Made arrangements for storing source documents, patient payment forms, enrollment logs, ICF for new constipation study and labels for study bin

Friday, Sep 14, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Filed the training certificate of old and new employees in the binder with their name tabs

Separated the patient charts for screen failed and randomized patients for hypertension study and stored in the study bin

Week 16

Monday, Sep 17, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Faxed the enrollment logs and data clarification form to the sponsor

Made the patient chart and updated the information in CTMS system

Read the study start up SOPs

Made arrangements for storing study supplies and set up bins for new upcoming studies

Tuesday, Sep 18, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Stored the CDA in labeled file folder and submitted to the CRC

Filed the IRB site questionnaire for new upcoming diabetes study

Filled the Form FDA 1572 for a new diabetes study

Complete the Financial Disclosure Forms for PI and SIs listed on Form FDA 1572

Worked on thesis writing

Processed the laboratory specimen of visit 1 for migraine study and shipped the specimen

Set up study bin for diabetes study and made arrangements for storing study bin

Wednesday, Sep 19, 2012

Filled additional site questionnaire for new diabetes study

Ordered the laboratory kits for migraine study

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Thursday, Sep 20, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Completed the site questionnaires for study start up

Discussed the outline of the thesis with Heema

Filled the site questionnaire and submitted to Research Director

Made list of the day care centers for kids in Plano and submitted to the Research Director

Friday, Sep 21, 2012

Processed the laboratory sample of visit 1, 2 and 3 for migraine study and shipped the specimen

Assisted CRC in visit 1 of migraine study and observed the blood draw

Completed the list of day care for kids in Plano

Performed data entry in eCRF for migraine study

Week 17**Monday, Sep 24, 2012**

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Faxed the enrollment logs for allergy study to the sponsor

Processed the laboratory specimen of visit 4 for diabetic neuropathy and shipped the specimen

Set up the regulatory binder for new constipation study

Processed the laboratory specimen of visit 2 for migraine study and shipped the specimen

Tuesday, Sep 25, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Created an email for giving information of current enrolling studies to the new patients in database

Filed the regulatory documents in the binder

Performed the data entry in eCRF of migraine study

Wednesday, Sep 26, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Processed the laboratory specimens of different visits for hypertension, migraine and diabetes study and shipped the specimens

Filled the new ICF in the binder

Made patient chart and updated the information in CTMS system

Arranged the patient chart for children allergy according to the randomization number

Thursday, Sep 27, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Friday, Sep 28, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Completed the study feasibility questionnaire for over reactive bladder and intrauterine contraception study

Processed the laboratory specimen of visit 1 for migraine study and shipped the specimen

Received the new patient phone calls and gathered the basic information

Filed the regulatory documents for constipation study in the binder

Week 18

Monday, Oct 1, 2012

Went to the University to complete paper work for Optional Practical Training (OPT)

Tuesday, Oct 2, 2012

Performed the chart review for children allergies to identify potential in-house patients

Processed the laboratory specimen of visit 1 for migraine study and shipped the specimen

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Filed the regulatory documents in the binder for various studies

Made patient charts and updated the information in CTMS system

Stored CDA in labeled file folder and submitted to the CRC

Wednesday, Oct 3, 2012

Went to the University to confirm the submission packet for OPT and also scheduled the room for the defense

Thursday, Oct 4, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Made patient charts and updated the information in CTMS system

Filed the regulatory documents in the binder

Arranged the migraine study kits in the laboratory and filed the shipment confirmation in the binder

Filed new Spanish consent for diabetes study and saved on the server

Processed the laboratory specimen of visit 1 for diabetes study and shipped the frozen and ambient specimens

Friday, Oct 5, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Performed the chart review for children allergies to identify the potential in-house patients

Responded to the laboratory query for diabetes study

Stored the CDA in labeled file folder and submitted to the CRC

Made patient chart for allergy study and uploaded the skin test in CTMS system

Performed data entry in eCRF for migraine patient

Worked on site information documentation of endometriosis study

Week 18

Monday, Oct 1, 2012

Went to the University to complete paper work for Optional Practical Training (OPT)

Tuesday, Oct 2, 2012

Performed the chart review for children allergies to identify potential in-house patients

Processed the laboratory specimen of visit 1 for migraine study and shipped the specimen

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Filed the regulatory documents in the binder for various studies

Made patient charts and updated the information in CTMS system

Stored CDA in labeled file folder and submitted to the CRC

Wednesday, Oct 3, 2012

Went to the University to confirm the submission packet for OPT and also scheduled the room for the defense

Thursday, Oct 4, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Made patient charts and updated the information in CTMS system

Filed the regulatory documents in the binder

Arranged the migraine study kits in the laboratory and filed the shipment confirmation in the binder

Filed new Spanish consent for diabetes study and saved on the server

Processed the laboratory specimen of visit11 for diabetes study and shipped the frozen and ambient specimens

Friday, Oct 5, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Performed the chart review for children allergies to identify the potential in-house patients

Responded to the laboratory query for diabetes study

Stored the CDA in labeled file folder and submitted to the CRC

Made patient chart for allergy study and uploaded the skin test in CTMS system

Performed data entry in eCRF for migraine patient

Worked on site information documentation of endometriosis study

Week 19**Monday, Oct 8, 2012**

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Faxed the enrollment logs for allergy study to the sponsor

Discarded the expired study kits and made space for new study kits

Tuesday, Oct 9, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Performed the chart review for children allergies to identify the potential in-house patient

Attended the staff meeting for new diabetes study which included discussion of protocol, visit procedures and phone screen synopsis

Performed the study close out task for hypertension study

Processed the laboratory specimen of visit 1 for hypertension and diabetic neuropathy study

Wednesday, Oct 10, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Helped the CRC in arranging the study kits

Scanned and saved the new patient forms and medical records

Completed inventory checklist for study close out task and filed in the binder

Thursday, Oct 11, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Scanned and saved the new patient forms and medical records

Made the patient chart and updated the information on CTMS system

Filed the new ICF for diabetic neuropathy study and provided the copy to the CRC

Faxed the medical records release form for the patients

Processed the laboratory specimen of visit 8 for diabetes study and shipped the specimen

Filed the IND safety reports in the binder

Friday, Oct 12, 2012

Went to the University to submit intend to defend form and discussed the thesis writing with

Dr. Gwartz

Week 20

Monday, Oct 15, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Faxed the enrollment logs for allergy study to the sponsor

Filled the Form FDA 1572, Financial Disclosure Forms, Site Questionnaire, additional site questionnaire for pediatric allergies and submitted to the Regulatory Specialist

Discussed the SOPs, study start up chart and regulatory documents with Heema for writing the thesis

Tuesday, Oct 16, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Processed the ambient and frozen laboratory specimen of visit 3 for diabetic neuropathy study and shipped the specimen

Completed the site assessment questionnaire for the new study and submitted to the Research Director

Processed the laboratory specimen of visit 9 for hypertension study and shipped the specimen

Filled the IRB approved advertisement, IRB site questionnaire in the binder

Wednesday, Oct 17, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Processed the laboratory specimen of visit 1 for diabetic neuropathy study and shipped the specimen

Created CV for new CRC in required format

Filed the Form FDA 1572 and Financial Disclosure Forms for new pediatric allergy study

Thursday, Oct 18, 2012

Sent an email blast to the patients in database to give updates of new enrolling active studies

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Worked on compiling PI and SI information such as name, expertise, License number and expiration date of license required for completing site questionnaires and Form FDA 1572

Made patient chart and updated the information in CTMS system

Friday, OCT 19, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Ordered the study supplies for migraine study

Made patient chart and updated the information in CTMS system

Processed the laboratory specimen of visit 3 for migraine study

Week 21

Monday, Oct 22, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Requested the medical records of the patient

Discussed with the CRC the specimen handling and shipping for the new diabetes study and processed the ambient, frozen and refrigerated laboratory specimen of visit 1

Tuesday, Oct 23, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Checked the inventory and ordered the study kits for diabetic neuropathy study

Filed the new ICF for diabetes study

Made patient charts and updated the information in CTMS system

Worked on filling the IRB site questionnaire for new gout study

Wednesday, Oct 24, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Worked on thesis writing

Thursday, Oct 25, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Worked on creating template for filling the site questionnaire

Worked on thesis writing

Friday, Oct 26, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Worked on creating template for filling the site questionnaire

Performed the chart review for the children allergy study to identify the potential in-house patients

Week 22**Monday, Oct 29, 2012**

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Faxed the enrollment logs to the sponsor

Processed the laboratory specimen of visit 4 for the diabetic neuropathy study and shipped the specimen

Processed the laboratory specimen of visit 1 and visit 3 for the migraine study and shipped the specimen

Filed the study status report in the regulatory binder for the diabetes study

Created the patient chart and updated the information on the CTMS system

Tuesday, Oct 30, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Faxed the enrollment logs to the sponsor

Created the patient chart and updated the information on the CTMS system

Arranged the IRB approved advertisements on the server

Worked on the study close out task and created the ICF binder

Wednesday, Oct 31, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Thursday, Nov 1, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Worked on study close out task

Filled the study status report for the asthma study

Processed the laboratory specimen of visit 3 for the migraine and visit 4 for the diabetes study

Filled the site questionnaire for the migraine study

Worked on the defense presentation

Friday, Nov 2, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Created the patient chart and updated the information on the CTMS system

Processed the laboratory specimen of visit 1 for the diabetes study and visit 1 for the hypertension study

Filled the regulatory documents in the study binder

Week 23**Monday, Nov 5, 2012**

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Faxed the enrollment logs for allergy study to the sponsor

Arranged the laboratory kits and the study supplies for the diabetic neuropathy study

Placed an order for visit 1 kit and butterfly needle for the diabetes study

Created the patient chart and updated the information on the CTMS system

Processed the laboratory specimen of visit 3 for the diabetic neuropathic study

Edited the practicum report

Tuesday, Nov 6, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Faxed the enrollment logs for allergy study to the sponsor

Performed chart review to identifying potential patients for the children allergy study

Processed the laboratory specimen of visit 1 for the diabetes study and shipped the specimen

Assisted the CRC in the patient visit

Completed the OSHA training and the quiz

Wednesday, Nov 7, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Performed the chart review to identify the potential patients for the children allergy study and updated the information on the outlook calendar

Filed the IRB re-approval notice for the allergy study

Processed the laboratory specimen of the visit 1 for the hypertension study and shipped d the specimen

Thursday, Nov 8, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Worked on study close out task

Filed the regulatory documents for the various

Performed the chart review to identify the potential patients for the children allergy study and

updated the information on the outlook calendar

Filed the new ICF for the constipation study and replaced in all the patient's chart

Friday, Nov 9, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Filled the regulatory documents in the binder

Processed the laboratory specimen of visit 1 for the hypertension study

Week 24

Monday, Nov 12, 2012

Went to the University to give a mock presentation of the practicum report

Tuesday, Nov 13, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Processed the ambient, refrigerated and frozen laboratory specimen of visit 1 for the diabetes study and shipped the specimen

Faxed the enrollment logs to the sponsor

Wednesday, Nov 14, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

Worked on the presentation of the practicum report

Thursday, Nov 15, 2012

Reported patient messages in the patient message booklet

Updated the temperature logs for the freezers

Kept ready the source documents for the next day's patient visits

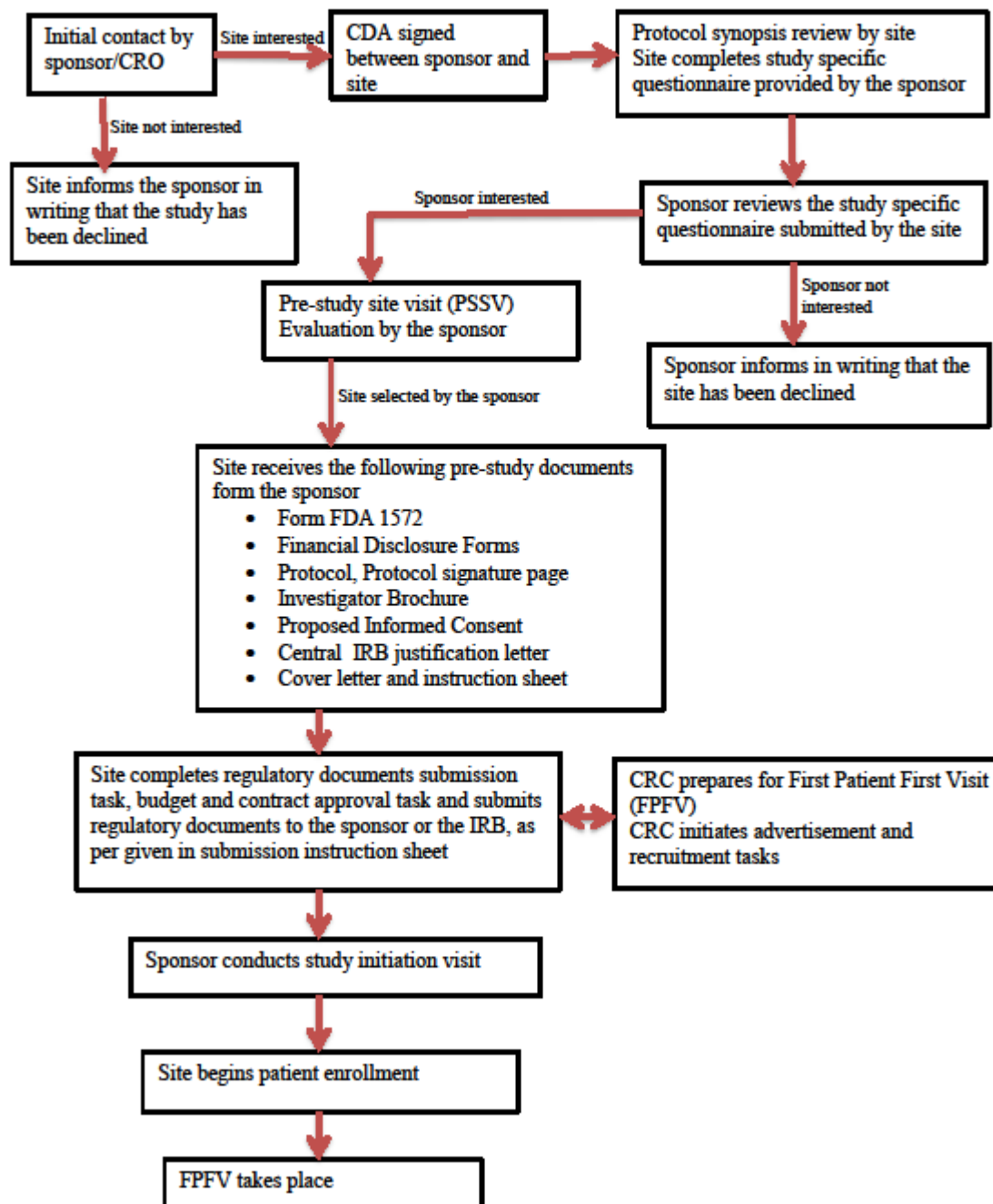
Worked on the CVs of the PIs and the SIs

Worked on the presentation of the practicum report

Appendix C

Flow chart for study start up process

FLOW CHART FOR STUDY START UP PROCESS



Appendix D

IRB documents

DATE: 11 July 2012

TO: Patricia Gwirtz, PhD
(with Clinical Research Management student Priyanka Chaudhari)
Clinical Research Management Program
Graduate School of Biomedical Sciences

PROTOCOL: #2012-143

"Overview of Study Start Up for Clinical Trial at an Investigative Site"

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 (1).

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 Peña 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,



Brian Gladue, PhD
Chair, UNTHSC Institutional Review Board

cc: I. Peña Pérez, OPHS

**UNT Health Science Center
Office for the Protection of Human Subjects
Institutional Review Board
BOARD ACTION**

IRB Project #: 2012-143

Date Submitted: July 10, 2012

Principal Investigator: Patricia Gwirtz, PhD with CRM student Priyanka Chaudhari

Project Title: Overview of Study Start Up for Clinical Trial at an Investigative Site

Sponsor Protocol #: _____

Department: Clinical Research Management / GSBS

Contact Info: _____

In accordance with UNT Health Science Center policy on the protection of human subjects, the following action has been taken on the above referenced project. Approval, when given, is **only** for the project as submitted. **No changes** may be implemented without first receiving IRB review and approval.

The Principal Investigator must notify the IRB immediately if any new potential conflict of interest arises or if CITI educational training lapses for any of the Key Personnel involved with the study.

- ☐ Project has received approval through: _____
- ☐ Informed consent(s) approved as submitted on: _____

You **MUST** use the version (s) attached rather than previously approved versions. In addition, only consent documents which bear the official UNTHSC IRB approval stamp can be used with subjects.

*Including: _____

- ☒ Study Protocol dated July 11, 2012 approved as submitted.
- ☐ Investigator's Brochure _____ approved as submitted.
- ☒ Protocol Synopsis approved as submitted on: July 11, 2012
- ☐ Amendment _____ to the protocol approved as submitted.
- ☐ Progress Report/Continuing Review completed, project has received approval through: _____
- ☐ Project has been reviewed. In order to receive approval, you must incorporate the attached modifications. You must submit one "tracked changes" version showing the markup and one "clean" copy of the revised protocol synopsis, informed consent, and advertisements to the IRB for review. **YOU MAY NOT BEGIN YOUR PROJECT UNTIL NOTIFIED BY THE IRB.**
- ☐ Project is disapproved for the reason(s) outlined (see attached).
- ☐ Consideration of the project has been **DEFERRED** pending resolution of the issues(s) outlined (see attached).
- ☐ Completion of project is acknowledged and all required paperwork has been received.
- ☒ Special Findings/Other

Project meets the necessary requirements to qualify for EXEMPT category review. Subsequently, approval granted under the provisions of 45 CFR 46.101 (b) category (1). Please note that ANY protocol modification, even if minor, requires OPHS review prior to implementation.


Chairman, Institutional Review Board

July 11, 2012
Date IRB Form 2 (revised March 2011)

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