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IDENTIFYING AND OVERCOMING BARRIERS IN CLINICAL RESEARCH MANAGEMENT: A REVIEW OF CLINICAL TRIALS WITHIN AN ACADEMIC MEDICAL CENTER

An Internship Practicum Report

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CHAPTER I

INTRODUCTION

Over the decades, clinical research has grown and evolved into what one would consider now as the cornerstone of medical advancement. Through the use of clinical trials, new and improved prevention and treatments continue to be discovered. These trials are not only an essential part of the process of drug discovery and development, but are required for drug approval.[1]

Conducting these clinical trials takes diligent cooperation between the pharmaceutical industry, government agencies, investigators, and academic medical centers (AMC's). With the implementation of new regulations as well as continual changes to policies and procedures overseeing clinical research, management of such trials has become a very meticulous and a lengthy process. Additionally, escalating costs of drug development[2,3] and an increased need for new treatments in the market at faster rates[4] have made the need for more effective and productive means of conducting clinical trials a priority for competitive research sites.[5]

With the landscape of clinical research constantly evolving, adaptation of study management and procedures is a continuous hurdle that clinical research sites must

overcome. Changes in regulations, limitations of funds and the need for more effective subject recruitment methods are all barriers that most AMC's are facing today.[6,7,8] Finding ways to overcome these obstacles is an essential part of conducting effective and productive clinical trails. In order to keep up with this change and maintain a high quality of research, continual review and audit of current research standards and procedures has become a necessity. Review of standard operating procedures and study documentation can help identify barriers which inhibit the process and initiate appropriate modifications in order to maintain efficient and effective study trials.

As such, for this Internship Practicum Project, the intern reviewed the standard procedures and monitored clinical studies with the Gastrointestinal Disease Oriented Team (GI DOT) in an attempt to identify barriers affecting the overall productivity and efficiency of the team. Once these barriers had been outlined, recommendations for changes in standard procedures were made in order to help improve the functionality of the GI DOT and, subsequently, enhance the success of GI protocols within the Simmons Cancer Center Clinical Research Office.

CHAPTER II

PRACTICUM PROJECT

Part 1: Project Design

Background and Literature Review:

Since the passing of the Kefauver-Harris Drug Amendments in 1962, clinical research trials have evolved into a staple of new drug development and safety evaluation.[9] Today, with approximately 33,502 clinical trials currently being performed in the United States alone,[10] clinical research management has grown into its own entity in the clinical research industry. Along with this increase in demand has also come an increase in regulations, length in study completion times and increased costs.[11] With steady growth expected over the next decade due to increases in life expectancy and a rise in the number of patients diagnosed with chronic illnesses,[12] the focus of many Academic Medical Centers (AMC's) is to recognize barriers within the clinical trials process and eliminate obstacles to help make trials more efficient, productive, and cost effective.

Today, the process of new drug discovery is a product of multifaceted cooperation of industry, research and healthcare.[4] While industry is a major source of innovation and drug discovery, researchers in academia, medical centers and governmental agencies have been a driving force conducting basic and clinical research. Due to their

commitment to the improvement of the nation's health and well being, AMC's have been imperative in the development and testing of new treatment modalities.[13] In the past, AMC's have had a significant role in conducting a majority of clinical trials. However, recent data suggests a trend of fewer AMC's being utilized to conduct clinical trials. In an article published in the *New England Journal of Medicine*, statistics showed that the percentage of clinical trials being preformed at academic medical centers had declined from 63% in 1994 to only 26% in 2004.[14]

Although the exact reason for the shift was not determined in the 2004 survey, speculations focused on the several important differences between academic and private practice which may have been the factors influencing the new trend. This assumption was built upon in an article by Scott which suggested that the continuing increases in the amount of time to complete studies as well as increasing cost within academia was pushing industry to use more independent or private practice sites.[15] Over the past decade, industry has seen an overall increase in both the amount of time it takes for drug development as well as cost. Total time for the development of a new drug currently takes on average of 10-15 years.[4] Time not only inhibits the ability of the company from placing the drug on the market it also increases the overall cost of development. In 2004, cost for the development of one drug was estimated at approximately $800 million.[2] Today current estimates have seen that number rise to $1.3 billion per drug.[3] Such substantial increases in time and cost has forced the pharmaceutical industry and governmental agencies to look for ways to shorten and decrease the cost of the clinical trial process. For site selection, both entities are now looking closer at study endpoints

such as the generation of high quality research, completion of a trial within budgeting limits, as well as feasibility of study completion.[5,16] Where academic sites are hindered by a lengthy process involving many steps, private practice sites are able to eliminate steps in order to make the process more effective and efficient.

The lengthy process associated with conducting clinical trials at AMC's can produce many potential barriers for conducting effective and efficient trials. In 2006, an article by Dilts and colleagues reviewed the timelines of 211 clinical trials at Vanderbilt University in order to identify the barriers impacting study startup.[6] They identified several administrative barriers within procedural, structural and infrastructural processes and outlined 60-110 steps within the studies which had to be completed in order to reach approval.[6] Accumulation of steps within the AMC infrastructure leads to many possibilities of process breakdown. In order for AMC's to continue to bring their patients the most updated treatments and paramount quality of care, several areas of research administration and procedures must be improved in order to attract new industry studies and governmental research grants. Collection of high quality data, completion of trials within reasonable costs, and expeditious patient recruitment to help facilitate study completion are just a few areas which affect the overall productivity of the research site.

The generation of high quality research is pertinent to both study sponsor and the research site. Quality research ensures the integrity of the data collected but also ensures the safety and welfare of the research patient.[17] In order to maintain the safety and efficacy of research trials, regulations such as *Code of Federal Regulations (CRFs), Good*

Clinical Practices (GCPs), and *Human Subject Protections* must be followed. To ensure that research trials are being conducted up to these standards, continual monitoring of study documentation for organization, accuracy and discrepancies is needed. Disorganization and random errors can lead to inaccuracy of study outcomes and may endanger the welfare of study participants. Clinical monitoring is a way to provide a direct assessment of these aspects and helps to identify shortcomings or obstacles in conducting efficient clinical trials.[17] Once aspects of the system which impede quality of data or protection of human subjects are identified, corrective measures should be taken. Standardizing all aspects of the clinical research office including organization of study documentation, case report forms, and internal data auditing[17] are ways in which the AMC can protect both their patients and the quality of data produced while increasing productivity. Another efficient way to help plan out study execution and eliminate the possibility of discrepancies is to implement project plans. Project plans provide a detailed description of the study process, delegate roles and responsibilities of research team members, and help to increase communication between research staff.[18]

To improve the productivity of an AMC, you must also improve the cost-effectiveness of the clinical research department. The ability to complete trials within a reasonable budget, one that is beneficial to both the sponsor and site, is also important for cost effectiveness. In a study conducted by Emanuel and colleagues, data collected from 21 clinical sites were used to determine the cost of conducting a trial as compared to the estimated income received from governmental or industrial funding.[7] Overall, the study found that payment received for study costs did not cover all expenditures for conducting

the trial. Their study suggested that conducting clinical trials and enrolling a subject into research can actually cost clinical sites money.[7] Discrepancies in budgeting are mostly due to budgeting issues, as well as complex billing procedures. Surveys reviewing budget development have shown inadequate estimates of cost for clinical trial administration and research procedures.[19] Simplified study budgets lacking detailed procedures may not take into consideration all clinical procedures, especially those which are deemed non-clinical. For instance, in the study by Wright and colleagues, clinical sites did not charge for or receive an overhead fee from studies organized by cooperative groups. In reality though, those administrative costs, such as salaries, were still accumulated and ultimately had to be absorbed by the clinical site. Another problematic aspect of study budgeting includes the complex billing process utilized in clinical research.[11] With the National Coverage Decision (NCD) of 2000 requiring the Centers for Medicare and Medicaid Services to pay for all routine costs within a protocols of a clinical trials,[20] determining which procedures are routine versus those which are specifically research related may be confusing and problematic for clinical research sites. Correcting budgeting pitfalls and generating study budgets which can support all cost endured by trial conduction, can help increase the efficiency and overall effectiveness of the AMC site. Extensive review of projected study costs should be done prior to financial negotiations.[20] Critical constraints such as estimated investigator and coordinator time, management overhead, and expected research clinical costs should be analyzed and represented within the budget. Site specific budgeting outlines and management software developed from estimated site costs can help facilitate standards for future budget and

financial negotiations and help reduce the amount of time for financial negotiations and decrease loss of revenue.[19]

Expedited subject accrual and shortened timelines to study completion are other barriers faced by most AMC's. Depending on the structure of the study protocol, subject recruitment and accrual can be difficult and study execution can run into procedural barriers. When the protocol for the study is too complex or has strict inclusion and exclusion criteria, the study timeline can be lengthened. Clear, well designed protocols are the core of clinical trials. All aspects of the protocol including complexity and entry criteria should be under scrutiny from the beginning of the contracting process in order to assure that the recruitment rates and study completion will be successful.[8] In addition, subject accrual feasibility should be determined prior to study approval.[8] This may include an analysis of the AMC's current clinical patient population to access the availability of participants who may meet specific study requirements.

In summary, there are many barriers which may arise during the process of conducting clinical research trials. All barriers inhibiting the conduction of efficient, productive and cost effective clinical trials are important to identify when managing trials within an AMC. In order to continue to attract industry trials and maintain grant-funded research, AMC's must find ways to decrease the amount of time and cost associated with conducting clinical trials[21] while maintaining study validity and patient welfare.

Specific Aims:

Administration in clinical research is continually changing due to increasing demand, more stringent regulatory guidelines, and mounting costs. In order to help identify and eliminate barriers which contribute to a decrease in efficiency and productivity, continual review of study procedures is required. In order to evaluate the standards and procedures currently in place and recognize barriers which hinder this process within the clinical research office of an academic medical center, the following specific aims were completed during this practicum:

1) Monitored open, active and closed GI protocols for compliance, organization and accuracy. as well as reviewed financial agreements and protocol feasibility based on patient population for each study.
2) Identified barriers associated with the management of clinical trials within the Clinical Research Office and developed recommendations for improvement.
3) Implemented suggested solutions within the Clinical Research Office.

Significance of Practicum Project:

Throughout the internship, the majority of the practicum was spent working within the Gastrointestinal Disease Oriented Team (DOT). The GI group specifically focuses on research trials involving esophageal, gastric, colorectal, hepatic and pancreatic cancers. With colorectal cancer being the third most newly diagnosed cancer among women and men,[22] one would expect the GI DOT to be successful in protocol completion and productivity. However, study records and patient accrual logs show that the GI DOT is not as productive as other disease groups in the Cancer Center's CRO. In order to

identify the limitations which are hindering the productivity of the GI group, study policies, procedures and implementation should be continually monitored and reviewed to minimize administrative barriers and increase departmental productivity. In an attempt to assess what barriers were limiting the efficacy and productivity of the GI disease group, a full review and audit of all active and closed GI studies for procedures, documentation, financials and patient recruitment was completed.

Materials and Methods:

Specific Aim 1: The following methods where utilized in order to monitor all open, active GI protocols for compliance, organization and accuracy, as well as review of financial agreements and protocol feasibility for each study.

1) *Monitoring Review of all GI Study Documentation*: For each study protocol, study documentation was monitored for completeness, accuracy and organization. Standards set forth by the Good Clinical Practice Guidelines (GCP) and all site regulatory guidelines where used to determine if the documentation required was complete and accurate. Auditing tools already in place by the Simmons Cancer Center Clinical Research Office (SCC CRO) were revised and utilized in order to help facilitate the review. Study documentation was reviewed for the following:

    a) Regulatory documents were reviewed to assess if the following documents where on file, completed and accurate:

        - FDA 1572

- **Current curriculum vitas, license, and financial disclosures of all investigators**
- IRB assurances and rosters
- Lab certifications and lab reference ranges
- Signature logs and staff delegation logs
- NR1 & NR3 forms
- IRB approved project summaries and protocols
- Protocol amendments (if applicable)
- Investigator brochure and package insert (if applicable)
- Lab manuals (if applicable)
- IRB approved informed consents for treatment, Spanish informed consent version (if applicable), and informed consents for DNA, genetic, blood and tissue collection and storage (if applicable).
- IRB approved HIPAA consent documentation
- All IRB approvals
- Committee approvals to include Protocol Review and Monitoring Committee (PRMC), co-op groups (e.g., ECOG approval), Radiation Safety Committee, Parkland Health and Hospital System (PHHS) and Research Compliance Committee (if applicable).
- IRB and general correspondence
- IND safety reports, SAE reports, and deviation reports

- Enrollment and screening logs

b) Patient case binders of consented subjects in each of the GI studies were reviewed for completeness and accuracy of the following forms and documentation:

- Informed consents were reviewed to ensure it was signed and dated, correct IRB version was used, consent occurred prior to any study procedures, person obtaining consent was authorized to consent study patients, and that the consent process was noted in chart and documentation was present that a copy of the consent was given to the study subject.
- HIPPA authorizations were reviewed to insure accuracy of signatures and dates, the most current IRB approved version had been used, and that the person obtaining consent was authorized to do so.
- Assessment of patient eligibility was reviewed by ascertaining that patient met both inclusion and exclusion criteria established by the study protocol and eligibility had been reviewed by either PI or Sub-investigator. Inclusion and exclusion checklists were reviewed for accuracy (if utilized by study coordinator).
- Patient case report forms along with source documentation were reviewed for accuracy of protocol procedures. Documentation was assessed to make certain registration,

randomization, screening, lab testing and diagnostics, and dosing were completed per protocol stipulations. Physician orders were reviewed for signatures and dates. If subject completed study, off treatment procedures were reviewed for accuracy, completeness and protocol compliance.

- Subject source documents were reviewed to assure all Adverse Events (AEs) and Serious Adverse Events (SAEs) had been documented correctly and reported to the IRB and study sponsor as outlined by the protocol and IRB regulations.

c) All regulatory and patient case binders were reviewed for organization of documentation.

2) *Audit of Financial Agreements and Budgets*: Financial agreements and budgets for each protocol were reviewed for accuracy, completeness and organization of documentation.

a) Financial agreements and amendments were reviewed for all GI studies. Stipulations and procedures outlined in each individual agreement were delineated and a comparison was completed between studies. Special attention was placed on reviewing those items which dealt with standard of care procedure payments, invoiceable study costs, payment schedules and study drug supply.

b) Study budgets were reviewed and checked for accuracy of account and viability of budget agreement. Procedures completed in review for each study budget included:

- Review of study invoiceables to verify all study procedures which were reimbursable had been accurately invoiced for.
- Review of account transactions to verify all appropriate study payments had been received by the CRO.
- Comparison of agreed budget cost to actual cost of study implementation.
- Comparison of those procedures considered standard of care within study budget as compared to guidelines for standard of care outlined in recent literature.

3) *Assessment of New Patient Population and Protocol Feasibility*: Assessment of protocols and current cancer center patient population for feasibility of study completion was done.

a) Patient accrual numbers for the past year for the GI disease group were obtained from the Assistant Director. The statistics were reviewed and compared to other study groups within the CRO.

b) New patient reports for both the Simmons Cancer Center (SCC) for the past three years and Parkland Health and Hospital System (PHHS) ambulatory clinics were obtained. Review and analysis of the patient demographical data including type of patient visit and disease location

was completed in order to assess trends found within the patient data. These trends were then used to determine which types of protocols would be most feasible in completion for the CRO GI disease group. Feasibility was determined by comparing patient demographic trends to study protocol inclusion and exclusion criteria.

Specific Aim 2: The following methods where utilized to identify barriers associated with the management of clinical trials within the Clinical Research Office and develop recommendations for improvement.

1) *Literature Review*: Ovid Medline was utilized to search for relevant articles and reports. Relevant articles pertaining to study procedural, infrastructural and financial barriers were compiled and reviewed to assist in identifying limitations and potential recommendations for improving the research study process.
2) *Regulation Review*: Study governmental and institutional regulations including Code of Federal Regulations (CRFs), Good Clinical Practices (GCP), Health Insurance Portability and Assurance Act (HIPAA), Human Subjects Protection and Institutional Review Board (IRB) guidelines were reviewed to assure that all regulations applying to clinical research study management and implementation would be adhered to and potentially improved upon during the recommendation process.
3) *Documenting Limitations Identified during Review*: During the process of reviewing and auditing study documentation, patient charts, financial

information, and patient recruitment measures, problematic issues related to the completeness, organizational structure and process were identified and documented.

Specific Aim 3: The following methods were utilized to implement suggested solutions within the Clinical Research Office.

1) *Reporting of Discrepancies:* All discrepancies identified within the review and auditing process where reported to Lynn Baker, the Assistant Director, and any other appropriate departmental personnel within the Clinical Research Office. Regulatory discrepancies found in review of protocol and regulatory documentation were reported to the regulatory supervisor. Inaccuracies or missing information found on review of case report forms and patient case binders were reported to the appropriate study coordinator. Financial discrepancies and issues were reported to the CRO accountant for review and reconciliation.
2) *Implementation of Recommendations:* Recommendations for improvement in study procedures and policies approved by the Assistant Director of the CRO were implemented within the department. Cooperation from study coordinators, regulatory and accounting personnel was utilized to implement changes. Execution of suggested changes within the GI group was limited by time constraints of the research internship. Only those which the Assistant Director and Intern felt could be accomplished within this time frame where implemented.

Part 2: Project Findings

Review of GI Study Documentation:

During review of all GI studies within the Simmons Comprehensive Cancer Center Clinical Research Office (SCCC CRO), the documentation was divided into two categories, regulatory documentation and patient case binders. Within the Cancer Center CRO, all regulatory documentation is maintained by the regulatory team and the maintenance of the patient case binders is the responsibility of the individual study coordinator. Overall, the regulatory and patient case binder documentation for ten active and closed GI studies were reviewed for completeness, accuracy and organization.

Regulatory Documentation: Completeness of the regulatory documentation was verified using a modified quality assurance tool already established within the CRO. Overall, findings for the regulatory section of the review found complete and current records on hand. Two of the ten studies reviewed showed no discrepancies at all and the other eight studies only had minor discrepancies found. Most discrepancies noted were the result of location of regulatory documentation and was not due to incompleteness or inaccuracies. This has been described in more detail below when discussing the organization of the regulatory documents. In regards to completeness and accuracy of records kept in the regulatory binders and files, several trends which were observed when completing the review have been expanded on below:

- *Investigator and Sub-Investigator Curriculum Vitae (CV) and License:* During review of the regulatory binder and files of the GI studies it was noted that

nine out of ten studies either did not have a current license or a current and signed CV in the binder for all investigators and sub-investigators.

- *Financial Disclosures*: Seven out of ten of the studies reviewed did not have a current financial disclosure on file in the regulatory binder.
- *Screening Enrollment Log*: Although required by most studies, copies of patient screening logs could not be located within the regulatory documentation in seven of the ten studies. Although, the log was not readily accessible in the regulatory file, several of these studies did have screening logs either kept on computer by the coordinator or had a separate folder for the log.
- *Signature Sheet and Staff Delegation Log*: Upon review it was noted that several of the studies (six of ten) did not have a signature sheet or staff delegation log located within the regulatory binders.
- *Lab Certifications & Reference Ranges*: Lab certifications and references ranges must be kept up-do-date in regulatory documentation. During review it was found that five of the studies did not have any lab certifications or lab references on file in the regulatory binders.

Although, most GI studies reviewed were missing copies of the appropriate and most up to date regulatory documentation, most missing forms could be located in other locations within the SCCC CRO or online within the research database. For example, current copies of all investigators and sub-investigator's CV and license could be located online within a research file folder. This research folder was kept up to date by members of the

regulatory team with all other staff within the Cancer Center CRO having access to this file folder. All regulatory forms missing from the regulatory binders could be accounted for online and once located were current and accurate. However, for review of completeness of each regulatory binder, it must be noted that current copies of some of the regulatory documentation were not present within the regulatory binders.

Although the regulatory files were accurate and ultimately complete, finding the location of many of these documents became a cumbersome task at times. Most of the regulatory documentation was very dispersed within the Cancer Center CRO. Many of the studies had more than one regulatory binder in place, sometimes located in different locations. For instance, for some studies regulatory forms would be dispersed between the SCCC CRO regulatory binder, study sponsor binder and coordinator binder. Additionally, some current regulatory documentation which was not found within any binder may have been found filed within the regulatory file cabinets. Furthermore, forms were not only located in several different binders or in different locations within the Cancer Center CRO, but they also were stored in several different media format types (either paper or electronic). Overall, having the regulatory documentation located in several different locations and in several different types of media formats instead of one main binder or file made locating all the documentation for review onerous.

Additionally, when reviewing each individual regulatory binder, it was noted that there was no standard organizational format used within the binders. Some sets of regulatory study binders seemed to follow a similar pattern in regards to the order of the regulatory

documentation, however, overall there were several different organizational patterns noted. Ultimately, this lack of cohesiveness of organization from binder to binder may be attributed to either the regulatory team member's personal style as well as sponsor specific recommendations for an individual study binder formats. In contrast, the file cabinets where some regulatory documentation were also stored followed a strict organization pattern. Each section for each study had been organized with the same style, making it easy to access regulatory documentation. This type of standard organization made finding forms within the cabinet filing system much easier than when having to search through several different binders. Better organization of study regulatory documentation could make the location and review more readily possible.

Patient Case Binders: As with the regulatory documentation, patient case binders were also reviewed for completeness, accuracy and organization using a modified version of a quality assurance tool already established within the CRO. Of the ten studies which were reviewed for regulatory documentation, patient case binders were not reviewed for two of the studies since no subjects had yet been enrolled into these studies at the time of review. As such, only the patient case binders of eight studies were reviewed and are described in this section.

Overall, most patient binders were complete and accurate upon review. The patient case binders of two of the eight studies reviewed showed no inaccuracies and had all forms present and complete. For those studies in which discrepancies were noted, most inaccuracies or missing documentation had already been queried either by an internal

review or a sponsor review and had been corrected. As seen with the regulatory documentation, missing forms which could not be located in the patient binder could be found online. With the advancement of technology, most Case Report Forms (CRFs) are conveniently located online by the sponsor and paper copies are not always provided or utilized. However, to help distinguish areas in need for improvement to help eliminate discrepancies and to help decrease the amount of coordinator time spent on correcting queries or protocol deviations, trends found within review are described below:

- *Inclusion/Exclusion Checklists:* During review, it was observed that half of the reviewed studies did not have an inclusion/exclusion checklist within each patient binder. Those studies which did have some form of inclusion/exclusion checklist mostly utilized a copy of the protocol page outlining the criteria and had coordinator's notes written in the margins.
- *Source Documents or Study Worksheets:* When reviewing source documents and sponsor provided worksheets it was noted that in two of the studies not all documentation was complete or located in the chart. In particular, some studies were missing source documentation for study values entered on study case report forms (CRFs). Additionally, it was noted that for studies where the sponsor had provided source documents or worksheets, most were incomplete or had not been utilized.
- *Copies of Case Report Forms (CRFs) in Shadow Charts:* Currently, most sponsors are moving to utilizing electronic CRFs. Most are accessible online and paper forms are no longer utilized or kept on file. However, it was noted that for the couple of studies which still had paper CRFs in place, some forms

were missing from the shadow charts which were kept in house after the originals had been sent to the sponsor.

- *Coordinator Progress Notes:* In several of the studies, it was noted that there were no coordinator notes within the source document binder. These notes can be important when clarifying queries or protocol deviations and should be done at each visit to outline which procedures were completed at each study visit.

In addition to the review of the completeness of the patient binder charts, accuracy of documents found within the binders was also reviewed. Although queries and protocol deviations can be expected to occur on a limited basis when conducting clinical trials, it is important to eliminate errors in the reporting of data as much as possible. Most discrepancies within reporting lab values, treatments or procedures seemed to occur most often within studies whose protocols were more complex. It was noted that most studies did not have visit worksheets to help assist in data collection, and even within those limited studies which did have visit worksheets, it was noted that the worksheets were not visit specific and outlined all research protocol procedures not just the ones specific to that study visit. For instance, a majority of the protocols included more than one treatment arm in the study. Each arm had different stipulations for study procedures which should be completed at each visit or had differences within treatment dosages to be given. Having such variation not only visit to visit, but treatment arm to arm makes it more likely that discrepancies can occur. In these more complex protocols, there were a relatively higher number of queries or protocol deviations noted. For instance, in one

Eastern Cooperative Oncology Group (ECOG) study some visits required a treatment doses and other visits did not. However, all CRF's for this study had the treatment dose present for all study visits. As such, several queries had been initiated when the coordinator mistakenly marked that a dose had been given on a visit that it was not scheduled. On review of source documentation, it was noted that the dose had not actually been given to the subject, but was just mistakenly marked by the coordinator. If each CRF had been visit specific so that the treatment dose was not listed on study visits that it was not scheduled to be given, this query would have been eliminated.

Additionally, it was noted that several studies had protocol deviations which were due to inaccurate regulatory documentation which had not been noticed by the regulatory team or the coordinator after initiation of the study. For example, in one study which had several corrected protocol deviations, these deviations were due to inaccurate inclusion/exclusion criteria within the study protocol. It had been discovered, on internal review, that the first few patients enrolled in the study had not truly met the protocol inclusion/exclusion criteria as outlined. However, on further review it was also noted that the protocol criteria was incorrect. Although in the study title and through the rest of the protocol, the study was designated for subjects with unresectable gastric cancer, within the criteria it stated the subject must have metastatic gastric cancer. Due to this discrepancy in wording in the inclusion criteria, the first few subjects enrolled in the study that had unresectable, non-metastatic gastric cancer did not meet the inclusion criteria as printed in the protocol. Although this deviation was noted and a change to the protocol inclusion/exclusion was made, it did cause many hours of coordinator time to be

spent on correcting the deviations found but working with the regulatory team to make protocol modifications. Additionally, there were other queries noted in that same study which pertained to regulatory oversight as well. Again on internal review, it was noted that several patients had been consented by a person not designated to obtain informed consent. This was due to a change in coordinator on the study protocol. As one coordinator left, another took over the study and a modification to the consent was not completed. This was more than likely due to a miscommunication between the regulatory team and DOT. Again, although this oversight was noted and was corrected prior to any additional study patients being consented, it still took additional coordinator and regulatory team time to correct the deviations and modify the consent.

Again it must be stated that most patient case binders reviewed in this audit were found to be complete and accurate. The queries and protocol deviations focused on in the above paragraphs were found only in limited number of the studies and had already been corrected within the study charts. However, time was spent focusing on these discrepancies in this report in order to help identify patterns which may lead to inaccuracies. By pointing out where and how discrepancies occurred within one study, it can help eliminate them from being repeated in future studies.

Organization of patient case binders was also a focus of this review as with review of regulatory documentation. Similar to the regulatory review, organization of patient case binders was found to be varied from study to study. Organization within each individual binder seemed to vary from coordinator to coordinator and study to study. Some patient

binders put the most recent visit in the front of the binder and others put the most recent toward the back of the binder. This variation was sometimes even seen when comparing the CRF binder and source binder for the same patient in one study. For example, some CRF binders had the visits organized with the newest visit to the back, but in the patient source binder the newest visit was placed in the front of the binder. Overall, no standard of organization was noted in the binders. Additionally, as noted in the regulatory review, patient CRF's and source binders were located in several different locations either at a location by the coordinator overseeing the trial or within file cabinets. It was even noted that in some cases, binders and source documents for the same study were located in separate file cabinets in different locations. At first, the reviewer thought that source documentation was missing, but with searching through more cabinets, the additional study documentation was found in another file cabinet all together. Furthermore, it was noted that most file cabinets had no indication as to which studies were stored inside, and those that did were not always marked correctly.

Audit of GI Study Financial Agreements & Budgets:

Review of the study financial agreements and budgets within the Simmons Comprehensive Cancer Center Clinical Research Office (SCCC CRO) consisted of a review of the financials of five industry sponsored studies as well as a review of budgeting information for four Eastern Cooperative Oncology Group (ECOG) studies. Financial agreements and budgets for each protocol were reviewed for accuracy, completeness, organization of documentation and trends.

During review of the industry sponsored study agreements and budgets, special attention was placed on invoiceable billing items, study drug supply as well as payment schedule outlines. Most agreements and budgets throughout the review were standard and consistent with each other, however, some minor differences were noted. A review of important trends seen during assessment of the financial documentation is listed below:

- *Subject Enrollment Numbers*: Contracted enrollment numbers are found within the financial agreement. This number of expected patient enrollment is individually based on overall anticipated study enrollment for each protocol.
- *Study Drug Supply*: The financial agreement usually outlined how the study drug would be supplied, stored and returned after study. For studies using Investigational study drug, it was supplied directly to the site by the sponsor. If the protocol outlined a treatment arm which used a treatment already considered standard of care, this therapy was not supplied to the patient by the sponsor but instead was charged to the patient or their insurance. However, in one trial, the study sponsor did agree to reimburse patients if an additional chemotherapy agent was recommended by their primary oncology physician and was prescribed.
- *Cost per Patient*: An overall cost per patient was typically outlined in each financial agreement or study budget. The cost per patient was determined by calculating the total cost of study visits and procedures as outlined within the study protocol.
- *Invoiceable Items*: It is important to take special notice of invoiceable items found within the study agreement. Such items typically consisted of the

Investigational Review Board (IRB) fees, costs for additional lab or imaging done outside of the regimen of standard of care, and payments for completion of Serious Adverse Event (SAE) Reports. However, since most research procedures are paid to the site on a regularly scheduled basis and typically based upon CRF completion, it is easy to overlook the billing of invoiceable items. During review of the five industry trials, it was found that two studies had items within their contract which had never been invoiced so site reimbursement was never made.

- *Startup Costs*: All studies within this review, with the exception of one, had startup costs figured into the study budget. This money is distributed at the beginning of the study and typically consists of the cost for the administrative start-up fee ($4550.00) and pharmacy set up fee ($1950.00). In several of the studies, the local IRB fee ($1500.00) was included in the start-up costs as well.
- *Initial and Final Payments:* Another option for payment is for the sponsor to give an initial payment. Examples of initial payments seen on review were an initial payment which was a percentage (e.g., 10%) of the total anticipated study budget or payment for one full patient at the beginning of the study. When an initial payment was given, all start-up costs and any study visit payments incurred after that payment were applied against the sum of the initial payment first. No additional payments are made from the sponsor until the original first payment has been completely utilized. Additionally, some study budgets where designed to withhold a percentage (10%) of the overall

study budget until the end of the study as a final payment. This payment was made upon completion of the study, closing procedures and return of all queries.

- *Payment Schedule:* All studies within this review used a quarterly payment method. Payments were made every three months for study visits which had occurred and completed CRFs had been turned into the sponsor.
- *Standard of Care (SOC) Items*: Due to regulations set forth by the national government, items which are to be considered Standard of Care (SOC) should be charged to the patient's insurance. These SOC items are typically outlined within the study budget and consist of procedures or treatment which would routinely occur even if the patient was not enrolled in a clinical trail. Of specific importance during review is to monitor if the standard of care is being followed. For instance, in one study, the protocol requested that a CT scan should be performed every six weeks. However, as outlined by the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines for Oncology, CT monitoring for cancer progression should occur at a rate of 8-12 weeks.[23] Thus, scans occurring every six weeks falls outside of the standard of care. In this case, the sponsor of the study did agree to pay the cost of every other scan for the patient. Another important aspect when dealing with SOC items is to monitor the billing of these items. When items do fall outside of the SOC and cost is being paid by study sponsor, it is important to monitor the billing of these items to insure that double billing does not occur for procedures being covered by sponsor funds. As in the case

of the above, without monitoring the billing for the CT scans, the patient's insurance was incidentally charged for CT which where already being covered by the sponsor. In this instance, the scans were not only charged to the patient insurance but payment for the scans was also received from the sponsor as well. This produced a double charge for the scans and extra time for both the coordinator and accountant had to be devoted to getting refunds to for the patient's insurance and to the patient for payments and co-payments made toward these scans.

- *Coordinator and Investigator Fees:* Another important area of note within the study budget is the coordinator and investigators fee. Within this review, fees for coordinator time at each study visit ranged from $118.50 to $240.00 per visit. Additionally, two studies also provided an administrative data entry fee ($40-65.00 per visit) to compensate for coordinator time spent entering data. Within all study designs, study coordinators were only paid on a per visit basis, with the exception of one study which did pay for completion of SAE reports. Payment was not made for coordinator time used for pre-screening, time spent answering queries or time spent preparing and participating in monitoring visits. Also, none of the studies included payment for visits which had to be delayed or treatments withheld. For example, within one study on two separate occasions the study patient had an adverse event. When they presented to clinic and the adverse event was noted, their chemotherapy treatment was delayed until the following week. Although the coordinator used time to see the patient and gather documentation, since no CRF was

completed on this patient for the time spent on this visit, there was no payment given by the sponsor. As such, the coordinator time spent with this study subject was not compensated. Additionally, it was noted that investigator fees were only supplemented within one study budget. Within that specific protocol the investigator was performing injections directly into tumor done with the assistance of ultrasound. Since this was outside the standard of care, the investigator was paid for their time at a rate of $600.00 per visit in which the procedure was performed. Most studies included investigator time with the patient as standard of care, so it was not reimbursed.

Study protocols sponsored by cooperative groups such as the Eastern Cooperative Oncology Group (ECOG) do not have the same agreement and budgeting as the industry sponsored trials which were described above. Instead, sites who become members of the cooperative group are paid at a set rate per subject enrolled. For instance, with ECOG pays the Cancer Center a total of $1,770.00 per patient enrolled into an ECOG study protocol. Since the Cancer Center is part of a large academic institution, a percentage of this payment is used for overhead costs for the institution. At a rate of 26%, approximately $370.00 is taken by the institution to help pay for overheard. This leaves roughly $1,400.00 to pay for all per patient costs associated with being enrolled in the study. Since the procedures and treatments vary depending on the study protocol, this set amount of payment per subject has to be used to cover different types of research procedures and treatments. However, in order to help with additional costs that may be brought on by complex protocols, guidelines which allow additional monies to be

requested for ancillary testing are available. These ancillary testing monies are limited though and are only available for protocols which have excessive testing outside that of standard of care.

In order to assess whether or not ECOG funding was sufficient to cover all expenses associated with conducting a particular clinical trial, a budget was developed and compared to the $1,400.00 that was provided. When estimating all the costs for coordinator time, procedures not covered by the standard of care, as well as additional medications not covered within the standard of care, it was found that most ECOG studies produced costs that were way above the $1,400.00 per patient payment received. *See* Table 1. Although most procedures and treatment options outlined with the ECOG protocols were covered under the standard of care, coordinator time and some screening procedures were not. This led to three of the four studies costing markedly more than what each payment per patient covered. For instance, average cost per patient for ECOG E2204 was $6,139.00, ECOG E3202 was $7,826.00 and ECOG S0600 was $3,610.00. After deducting the per patient payment made to the site, this left $4,739.00 per patient in the E2204 study, $6,426.00 per patient in the E3202 study, and $2,210.00 per patient in the S0600 study to be covered by the Cancer Center CRO. The only study which did not excessively exceed the per patient payment was ECOG E5202, where cost per patient was estimated at $1,416.00 in the treatment arms of the study. Additionally, the cost per patient did not incorporate the startup costs for each study including local IRB fees, administrative start-up fees and pharmacy set up fees. These additional costs would

ultimately have to be covered by the SCCC CRO making the overall cost of conducting ECOG studies at the site even more costly.

Table 1: Cost of ECOG Study Management and Conduction

Study Title	Startup Costs[a]	Cost Per Patient within treatment arm[b]
ECOG E2204	$7,950.00	$6,139.00
ECOG E3204	$7,950.00	$7,826.00
ECOG E5202	$7,950.00	$1,416.00[c]
ECOG S0600	$7,950.00	$3,610.00[d]

[a] includes local IRB fee, administrative start up, and pharmacy set up fees.
[b] includes all non-standard of care costs and coordinator time for each study visit within treatment arm of the study.
[c] this cost represents the treatment Arms A&B of the study. Arm C was just observational consisting of only the initial screening visit and one follow-up visit.
[d] This cost represents the average of the costs for all three treatment arms. Arm 1 = $3,560.00, Arm 2 = $3,636.00, Arm 3 = $3,636.00.

Assessment of Patient Demographics & Protocol Feasibility:

In order to assess the potential productivity of the Simmons Comprehensive Cancer Center Clinical Research Office (SCCC CRO), a complex evaluation of patient accrual to study, availability of potential new patient visits, and presenting cancer locations as compared to protocol types was completed.

Assessment of Subject Accrual: Subject accrual data for years 2005-2008 were obtained from the ONCORE patient data system. Each report included the total number of patients recruited within the 12 month period, with the exception of the 2008 report. Since the internship was completed in 2008, the report was only available for the months of January though the end of August. Enrolled subjects were recruited from two research study sites which included the Simmons Comprehensive Cancer Center (SCCC) and Parkland Health and Hospital System (PHHS) and were enrolled to either therapeutic or non-therapeutic trials.

When reviewing yearly accrual reports, variation from year to year is noted in the number of patients recruited within the Cancer Center CRO. *See* Table 2. In 2005, recruitment was at an all time high for the four year span with a total of 406 patients enrolled in either therapeutic or non-therapeutic trials. In 2006, overall patient recruitment decreased drastically with a total of only 182 patients being enrolled for the year. Patient recruitment numbers again increased in 2007 to 366 patients, with overall patient accrual for the 2008 year seemingly on tract with the same projections as seen in 2007. At the end of August, accrual had reached a total of 278 from beginning of year to date.

Table 2: SCCC CRO Subject Accrual Per Year

Disease Oriented Team	2005	2006	2007	2008[a]
Gastrointestinal (GI)	56	13	29	8
Brain	0	8	8	8
Breast	209	79	126	130
Genitourinary (GU)	5	7	30	16
Gynecological (Gyn Onc)	36	25	63	37
Head & Neck	2	1	4	3
Hematology	78	30	18	16
Lung	14	19	71	60
Skin (Melanoma)	6	0	17	0
Total for all DOTs	406	182	366	278

[a] accrual is from January 1, 2008 through August 31, 2008.

As part of the summary of each yearly report, each disease group total patient accrual is also reported. *See* Table 2. By looking at recruitment numbers throughout the four year span, it can be noted that Breast DOT tends to have the highest patient recruitment, usually followed by GU, Hematology, and Lung DOTs. Although, GI DOT may not have the highest recruitment, it can be seen when examining the table that similarly to all groups, the GI DOT has an unstable cycle in the number of subject's recruited over the

years reviewed. GI patient recruitment was at its highest number in 2005 with 56 patients. It then followed the dip seen within overall recruitment in 2006, with only 13 total patients recruited. An increase was seen within recruitment in 2007 with 29 patients. For 2008, since the beginning of year to the end of August, only a total of 8 patients have been recruited into trials, but with several months of the year still ahead the numbers seen in 2007 still have a chance to be met.

Although we can see a similar wavering pattern of recruitment when looking at the numbers of each individual disease group and total numbers from year to year, if we take a closer look at the percentage of patients recruited by the GI disease team as compared to the overall recruitment numbers, a slow continual decline becomes apparent. *See* Table 3. For instance, in 2005 the percentage of patients enrolled who were participating in GI studies was 13.8%. This percentage decreased to 7% in 2006 and 8% in 2007. Currently, the number of patients enrolled in GI studies as compared to the total number of subjects accrued within the Cancer Center CRO for the year 2008, the GI accrual has reached an all time percentage low of only 2%.

Table 3: GI Disease Oriented Team Accrual Percentages

	2005	2006	2007	2008[a]
CRO Total Patient Accrual	406	182	366	278
GI DOT Patient Accrual	56	13	29	8
Percentage Patients in GI Studies	13.8%	7%	8%	2%

[a] accrual is from January 1, 2008 through August 31, 2008.

Assessment of New Patient Visits: One factor which is a direct determinant of subject accrual is sufficient access to the targeted patient population. In order to determine if an

adequate population pool was available to the GI DOT for recruitment, an analysis of patient visit types was completed for the years 2005-2008. Since most GI studies protocols exclude patients who received adjuvant therapies prior to beginning a study trial, the number of new patient visits per year strongly influences the recruitment potential. In order to determine the number of patient visits per year, yearly reports consisting of all patient visit types for both the Simmons Comprehensive Cancer Center (SCCC) and Parkland Health and Hospital System (PHHS) ambulatory clinics were obtained. Yearly visits were then organized into patient types based on CPT procedure coding. The new patient visits were then categorized further into disease type. All new patient visits which would fall into the GI DOT were then distributed by primary tumor location site in order for a comparison to be done against the number of new patient visits for each type of cancer as compared to the number of current protocols available for that cancer type. As seen above, special note must be made that when looking at the number of visits in each category, for all years except 2008, the number of visits for a full twelve months was reported. Again here as with patient accrual, it must be noted that the number of visits for 2008 was from the beginning of January to the end of August 2008.

Overall, a steady increase in the number of overall patient visits, as well as new patient visits can be seen at the clinics over this four year span. *See* Table 4. Over the three year period from 2005 to 2007, an increase of 8628 total patient visits and an increase of 383 new patient visits occurred. This increase in both the total number of patient visits as well as an increase in the total number of new patient visits for each year maintains the percentage of new patient visits which are seen each year. A steady rate of 3.4-3.8% of

new patient visits as compared to all visits seen either at the SCCC and PHHS clinics can be observed. In contrast to the numbers seen within total patient accrual of the Cancer Center CRO, there are no noted increases or decreases in overall number of visits. This does not follow the same alternating pattern seen in subject accrual which leads one to believe that the instability of subject recruitment was not due to any changes in the number of patients seen within the ambulatory clinics.

Table 4: Number of Patient Visits per Year by Type

Type of Visit	2005	2006	2007	2008[a]
All Visit Types[b]	14,776	19,667	23,404	9,233
New Patient Visits	518	748	900	314
Percentage of Visits which are New Patients	3.5%	3.8%	3.8%	3.4%

[a] accrual is from January 1, 2008 through August 31, 2008.
[b] includes all visits types such as new patient, established patient, follow-up, and procedure visits.

However, by looking closer at just the GI new patient visits, we see a different pattern. In order to take a closer look at the number of new patient visits available for GI DOT recruitment, new patient visits were classified by each disease oriented team based solely on tumor location. For those new patients in which the primary site of the cancer was mentioned, they are listed under the corresponding DOT. However, if primary site was not specified within the patient report, the visit was filed under "unspecified" category. *See* Table 5. Of all 518 new patient visits seen in 2005, 14.8% of the visits (77 visits) were involving cancers of the GI tract. Following the cyclical pattern which was seen in GI DOT patient accrual numbers, a drop in the number of GI new patient visits to 6.2% was seen in 2006 with a slight increase in 2007 to 8.4%. This percentage has continued to increase in 2008 to 9.8% so far from this start of year until the end of August. It can

be concluded by this data that although the number of total visits of new patients only increased from year to year (as seen in Table 4), the number of new GI patient visits did have the same cycle of increases and decreases as seen in the overall subject accrual. Thus, this cyclical pattern could have played a role in causing the unpredictable pattern of recruitment seen specifically within the GI DOT.

Table 5: New Patient Visits per Year by Disease Oriented Team

Disease Oriented Team (DOT)	2005	2006	2007	2008[a]
Gastrointestinal (GI)	77	47	76	31
Hematology Oncology (Hem Onc / BMT)	49	112	98	45
Brain	4	37	24	3
Breast	68	120	133	28
Genitourinary (GU)	50	43	55	27
Gynecological (Gyn Onc)	123	164	227	49
Head & Neck	2	8	17	9
Lung	22	50	77	24
Skin (Melanoma)	31	15	19	14
Unspecified	90	152	173	84

[a] accrual is from January 1, 2008 through August 31, 2008.

Assessment of Current Study Protocols and GI Cancer Locations:

Another important factor for subject accrual, is to assess if the most relevant protocols are being initiated as compared to the patient population available. In order to assess if current active study protocols are feasible, they must not only be compared to the number of new patients seen with gastrointestinal cancer but also a comparison must be done. This included categorizing all new GI patient visits by location of the primary cancer tumor. Although variations of the percentages of types of cancer vary from year to year within the gastrointestinal group, the highest number of patients seen each year overall present with colon cancer. *See* Table 6. Pancreatic and hepatic are the next most

commonly seen cancers within this group, with gastric, esophageal and cancers of the biliary tract presenting less often.

Table 6: Number of New GI Patient Visits Distributed by Primary Cancer Location

Primary Location of Cancer	2005	2006	2007	2008[a]
Anorectal	11	5	6	3
Colon	32	20	26	7
Esophageal	4	4	8	6
Biliary tract (Gallbladder)	3	0	0	2
Hepatic	8	6	12	3
Pancreatic	13	8	14	6
Gastric	6	4	10	4

[a] accrual is from January 1, 2008 through August 31, 2008.

When compared to the number of active protocols, we see increased competition between study types for a very limited number of patients in each disease site. *See* Table 7. Currently there are six open active GI studies within the Cancer Center CRO. Of the five active studies, three are pancreatic, one is hepatic, one is colorectal and one is for rectal cancer. With three of the six studies currently active within the CRO competing for the total of six new pancreatic patients seen so far this year, it is hard to see how sponsor recruitment goals can be met. Not only are you dealing with a limited target patient population, but competition between studies will further limit the number of subjects enrolled in each. Although the total number of new patients may still be a barrier to the patient recruitment, enrollment goals have a better chance of being met without additional competing protocols opened for the same target population.

Table 7: Current Active GI Protocols & Accrual Goals

Protocol	Primary Cancer Site	Accrual Goal
BMS Ca182-006	Hepatic (unresectable, locally advanced, metastatic)	24
GenVec TNFerade	Pancreatic (unresectable, locally advanced)	10
Pfizer 1020	Colorectal (metastatic)	30
Pfizer 1028	Pancreatic (unresectable, locally advanced or metastatic)	15
ECOG E5204	Rectal (Stage II or III, pre-operative)	10
Reata	Pancreatic (locally advanced, can be metastatic)	10

Overall, with the very limited number of new patients seen each year for each primary cancer site, subject enrollment may be limited even with just one active protocol open at any time for any one site. In order for a protocol to have high feasibility to completion, higher numbers of patients must be seen within the clinic. Other factors such as protocol inclusion/exclusion, protocol complexity, as well as a patient's willingness to enroll are other factors which ultimately limit the number of subjects which can be recruited for a trial. Only with higher numbers of new patients to screen and approach for trials will subject accrual be able to increase within the GI DOT.

Part 3: Summary and Conclusion

Discussion of Findings:

There are many obstacles which may affect the quality, cost effectiveness and productivity of a clinical trail. Through the implementation of this Practicum Project, several potential barriers to conducting efficient trials and producing quality data were identified within the GI DOT.

Quality of Research Barriers and Recommended Modifications: The quality of research is an important aspect when conducting clinical trials. By conducting high quality research trials, the safety and welfare of the research subject is protected, as well as the integrity of the research data collected.[17] In order to guarantee the safety of the subjects and the quality of the data, there are many regulations and guidelines which must be followed when conducting clinical trails. To be certain that these standards have been maintained, continual review of regulatory and subject documentation must be conducted.[17] During the review of GI DOT study regulatory and subject data, several potential barriers to maintaining effective clinical trials while ensuring data quality and patient wellbeing were identified.

Although the majority of the regulatory and subject documentation reviewed during the internship was found to be complete and accurate, the lack of an organizational standard of documentation with the GI studies could potentially be a hindrance to making certain all regulations and guidelines requirements have been met. Standardizing all aspects of

the clinical research office, including organization of study documentation,[17] are ways in which the AMC can protect both their patients and the quality of data produced. Varying organization of study documentation not only makes it harder to locate the necessary forms when needed, but also makes it more likely that forms may be misplaced. If a standard format for regulatory binders, as well as for patient case binders was established within the SCCC CRO, this would make monitoring and reviewing study documentation more straightforward and less problematic. Additionally, a standard format could have other benefits within the Cancer Center CRO. This could also make transitions due to either new staff hires or changes in responsibilities easier. Currently, with no standard in place, when a new staff member is hired they have to adapt to several different methods of organization. If only one type of organizational system was in place for all studies, transitions could be less complicated and more readily made. Furthermore, putting a labeling system in place for the file cabinets in order to identify the location of each study's file will consistently help eliminate misplacement of source documents or study forms. Overall, organization of study documentation within the GI DOT would help to eliminate potential mistakes and make monitoring, reviewing and accessing study files more readily available to the staff.

Another potential barrier to maintaining quality research standards is the potential for a breakdown of communication between CRO teams. With the Cancer Center CRO being organized into different teams, there is an increased potential for communication barriers to be encountered. For instance, although the majority of the regulatory and subject documentation was found to be accurate and complete, there were some deficiencies

which appeared to be due to a lack of open communication between the GI DOT and the regulatory team. In this case, it was noted that in one particular study the consenting coordinator was not listed on the consent form or on the study delegation list. This was retrospectively corrected and the coordinator was added to the consent form. However, in order to conduct quality clinical research, oversights such as this must be avoided as much as possible. In order to prevent such discrepancies, open and consistent communication between teams is important to ensure all federal and internal guidelines for study conduction are maintained. Meetings consisting of the GI DOT coordinators and their regulatory team members should occur on a routine basis. Potential modifications to study protocols or consents as well as upcoming IRB reviews should be discussed at these regular meetings. Additionally, development of detailed project plans which delegate the roles and responsibilities of each team member could help increase communication between the research staff. By having scheduled meetings and project plans in place, it is less likely that changes, such as the one described above, will be overlooked. Ultimately, these recommendations can help eliminate lapses within maintaining regulatory guidelines.

Besides maintaining regulatory guidelines, it is also important to maintain the integrity of the research data collected and to limit data queries and protocol deviations. Although queries and deviations are expected when conducting a clinical trail, an increased number of them appeared to occur when reviewing the GI DOT patient case binders. Overall, a majority if the deviations and queries found seemed to occur most often within those study protocols which were more complex. For example, more discrepancies were noted

in those studies consisting for more than one treatment arm. These studies typically consisted of one or more treatment arms and an additional standard of care or observational arm. Within each arm of the study, different labs procedures and different treatment regimens were utilized. As such, protocols with different arms could easily become complex and, at times, confusing. This complexity can then lead to data inaccuracies or deviations form the protocol which can ultimately endanger the study subject. As such, limiting the amount of queries and deviations is extremely important when conducting clinical trails. In order to help ensure the safety of the subject, the use of visit specific worksheets should be implemented. Visit specific worksheets or source documents can be used to outline procedures and treatments which should be conducted at each individual study visit. By adding specificity to each visit document, the deviations and data inaccuracies can be diminished. Additionally, coordinator visit notes and patient study calendars should be utilized by the GI DOT coordinating staff. Coordinator progress notes can help ensure safety and efficacy within the study by clearly documenting the procedures completed at each visit. Patient visit calendars can also help to not only keep the coordinating staff aware of the visit schedule, but also be used to help inform the patient and clinic staff of upcoming research visits. By implementing techniques to limit the confusion of study visit procedures and treatments, discrepancies can be more readily evaded.

Furthermore, other changes within the GI DOT can help to maintain the quality of the trials performed. Clinical monitoring is a way to provide a direct assessment of the regulatory maintenance and data quality and can help identify shortcomings or obstacles

in conducting efficient clinical trials.[17] Continuation of regularly scheduled internal audits by the Quality Assurance and Educational Coordinator should be continued in order to assure that research subjects are being protected and the data produced is of the utmost quality. Continuation of these internal audits can help identify and eliminate where deviations and queries are most likely being produced. Once identified, changes within the GI DOT can continually be made in order to diminish discrepancies and increase the quality of data and patient safety.

Additionally, implementing coordinator educational programs can also help reduce deviations from regulations or study protocols. Regular educational programs should be conducted by the Quality Assurance and Educational Coordinator. Pertinent clinical research topics discussing regulatory guidelines such as *Code of Federal Regulations (CRFs), Good Clinical Practices (GCPs),* and *Human Subject Protections* or describing local Institutional Review Board guidelines should be scheduled throughout the year to help keep the administrative, regulatory and coordinating staff up to date on all relevant guidelines. In addition, staff should also be encouraged to complete outside continuing education training programs such as training for Certified Clinical Research Coordinator (CCRC). Currently there are two organizations which provide certification for clinical research coordinators which includes the Association of Clinical Research Professionals (ACRP)[24] and the Society of Clinical Research Associates (SoCRA).[25] In order to help encourage the staff to participate in these type of certification programs, incentives or reimbursement for this additional training should be provided by the SCCC CRO if available. Overall, continuing internal monitoring and increasing the educational

opportunities will help to increase the knowledge of the GI DOT staff and help to alleviate potential barriers to maintaining quality research within the SCCC CRO.

Financial Productivity Barriers and Recommended Modifications: The ability to complete trials within a reasonable budget, is an important cost effective barrier faced by most AMC's.[7] There are several aspects of the negotiation process and development of study budgets which can impede coverage of all research related costs incurred by the research site. When reviewing the GI DOT several different barriers which can reduce the cost effectiveness of the Cancer Center CRO where identified.

Almost certainly, the most important factor hindering the cost effectiveness of the GI DOT is the lack of appropriate funding for cooperative group study trials. Similarly, as with the data produced by the study conducted by Emanuel and colleagues,[7] it was found that within the GI DOT study protocols sponsored by the Eastern Cooperative Oncology Group (ECOG), the cost of conducting most of these trials significantly outweighed the funding received from the sponsoring organization. As noted during the review, the majority of the ECOG study costs spent at the site are considerably higher than the limited funds provided. However, this is a difficult problem to fix. Since ECOG studies are paid only on a set per patient basis with limited negotiation room for ancillary funds, the best way for the site to manage within this budget it to streamline the research process as much as possible. The review found that most of the over cost was not due to study procedures, labs or treatment since most fell within the standard of care. The overage comes from coordinator and administrative staff time. In order to reduce the cost, the

time spent on each study must be reduced. The reduction of multiple steps in the process of study start-up and more efficient subject screening techniques could help reduce the time spent on each study. However, no direct recommendation can be made for change. All reviewed steps within the GI DOT are currently necessary in order to fully manage a clinical trail at the academic site setting. Ultimately, changes in procedures and internal processes should be reviewed on a regular basis in order to try to find new ways to limit administrative and coordinator time and reduce cost of study conduction.

Likewise, potential budget pitfalls within industry sponsored trails were also identified. Consistent with the survey data produced by Wright in 2005,[19] review of the GI DOT study budgets showed that most administrative and non-clinical research procedures were not always being sufficiently funded. Again here, as with the ECOG studies, it was found that most clinical procedures, including lab tests and therapies, were found to be covered by either the standard of care or funded by the sponsor. However, non-clinical procedures such as reimbursement for coordinator time or administrative start-up fees were not always compensated for fully. As mentioned above, negotiating sponsor budgets can be an impossible process. As such, the recommendations made can only be achieved with the cooperation of the industry sponsor.

Negotiation is key when working with the industry sponsor to agree upon a reasonable budget for both the sponsor and the research site. One important stipulation to try to negotiate into each financial agreement is initial start-up cost. Although most of the recently initiated studies with the GI DOT include this fee, some previous studies had

limited funds allotted for this. Prior to the first subject ever entering the clinic, costs of study start up are already being accumulated. If a study startup or initial payment is not made, the Cancer Center CRO is ultimately responsible for covering those costs. In order to avoid the accumulation of start-up costs, an initial fee covering all administrative startup fees, local IRB fees and pharmacy set up fees should be collected from agreeable sponsors. If an initial payment can be included in the study agreement, these funds can help cover costs associated with administrative startup time and IRB review.

Additionally, review of all critical constraints, such as investigator and coordinator time, should be analyzed and represented appropriately within each study budget[20] Within the review of the GI DOT study budgets, significant variation in the amount reimbursed for coordinator time was noted. For most studies, this per visit reimbursement was based on many factors including amount of time expected for each study, as well as the sponsors recommended rate. In order to be certain coordinator time is being sufficiently covered within the study budget, the Cancer Center CRO should establish a standard hourly rate for coordinator time. When developing a budget, this rate should be used to determine the cost for each subject visit. Additionally, the estimated amount of time the coordinator will spend screening subjects, participating in monitoring visits, entering data and adverse events as well as answering queries should also be included in the overall budget. With all time factors included, a reasonable study budget can then be negotiated with the study sponsor in order to produce a budget that will include sufficient funds for coordinator time.

Furthermore, an extensive review of all procedures or treatments considered standard of care (SOC) should also be completed with each budget. Since the passing of the National Coverage Decision (NCD) of 2000, determining what entity should cover procedures performed has become a daunting task.[20] For instance, when reviewing the GI DOT budgets, variation in the time frame for routine testing, especially imaging, varied from study to study. Some studies scheduled CT scans every 6-8 weeks, where as others had the imaging performed every 8-12 weeks. By the national guidelines produced by the National Comprehensive Cancer Network (NCCN),[23] the standard of care for monitoring for progression of disease in colon or rectal cancer by CT is every 8-12 weeks. For these studies in which CT's occur more often than the 8-12 week standard, reimbursement should be negotiated by the site since these procedures fall outside of the standard of care. In order to help estimate study budgets, a standard format for SOC procedures should be established with the GI DOT as well. This standard can then be utilized when developing and negotiating study budgets for new protocols and help eliminate oversights and loss of revenue for procedures which do not get covered.

In addition to setting up standards and guidelines for the negotiation of study budgets, continual review of study transactions and billing should be completed on a regular basis. Throughout the review of GI DOT study financials, oversights of invoiceable items were observed. One way to try to reduce this occurrence would be to include as many items as possible into the schedule of payments. However, for those items which the sponsor is unwilling to include, regular review by the accounting personnel should be done for each

study in order to ensure that all invoices have been sent and all accounts have been reconciled.

With the overall willingness of the sponsor to negotiate budgets being a prime limitation, some of the above recommendations made may be difficult to implement. However, if the GI DOT is able to implement some of the changes to help correct budgeting pitfalls and then are able to generate study budgets which can support all cost endured by trial conduction, it will be able to increase its overall efficiency and effectiveness.

Protocol Feasibility Barriers and Recommended Modifications: An additional barrier continually faced by AMC's when conducting clinical trials is protocol completion feasibility and subject accrual.[8] A significant amount of pre-trial preparation is utilized analyzing protocol feasibility during the initial phases study review. However, although GI DOT protocols are thoroughly reviewed, patient accrual into GI studies still seems to be an obstacle with the Cancer Center CRO. Numbers for the GI DOT accrual show a fluctuating pattern of patient recruitment over the past fours years. However, the percentage of patient recruited within the Cancer Center CRO into GI studies has been on a steady decline. Several factors, identified during completion of this Practicum Project, have been identified as possible barriers to effectively recruiting study subjects. First, when reviewing the current patient demographics within the Simmons Comprehensive Cancer Center and Parkland Health and Hospital System's ambulatory clinics, one can make some assumptions as to why recruitment is low within the GI group. Although there has been a steady increase in the number of new patients reporting to the clinics

each year, there is a substantially lower number of new patients presenting to the clinics with cancers of the GI tract as compared to the number of patients presenting for other cancer sites. For example, for this current year there were only a total of 31 new patients presenting with GI cancers from January to August 2008. Whereas, if you look at the new patients presenting to clinic with breast and lung the numbers are much higher at 130 new patients and 60 new patients, respectively. With a lower number of patients presenting within the target population for the GI DOT, meeting subject accrual goals becomes almost impossible.

The task of recruitment seems more impractical when you consider the number of patients presenting for each individual GI cancer site compared to the number of subjects outlined in accrual goals by the GI study protocols. For the 2008 year, at one time there were three pancreatic protocols active trying to recruit a goal of 35 patients total for all three studies. When compared to the total number of new patients seen in this year so far (only 6) these recruitment numbers seem unrealistic to be met for several years.

In order to help the GI DOT increase their subject recruitment numbers, several adjustments should be made. First, protocols should be stringently reviewed and only those which are reflected of the current patient population should be opened at the Cancer Center. As described above, there are currently too many pancreatic protocols open when compared to the available patient population. In order to adjust for this, less pancreatic oncology studies should be initiated. Instead, focus on spreading protocols out in several gastrointestinal areas should be done. An overall mix of study trials which is

tailored to the current patient population should be achieved. By completing annual reviews of the current patient population and comparing that to upcoming study trials, the GI DOT will be more effective at opening studies where recruitment is more feasible and meeting accrual goals is more likely.

Additional methods to help improve the recruitment process should also be considered. Regular administrative meetings between different disease groups can be utilized to help promote the exchange of ideas on how to overcome recruitment barriers. Discussion of obstacles faced by each DOT and ways to overcome these can help groups fine tune their subject accrual efforts. Furthermore, these meetings can also be utilized to inform each DOT about the open trials within the other groups. With overlap of patients within different ambulatory clinics, having all team members of the Cancer Center aware of which studies each DOT has enrolling can help promote recruitment in all areas. By enlisting all DOTs within the Cancer Center to work together and share ideas, increased enrollment not only with the GI DOT but all DOTs can be achieved.

Implemented Changes within GI DOT: Overall, reaching the goals set for the GI DOT will take time, but by implementing changes to study execution and conduction, these goals can eventually be achieved. Implementation of these changes will have to occur as a developing process. As of the date of the end of the internship, some organizational changes within the GI DOT had occurred. Patient binders and development of study specific source documents had been started by the intern and GI DOT coordinators. Study budgets with the GI DOT had been reviewed by the intern and account

discrepancies had been identified to the accountant and reconciliation was in process. However, as described within the Project Limitations, the limited time available to the intern to complete this project during the internship hindered the initiation of many of the above recommendations. Further implementation of recommendations will continue to be made as the GI DOT coordinators and Assistant Director of the Cancer Center CRO continue to improve the productivity of the team.

Summary of Findings:

Throughout the Internship Practicum Project, there were several barriers noted which may impede the productivity and efficacy of the GI DOT. By making subtle changes to the organization, budgeting and protocol selection, improvement of the GI DOT can be made. To help the GI DOT become productive, it is probably most important to reevaluate the selection of study protocols and to make certain that new protocols opened within the GI DOT are in line with the current patient population. By achieving a viable mix of study protocols, subject accrual can be improved. Additionally, more standardized formats for organization and budget development and negotiations should be implemented within the GI DOT. By making standardized formats for each, oversights of regulatory guidelines or substantial study funding can be reduced. Continual review and modifications must occur within the GI DOT in order for it to become a productive and efficient part of the Simmons Comprehensive Cancer Center Clinical Research Office.

Project Limitations:

Several limitations to the conduction of the Internship Practicum Project have been identified. Such limitations include inadequate experience of the intern in regards to financial budgeting of clinical research trials, as well as limited knowledge of the facility patient database systems. In order to insure that the best outcomes were reached through the research project, the following measures were implemented in order to reduce any discrepancies caused by these limitations.

- The intern reviewed articles related to study budgeting and cost analysis.
- The intern had access to Cancer Center CRO personnel who are proficient in financial aspects of research management for advice and guidance. The intern collaborated with both the Assistant Director of the CRO as well as accounting personnel when reviewing financial documentation and developing recommendations for changes within the GI DOT.
- The intern also had access to Cancer Center personnel who are proficient with the database management systems used within the CRO. The intern was able to utilize patient information reports produced by the Senior Database Analyst. Specifications for the patient reports were outlined by the intern in collaboration with the Assistant Director of the CRO.

The most limiting factor of the conduction of the Practicum Project was time constraints. The intern and the Assistant Director of the CRO scheduled the completion of several projects to be discussed with the Practicum Project during the 24 week internship. Although, all scheduled analysis and reviews were completed during the time frame, time

constraints inhibited the amount of implemented changes which could be started with the GI DOT and SCCC CRO during the time frame of the internship. However, although implementation may have not been able to be completed during the set outlines of the internship, changes may still be completed within the GI DOT by the Assistant Director after the internship has concluded.

CHAPTER III

INTERNSHIP EXPERIENCE

Internship Site Description:

The internship was conducted at the University of Texas Southwestern Medical Center in Dallas, Texas, within the Clinical Research Office (CRO) at The Harold C. Simmons Comprehensive Cancer Center. The Cancer Centers CRO's primary focus is conducting clinical oncology research studies that test new drugs, drug combinations and novel therapies which promote the development of new treatment standards.[26] Although the CRO ultimately functions as one entity, the department's infrastructure is sub-divided into several different smaller groups. Departments within the CRO consist of the administration, a regulatory unit and nine Disease Oriented Teams (DOTs). Administration's main objective in the CRO is to oversee study approval, manage contracts and financials, and update the clinical research database. The regulatory unit interacts with the IRB and focuses on maintenance of all regulatory documents for all studies within the Clinical Research Office. Clinical coordinators, research nurses and clinical data specialist are subdivided into nine different disease focused groups including brain, breast, head & neck, hematology oncology (BMT), gastrointestinal (GI), gastrourinary (GU), gynecology oncology, lung and melanoma. Each disease group's

responsibilities include patient recruitment and coordination and execution of all study protocols within their disease group.

Internship Experience:

During this internship, the majority of the practicum was spent reviewing and analyzing data from within the Gastrointestinal Disease Oriented Team (GI DOT). After completing a full audit and review of all GI study protocols, study documents, financials and patient recruitment statistics, the intern helped develop recommendations for all areas to help improve the efficiency of the GI disease group. Some of those suggestions were implemented by the assistant director and intern within the department; however, execution of changes was limited due to the time restrictions of the internship. Ultimately, the practicum focused not only on giving the intern the opportunity to increase her knowledge of the steps involved in clinical research management, but it also allowed the intern to actively participate in the development of procedural changes which may help to increase the productivity, cost effectiveness, and efficiency of the GI DOT.

Although the primary focus of this internship was to provide the student with first hand knowledge of clinical research management, the intern was also given opportunities to participate in various other aspects of study startup and execution of clinical trials. A Daily Research Activity Log which outlines the projects completed by the intern each day was kept throughout the internship. *See* Appendix A. Duties which were delegated to the intern either by the assistant director or the GI DOT manager and coordinators are described below:

- *CRO Staff Meetings*: During the internship the intern was able to participate in monthly staff meetings. These meetings were held to address the issues or challenges that had presented within the Cancer Center CRO. The intern was able to learn through observation at these meetings, but was also able to take part in discussion to help make suggestions for improvement or resolution of obstacles faced by the CRO.
- *Training and Certifications*: At the beginning of the internship, the intern completed all required training which included Health Insurance Portability and Accountability Act (HIPAA), Human Subjects Protection, local IRB training and training for use of the Cancer Center CRO research database. In particular, the Human Subjects Protection and local IRB training was an excellent review of the regulations and guidelines which govern the conduct of clinical research trials. These training materials were utilized throughout the internship as the intern monitored and reviewed all study documentation for the GI DOT.
- *Simmons Cancer Center Clinical Research Office Training*: At the beginning of the internship, training was provided by the administrative and regulatory teams which described the steps involved in protocol review, acceptance and study initiation. This training described in detail the committees which have been established at the different levels of the academic medical center to insure that quality and safe research trails are conducted at this site. For new study approval, the new study protocol must pass several different levels of

review prior to being accepted and initiated by the Cancer Center's CRO. A protocol is first presented by the Primary Investigator (PI) to the DOT. If approved, it is then submitted to the PRMC and pre-IRB review. The PRMC is a committee established within the Cancer Center CRO to review the scientific merit and feasibility of all oncology clinical research protocols to be conducted at UTSW. Based upon review of the protocol the PRMC will make one of four choices regarding the approval. It can either be approved, approved pending response, deferred, or can be disapproved. If PRMC approves the protocol, and only when approved, it will then go to the local IRB for review and approval. Additionally at this time, other entities which will be involved in the execution of the study protocol must also grant approval. This includes approvals from the UTSW ambulatory clinics, the University Hospitals Research Compliance Committees (RCC) and the Radiation Safety Committee (RSC). If the study will enroll patients at Parkland Health and Hospital System (PHHS), it must also undergo review and approval at this facility as well. If all levels of approval are reached, then the study protocol can be initiated within the Cancer Center's CRO. Although the intern was not involved within the actual submission of new study protocols, the training provided by the CRO was informative and necessary to understand the administrative and regulatory requirements for study approval at the Cancer Center and the University.

- *Protocol Feasibility*: One of the most important initial steps of protocol approval and initiation is the review of each study protocol to assess whether it will be feasible to complete with the resources available within the Cancer Center CRO. To assess practicability, the manager for each resource that is being utilized reviews the protocol for feasibility and resource usage in their specific area. For example, the Investigational Drug Service pharmacist reviews the protocol for items such as amount of needed pharmacy staff and time, space for long and short-term storage, as well as proper equipment for drug storage and dispensation. The clinic managers, revenue cycle manager and clinical research managers all review the protocol for similar effects on their staff and resources. Once all resource managers have signed the Resource Approval form, the CRO Assistant Director signs the documents and the study can be opened contingent on all pending approvals. This review balances many aspects of study execution ranging from length of time for patient enrollment to study completion, the number of staff and the time commitment needed to complete the study, as well as the availability of the target population within the ambulatory clinics. As described within the methods section of the Practicum Project, the intern was responsible for an important aspect of protocol feasibility by completing an analysis of the patient demographics within the ambulatory clinics. *See* Chapter II: Practicum Project. These statistics where then used to estimate which type of protocols would be most productive within the GI DOT reaching their accrual goals and

help establish which types of protocols should be opened within the CRO for the GI DOT.

- *Study Financial Agreements & Budgeting*: Another important job of the administrative staff is to work with the sponsors to develop a reasonable budget for completion of the study protocols. In order to establish a complete budget the accountant must take into consideration the cost for non-standard of care procedures and treatments, cost for staff time and institutional overhead. In order to adequately access all costs involved in the execution of the study, the accountant and the study coordinator review the protocol in detail and develop an expense sheet of all costs which will be accrued during the study conduct. This includes costs of all supplies, procedures, equipment, coordinator time, as well as additional resources which may have to be utilized outside of the Cancer Center CRO. The intern was given the opportunity to help with the budgeting process by producing a cost sheet of routine procedures based on past protocol budgets, as well as listed invoiced costs from the utilized facilities. This cost sheet was used to compare cost of new study protocols to costs which where collected in the past. After procedure costs were determined by the study coordinator and the accountant, the institutional overhead is then added to these costs in order to produce a reasonable budget for execution of the protocol. Although negotiations and budget development are important aspects of research management, continual review and tracking of financial transaction and reconciliation of accounts must be maintained. As such, the intern played an important role in the

review of all financial agreements, budgets and transactions within the GI DOT. As described above, the intern completed a full review of all financial agreements and budgets for both open and closed GI protocols. *See* Chapter II: Practicum Project. Upon completion, the intern then worked with the assistant director and CRO accountant to reconcile all accounts.

- *Monitoring of Study Documentation:* In order to conduct effective and safe trials there are many regulations and guidelines which must be followed. To determine if these standards have been met, continual review of the regulatory documentation, case report forms and source documents must be done. Implementation of the Practicum Project required a complete audit and review of all GI study protocols, regulatory documentation and patient case binders. Steps taken to complete this review are described in detail in Chapter II: Practicum Project. The opportunity to monitor all the regulatory aspects of research management gave the intern a chance to focus on key regulations and guidelines which must be followed in order to conduct efficient, safe and quality trials.
- *Study Coordination and Implementation:* Study coordination is one of the most important aspects of clinical research. Coordinators are responsible for ensuring the safety of the subject while also maintaining the efficacy and productivity of the study. During the internship, the intern was given the opportunity to assist the GI DOT in several different aspects of study coordination and management. While in the internship, the intern worked along side the GI DOT coordinators to help in initiation processes, study

execution and management. Assisting with consent form development, production of subject screening logs, participation in study visits, development of source documents, assisting in the review of adverse events and data clarification queries, as well as participation in monitor and site initiation visits were all tasks made available to the intern. Prior to study initiation, the coordinator is responsible for assisting the regulatory and administrative teams with modifications to protocol and consents, as well as study budgeting. The intern had the opportunity to assist the GI DOT coordinator with consent development and modifications by gathering published data on possible drug side effects. This gathered data was then used to make modifications designated by the local IRB to protocols which were in review.

After approval has been reached on all regulatory documentation and a site visit has been completed, the next phase of study initiation is the site initiation visit. Since the intern was present at the site during a GI DOT site initiation, she was given the opportunity to participate in this event. Site initiations are important to the DOT's and regulatory team since they provide the teams an opportunity to review the basic science behind the study design, as well as get an in-depth review of the protocol itself. Initiation visits also allowed the Cancer Center GI DOT to clarify any questions they may have with the study protocol directly with the sponsor team onsite.

Once the site initiation was complete, screening and patient enrollment can begin. To help with this screening and patient enrollment, the intern was responsible to develop a log tracking the number of patients screened each month for each of the active studies within the GI DOT. This log was then utilized by the assistant director for administrative reports. Keeping a log of screened patients is fundamental in patient recruitment since it shows how many patients must be screened in order to enroll one into a study. This tool helps to determine if the patient population within the Cancer Center clinics is coinciding with study protocol criteria and helps to determine if a study will be able to maintain productivity.

Beside administrative measures, coordinators spend part of their time each week conducting study visits. As such, the intern was given the opportunity to accompany the GI DOT coordinator to study visits and observe. Through this process the intern was able to interact with the coordinator, principal investigator and study subject. She was able to observe the actual execution of study visits and all the requirements which must be completed at each. At each visit, the coordinator must meet with the patient, collect all necessary data outlined within the CRF's and study protocol to be inputted in the sponsor's data system. Although the intern was not able to conduct a study visit on her own, observation of such activities was a great learning experience into the process of protocol execution. Additionally, data collection is an important part of each study visit, especially the reporting of

adverse events. By being allowed to observe study visits, the intern also gained insight into the reporting of adverse events. When an adverse event is noted by the coordinator, it must be reported to the sponsor and the local IRB. This process was demonstrated to the intern by the GI DOT coordinator. The GI DOT coordinator also enlisted the intern's assistance with the clarification of data queries. The intern was given the responsibility of reviewing subject data and source documents to help answer queries.

One of the main assets the intern provided for the GI DOT study coordinators was to help with organization of patient case binders, study binders and source document development. As part of the Practicum Project, the intern was responsible for patient case binder review. During this task the intern also helped the study coordinators organize the study binders in an attempt to make the format more standardized. She also assisted in organizing study binders for each protocol to help place all recruitment, study visit and lab information in one location for easy access by the study coordinator. Additionally, as part of the study binders, the intern also developed screening tools based on protocol inclusion and exclusion criteria to be utilized by the coordinator for each study. Overall, by allowing the intern to participate in all aspects of the coordinator's responsibilities, she was able to gain great insight into all areas of clinical research conduction.

During this internship, the intern was given the opportunity to participate in many facets of the clinical research experience. The intern was able to gain substantial knowledge within administrative and regulatory processes, as well as study coordination and implementation. She was able to help identify potential barriers which may occur when conducting clinical trial and was given the opportunity to help find solutions for overcoming these barriers. Overall, this internship experience was an educational experience which will be utilized by the intern in her future endeavors within clinical research management.

APPENDIX A

RESEARCH DAILY ACTIVITY LOG

Daily Research Journal for Elisha Hatfield, MPAS, PA-C

Site: UT Southwestern Medical Center at Dallas
Clinical Research Office, Simmons Cancer Center
Dates of Internship: June 2, 2008 through November 14, 2008

Date	Daily Activities
WEEK 1	
Monday June 2, 2008	**Advisory Committee Meeting** ▪ met with assigned advisory committee consisting of Lynn Baker, MBA, UTSW Medical Center; Patricia Gwirtz, Ph.D., UNTHSC; and Rusty Reeves, Ph.D., UNTHSC. ▪ *Master of Science Designation of Advisory Committee* and *Master of Science Degree Plan* were reviewed and signed by the advisory committee ▪ discussed potential job duties and research assignments within the CRO. 1) Investigator Initiated Phase II Drug Trial in Breast Cancer Research, 2) Eastern Oncology Cooperative Group Study, other options include studies in hematological oncology, neuro or GI. ▪ thesis topic will be decided upon within first two to three weeks of internship and be submitted to Drs. Gwirtz and Reeves no later than the week of June 16, 2008. ▪ thesis proposal will be due to Drs. Gwirtz and Reeves by mid-July (July 14-18, 2008) ▪ will try to schedule thesis presentation for 2-3 weeks prior to Thanksgiving holiday.
Tuesday June 3, 2008	**Scheduled Day Off** – Awaiting UTSW HR Approval
Wednesday June 4, 2008	**UTSW Orientation and Training** ▪ Human Resources Orientation ▪ CRO Computer Orientation and Training
Thursday June 5, 2008	**UTSW Training** ▪ NIH Protecting Human Research Participants Online Training ▪ Computer Online Self-Training Modules **Research Material Review** ▪ review of CRA Monitoring Materials
Friday June 6, 2008	**Training** ▪ Computer Online Self-Training Modules ▪ research thesis topics and article review

Date	Daily Activities
WEEK 2	
Monday **June 9, 2008**	**Research Material Review** ▪ reviewed CRA Monitoring Guidelines ▪ article reviews for thesis topics **Research Study Review** ▪ reviewed Protocol SCCC-02107 ▪ reviewed Informed Consent for Protocol SCCC-02107
Tuesday June 10, 2008	**Research Study Review** ▪ review of Protocol SCCC-02107 ▪ review of pertinent journal articles related to study protocol including drug reference information, RECIST criteria and current guidelines for first line treatment of metastatic breast cancer **Research Orientation & Training** ▪ Research orientation and HIPAA training with Investigational Review Board (IRB)
Wednesday June 11, 2008	**Research Study Review** ▪ review of Protocol SCCC-02107 ▪ review of related journal articles and breast cancer management guidelines
Thursday June 12, 2008	**Research Study Review** ▪ review of related journal articles, breast cancer management guidelines, and obstacles in breast cancer research **Organization for Research Practicum** ▪ organization of timeline for Research Internship and Practicum Report ▪ search interesting research thesis topics and review pertinent articles to discuss with Lynn Baker
Friday June 13, 2008	**Research Practicum** ▪ locate journal articles for research thesis ▪ begin working on research proposal **CRO Training** ▪ met with Charla Dowell, Protocol Coordinator. Reviewed the new study approval process, role of the protocol review and monitoring committee, and the role of the data safety and monitoring committee. ▪ met with Deandrea Hendricks, Regulatory Coordinator. Reviewed role of the regulatory unit as well as their procedures.

Date	Daily Activities
WEEK 3	
Monday June 16, 2008	**Research Practicum** ▪ locate journal articles related to research thesis ▪ begin working on research proposal **Research Material Review** ▪ reviewed CRA Monitoring Guidelines
Tuesday June 17, 2008	**Research Study Review** ▪ review of related journal articles, breast cancer management guidelines, and obstacles in breast cancer research **Internship Practicum Meeting** ▪ meeting with Lynn Baker, MBA ▪ discussed potential research proposal suggestions. Narrowed suggestions down to two ideas: Obstacles faced in minority recruitment into clinical research trials and maintaining their enrollment. This would involve the development suggestions for increasing minority participation; or Review of GI studies in Developing Programs Department. This would require review of current studies' (10-12) protocols, IRB, CRFs etc. to find areas of discrepancies or areas in need of improvement. This would involve the development of suggestions for GI disease group improvements along with potential accountability measures. ▪ will try to meet with Rosalie Serrano, DOT Research Manager, and Celeste Skinner, Communications, to finalize decision on which proposal to pursue. ▪ once proposal has been decided upon will set up regular meetings with Lynn to discuss progress of proposal.
Wednesday June 18, 2008	**Research Practicum** ▪ located and reviewed journal articles dealing with either minority patient recruitment or research study management. ▪ correspondence to Drs. Gwirtz and Reeves regarding research proposal suggestions.
Thursday June 19, 2008	**Research Article Review** ▪ reviewed journal articles dealing with either minority patient recruitment or research study management. **CRO Staff Meeting** **Internship Practicum Meeting** ▪ meeting with Lynn Baker, MBA ▪ revisited topics for research proposal. We will meet again either tomorrow or Monday to finalize topic.
Friday June 20, 2008	**Research Article Review** ▪ review of related literature for research management and cancer treatment. **Internship Practicum Meeting** ▪ met with Lynn Baker, MBA ▪ we will discuss plan for implementing research topic next week. ▪ topic will focus on GI study review and management.

Date	Daily Activities
WEEK 4	
Monday **June 23, 2008**	**Research Article Review** ▪ reviewed book "The CRA's Guide to Monitoring Clinical Research" ▪ located and reviewed articles pertaining to quality assurance and management in clinical research
Tuesday June 24, 2008	**Research Practicum** ▪ established a proposal outline **Research Article Review** located and reviewed articles pertaining to quality assurance and management in clinical research
Wednesday June 25, 2008	**Research Practicum** ▪ began research proposal first draft **Internship Practicum Meeting** ▪ meeting with Lynn Baker, MBA ▪ will focus research internship and practicum within GI Study Group of the Developing Programs ▪ discussed development of research practicum which will include a complete review of all open and closed GI studies. Areas of review will focus on 3 main potential topics: financials – review of contracts and funding of each study; Study Audit – to include review of protocols, IRB forms, CRFs, adverse event forms, etc.; and Patient Recruitment – analyze patient population of GI clinic at the Cancer Center and Parkland to make suggestions for future studies which might be able to have better enrollment. Also review protocols and obstacles in clinic which might hinder patient enrollment and continuation in GI studies. ▪ will schedule a meeting for next Monday with Lynn Baker, Rosalie Serrano, DOT Research Manager and Antoinette Gonzales, QA Coordinator to discuss further details and involvement in the GI Study Group. **Research Article Review** ▪ located and reviewed articles by DM Dilts regarding obstacles and barriers in research administration
Thursday June 26, 2008	**Research Article Review** ▪ reviewed book "The CRA's Guide to Monitoring Clinical Research" ▪ reviewed articles relevant to clinical research study management and quality assurance
Friday June 27, 2008	**Research Practicum** ▪ redraft proposal outline and internship calendar of events **Research Article Review** ▪ review of articles related to study auditing and financials. ▪ review articles pertaining to patient recruitment.

Date	Daily Activities
WEEK 5	
Monday June 30, 2008	**Internship Practicum Meeting** ▪ met with Lynn Baker, MBA, Rosalie Serrano, DOT Manager and AntoinetteGonzales, QA & Education Coordinator ▪ discussed goals for internship practicum. It will focus on above mentioned areas to include study audits, financial and budgets reviews as well as patient population evaluation for the GI disease group. Upon completion of evaluation, study tools, guidelines and/or accountability measures may be developed for study improvements ▪ will complete auditing and financial review of each study prior to moving onto next. Will begin with all ECOG studies. ▪ will meet with Antoinette next week to review all auditing tools and materials. Will report any discrepancies found during study review to her. ▪ Rosalie will provide a list of ECOG studies, arranged in order of importance, for review ▪ Lynn will assist in financial review and discussions with budgeting **GI Study Audit/Review of Study Documents** ▪ review quality assurance guidelines and auditing tools **Research Practicum** ▪ finalize proposal outline
Tuesday July 1, 2008	**CRO Training** ▪ HIPPA Research Specific Online Training ▪ Good Clinical Practices Online Training **GI Study Audit/Review of Study Documents** ▪ review quality assurance guidelines and auditing tools
Wednesday July 2, 2008	**GI Study Audit/Review of Study Documents** ▪ began review of ECOG-E2204 Protocol
Thursday July 3, 2008	**GI Study Audit/Review of Study Documents** ▪ completed review of ECOG-E2204 Protocol ▪ began review of ECOG- E3204 Protocol
Friday July 4, 2008	**Scheduled Day Off** – Holiday

Date	Daily Activities
WEEK 6	
Monday July 7, 2008	**GI Study Audit/Review of Study Documents** • completed review of ECOG-E3204 Protocol • began review of ECOG- E5202 Protocol
Tuesday July 8, 2008	**GI Study Audit/Review of Study Documents** • completed review of ECOG-E5202 Protocol • began review of ECOG- SO600 Protocol
Wednesday July 9, 2008	**Audit Process Meeting & Discussion** • met with Antoinette Gonzales, QA and Education Coordinator • discussed auditing and report procedure and reviewed auditing tools **GI Study Audit/Review of Study Documents** • continued review of ECOG-SO600 Protocol
Thursday July 10, 2008	**GI Study Audit/Review of Study Documents** • completed review of ECOG-SO600 Protocol • began review of ECOG- SO600 Protocol
Friday July 11, 2008	**Research Practicum** • work on finishing up Research Proposal **Internship Practicum Meeting** • meeting with Lynn Baker, MBA • discussed background information for research proposal and decided on direction • will start setting up bi-monthly meetings to discuss progress of research thesis and will begin to review study financial agreements **Research Article Review** • review of articles related to study auditing and financials.

Date	Daily Activities
WEEK 7	
Monday **July 14, 2008**	**Research Article Review** ▪ review of articles related to study auditing and financials. ▪ review articles pertaining to methods to improve research department. **Research Practicum** ▪ completed Research Proposal
Tuesday July 15, 2008	**Scheduled Day Off** – Sick Day/Doctors Appt
Wednesday July 16, 2008	**Research Practicum** ▪ final review of research proposal draft **GI Study Audit/Review of Study Documents** ▪ review of ECOG-E2204 regulatory and patient case binders
Thursday July 17, 2008	**GI Study Audit/Review of Study Documents** ▪ review of ECOG-E2204 regulatory and patient case binders **CRO Staff Meeting**
Friday July 18, 2008	**GI Study Audit/Review of Study Documents** ▪ completed review of ECOG-E2204 regulatory and patient case binders ▪ complete review of ECOG-E2204 Pharmacy **Internship Practicum Meeting** ▪ met with Lynn Baker, MBA to discuss changes to Research Proposal ▪ discussed making changes to specific aims to generalize project more ▪ discussed additional information to include in background

Date	Daily Activities
WEEK 8	
Monday July 21, 2008	**GI Study Audit/Review of Study Documents** ▪ completed review of ECOG-E3204 regulatory **Research Practicum** ▪ make recommended changes to research proposal **Internship Practicum Meeting** ▪ met with Lynn Baker to clarify practicum proposal changes
Tuesday July 22, 2008	**GI Screening Log** ▪ created log to show all patients screened for the past six months within the GI DOT ▪ organized chart by number of patients screened each month per study **Internship Practicum Meeting** ▪ meet with Drs. Gwirtz and Reeves to get signatures for Declaration of Intent to Graduate. ▪ form turned into GSBS office.
Wednesday July 23, 2008	**Study Audit/Review of Documents** ▪ began audit of ECOG-3204 patient documents and binders
Thursday July 24, 2008	**GI Study Audit/Review of Study Documents** ▪ made study review checklist spreadsheet for all current active studies **Research Practicum** ▪ made final changes to Research Proposal
Friday July 25, 2008	**GI Study Audit/Review of Study Documents** ▪ finished study review checklist spreadsheets for all current GI studies ▪ created patient recruitment and accrual log for each GI study ▪ gather and make copies all current GI study protocols ▪ organize binder for study review materials

Date	Daily Activities
WEEK 9	
Monday **July 28, 2008**	**GI Study Audit/Review of Study Documents** ▪ completed audit of ECOG-S0600 regulatory documents, no patient binders to be reviewed. ▪ completed audit of ECOG-E5204 regulatory documents, no patient binders to be reviewed. ▪ review GenVec TNFerade protocol.
Tuesday July 29, 2008	**GI Study Audit/Review of Study Documents** ▪ review of GenVec TNFerade protocol. ▪ began review of GenVec TNFerade regulatory documents.
Wednesday July 30, 2008	**GI Study Audit/Review of Study Documents** ▪ reviewed GenVec TNFerade regulatory documents and patient case binders. ▪ reviewed Pfizer A4061020 regulatory documents
Thursday July 31, 2008	**GI Study Audit/Review of Study Documents** ▪ reviewed Pfizer A4061028 regulatory documents ▪ reviewed BMS HCC CA182-006 regulatory documents
Friday August 1, 2008	**GI Study Audit/Review of Study Documents** ▪ reviewed Gastric H3E-US-X005 regulatory documents ▪ reviewed Genetech AVF2941n regulatory documents ▪ began review of GenVec TNFerade patient case binders.

Date	Daily Activities
WEEK 10	
Monday August 4, 2008	**GI Study Audit/Review of Study Documents** ▪ continued review of GenVec TNFerade patient binders ▪ began protocol review for Pfizer 1028
Tuesday August 5, 2008	**GI Study Audit/Review of Study Documents** ▪ reviewed Protocol for Pfizer 1028 ▪ began Review of Pfizer 1028 Patient Case Binders **Internship Practicum Meeting** ▪ met with Lynn Baker to go over changes to research proposal ▪ discussed what will be expected during financial audit of all GI studies **Research Practicum** ▪ changes completed and final copy of research proposal was sent to Drs. Gwirtz and Reeves for approval ▪ once approved, will obtain signatures from advisory committee and submit to GSBS office.
Wednesday August 6, 2008	**GI Study Audit/Review of Study Documents** ▪ completed review of all Pfizer 1028 Patient Case Binders ▪ began review of GenVec TNFerade Patient Case Binders
Thursday August 7, 2008	**GI Study Audit/Review of Study Documents** ▪ completed review of GenVec TNFerade Patient Case Binders **GI Study Audit/Review of Financial Agreements & Budgets** ▪ assisted Rosalie Serrano, DOT Manager, in chart review for financial audit of Amgen study
Friday August 8, 2008	**GI Study Audit/Review of Study Documents** ▪ reviewed BMS HCC protocol ▪ started to review BMS HCC Patient Case Binders, however, unable to locate source documents ▪ reviewed Pfizer 1020 protocol

Date	Daily Activities
WEEK 11	
Monday August 11, 2008	**GI Study Audit/Review of Study Documents** ▪ Reviewed protocol for Genetech AVF294n study ▪ Started review of Genetech AVF294n patient case binders
Tuesday August 12, 2008	**GI Study Audit/Review of Study Documents** ▪ completed review of Genetech AVF294n patient case binders ▪ still unable to locate BMS HCC patient case binders ▪ reviewed Pfizer 1020 patient case binders
Wednesday August 13, 2008	**GI Study Audit/Review of Study Documents** ▪ completed review of Pfizer 1020 patient case binders ▪ began review of ECOG 3204 patient case binders
Thursday August 14, 2008	**Research Practicum** ▪ met with Dr. Gwirtz at UNTHSC for signature on finalized research proposal ▪ Dr. Reeves was out of town on vacation and was unable to sign, however, Dr. Gwirtz was going to keep the proposal to have him sign and then turn it into the GSBS office next week **GI Study Audit/Review of Study Documents** ▪ completed review of ECOG 3204 patient case binders ▪ worked on queries regarding AE submitted for ECOG 3204 patient
Friday August 15, 2008	**GI Study Audit/Review of Study Documents** ▪ round BMS HCC patient case binders ▪ began review of BMS HCC patient case binders.

Date	Daily Activities
WEEK 12	
Monday August 18, 2008	**GI Study Audit/Review of Study Documents** ▪ completed review of BMS HCC patient case binders ▪ found mission Genentech AVF2941n patient case binders and continued review
Tuesday August 19, 2008	**GI Study Audit/Review of Study Documents** ▪ completed review of Genentech AVF2941n patient case binders ▪ reviewed protocol for Gastric H3E-US-X005 study ▪ began review of Gastric H3E-US-X005 patient study binders **Internship Practicum Meeting** ▪ met with Lynn Baker to discuss process of completing study financial audits ▪ discussed parts of financial agreements and budgets ▪ will complete a review of each GI study and then setup meeting with Lynn Baker and Shirley Martin to discuss findings.
Wednesday August 20, 2008	**GI Study Audit/Review of Study Documents** ▪ continued review of Gastric H3E-US-X005 patient study binders
Thursday August 21, 2008	**GI Study Audit/Review of Study Documents** ▪ continued review of Gastric H3E-US-X005 patient study binders **CRO GI Group Meeting** ▪ met with Rosalie Serrano, Deny Von Merveldt, and Drs. Willson, Arriga, and Verma to discuss progress of GI studies ▪ discussed potential issues which may be encountered in upcoming Reata Pancreatic study. ▪ discussed strategies for patient recruitment
Friday August 22, 2008	**GI Study Audit/Review of Study Documents** ▪ completed review of Gastric H3E-US-X005 patient case binder.

Date	Daily Activities
WEEK 13	
Monday August 25, 2008	**GI Study Audit/Review of Financial Agreements & Budgets** ▪ reviewed financial agreement and budget for Pfizer 1020.
Tuesday August 26, 2008	**GI Study Audit/Review of Financial Agreements & Budgets** ▪ continued to review budget for Pfizer 1020. ▪ completed literature search for guidelines or articles to help determine the Standard of Care of patients who are receiving chemotherapy/radiation for colorectal cancer.
Wednesday August 27, 2008	**GI Study Audit/Review of Financial Agreements & Budgets** ▪ finished review of Pfizer 1020 budget. ▪ began review of Pfizer 1028 financial agreement and budget.
Thursday August 28, 2008	**GI Study Audit/Review of Financial Agreements & Budgets** ▪ continued review of Pfizer 1028 budget ▪ completed literature search for guidelines or articles to help determine Standard of Care of patients receiving chemotherapy/radiation for pancreatic cancer.
Friday August 29, 2008	**GI Study Audit/Review of Financial Agreements & Budgets** ▪ continued review of Pfizer 1028 budget
WEEK 14	
Monday September 1, 2008	**Scheduled Day Off** – Holiday
Tuesday September 2, 2008	**GI Study Audit/Review of Financial Agreements & Budgets** ▪ completed review of Pfizer 1028 budget ▪ began review of GenVec TNFerade financial agreement and budget
Wednesday September 3, 2008	**GI Study Audit/Review of Financial Agreements & Budgets** ▪ completed review of GenVec TNFerade budget ▪ began review of BMS HCC financial agreement and budget
Thursday September 4, 2008	**GI Study Audit/Review of Financial Agreements & Budgets** ▪ continued review of BMS HCC budget **CRO Coordinator Meeting** ▪ met to discuss patient screening and recruitment ▪ discussed ideas for logging patients screened ▪ discussed issues with decreased enrollment of Parkland patients **Consent Form Development/Article Review** ▪ ran a literature review for articles pertaining to the contra indications and adverse events of the use of CT contrast media. ▪ information to be used in consent form modifications for GenVec study
Friday September 5, 2008	**GI Study Audit/Review of Financial Agreements & Budgets** ▪ completed review of BMS HCC budget

Date	Daily Activities
WEEK 15	
Monday September 8, 2008	**GI Study Audit/Review of Financial Agreements & Budgets** ▪ began review of Genentech AVF2941n study agreement and budget
Tuesday September 9, 2008	**GI Study Audit/Review of Financial Agreements & Budgets** ▪ continued review of Genentech AVF2941n study budget
Wednesday September 10, 2008	**GI Study Audit/Review of Financial Agreements & Budgets** ▪ continued review of Genentech AVF2941n study budget **Chart/SAE Review** ▪ reviewed charts for SAEs filed for Genentech AVR2941n
Thursday September 11, 2008	**GI Study Audit/Review of Financial Agreements & Budgets** ▪ completed review of Genentech AVF2941n study budget ▪ made list of all study charges for procedures, administration and invoice fees for past GI studies
Friday September 12, 2008	**GI Study Audit/Review of Financial Agreements & Budgets** ▪ reviewed all study charges in GI studies to compose a list of all past charges used to develop budget ▪ reviewed SOC of procedures, imaging and lab to help establish outline for study budgeting

Date	Daily Activities
WEEK 16	
Monday September 15, 2008	**GI Study Site Initiation** ▪ attended site initiation meeting for Reata Study ▪ reviewed literature for antioxidant inflammation modulators **GI Study Development & Organization** ▪ began creating coordinator study binders for each GI study to organize all necessary paperwork in one location
Tuesday September 16, 2008	**GI Study Development & Organization** ▪ worked on creating coordinator study binders for each GI study to organize all necessary paperwork in one location ▪ organize study binders **Research Practicum** ▪ work on outline of Internship Practicum Report
Wednesday September 17, 2008	**GI Study Development & Organization** ▪ worked on creating coordinator study binders for each GI study to organize all necessary paperwork in one location ▪ organize study binders **Research Practicum** ▪ begin writing Internship Practicum Report
Thursday September 18, 2008	**GI Study Development & Organization** ▪ worked on creating coordinator study binders for each GI study to organize all necessary paperwork in one location ▪ organize study binders **CRO Staff Meeting** ▪ discussed upcoming events ▪ discussed use of ONCORE and access to folders **Research Practicum** ▪ begin writing Internship Practicum Report
Friday September 19, 2008	**GI Study Development & Organization** September 19, 2008▪ worked on creating coordinator study binders for each GI study to organize all necessary paperwork in one location ▪ organize study binders **Internship Practicum Meeting** ▪ met with Lynn Baker to discuss findings in financial audit ▪ discussed how ECOG studies are funded ▪ also discussed getting new patient demographic lists from SCC and Parkland for patient population analysis ▪ dived up research practicum report into sections and developed a calendar of when sections should be completed

Date	Daily Activities
WEEK 17	
Monday September 22, 2008	**GI Study Audit/Review of Financial Agreements & Budgets** ▪ estimated budgets of all ECOG studies in order to compare per patient actual cost to actual payment per patient. **Research Practicum** ▪ worked on Section I of Internship Practicum Report
Tuesday September 23, 2008	**GI Study Audit/Review of Financial Agreements & Budgets** ▪ estimated budgets of all ECOG studies in order to compare per patient actual cost to actual payment per patient. **Research Practicum** ▪ worked on Section I of Internship Practicum Report **Internship Practicum Meeting** ▪ met with Lynn Baker to discuss possible internship practicum presentation dates and times
Wednesday September 24, 2008	**GI Study Audit/Review of Financial Agreements & Budgets** ▪ estimated budgets of all ECOG studies in order to compare per patient actual cost to actual payment per patient.
Thursday September 25, 2008	**Internship Practicum Meeting** ▪ met with Lynn Baker for signatures ▪ discussed new patient demographics lists. Lynn is working on getting lists so that we can analyze the patient population in the clinics. **Research Practicum** ▪ worked on Section I of Internship Practicum Report
Friday September 26, 2008	**GI Study Development & Organization** ▪ worked on creating coordinator study binders for each GI study to organize all necessary paperwork in one location **CRO Staff Luncheon** **Research Practicum** ▪ worked on Section I of Internship Practicum Report

Date	Daily Activities
WEEK 18	
Monday September 29, 2008	**Research Practicum** ▪ completed first draft of Section I of Internship Practicum Report **GI Study Audit/Review of Financial Agreements & Budgets** ▪ worked on cost comparison of study cost and budget payments.
Tuesday September 30, 2008	**Clinical Research Subject Visit** ▪ went with coordinator to observe clinical research subject visit for Pfizer 1020 **GI Study Audit/Review of Financial Agreements & Budgets** ▪ worked on cost comparison of study cost and budget payments.
Wednesday October 1, 2008	**Analysis of GI Clinic Patient Demographics** ▪ received patient demographics for the Simmons Cancer Center and Parkland Health and Hospital Systems ambulatory clinics. ▪ began sorting data for analyzing **GI Study Development & Organization** ▪ worked on creating coordinator study binders for each GI study to organize all necessary paperwork in one location **Clinical Research Subject Recruitment** ▪ discussed issues facing patient recruitment with GI team and brainstormed ideas for ways to increase enrollment
Thursday October 2, 2008	**Analysis of GI Clinic Patient Demographics** ▪ continued to sort patient data by years. Information received was for past four years so data was sorted by year to help develop trends from year to year. **Research Practicum** ▪ worked on Section II of Internship Practicum Report
Friday October 3, 2008	**Analysis of GI Clinic Patient Demographics** ▪ continued to sort patient data by years. Information received was for past four years so data was sorted by year to help develop trends from year to year. ▪ began organizing 2005 data by CPT codes and location of GI cancers **Research Practicum** ▪ worked on Section II of Internship Practicum Report

Date	Daily Activities
WEEK 19	
Monday October 6, 2008	**Analysis of GI Clinic Patient Demographics** ▪ completed organization of 2005 data by CPT codes for new patient visits. ▪ organized new patients by disease group, then further organized GI group into groups determined by location of cancer. ▪ analyzed number for 2005 patient data. **Research Practicum** ▪ worked on Section II of Internship Practicum Report **Internship Practicum Meeting** ▪ met with Lynn Baker to discuss develop of patient demographic data as well as discuss the progress of Section II of the Internship Practicum Report
Tuesday October 7, 2008	**Analysis of GI Clinic Patient Demographics** ▪ began organizing 2006 data by CPT codes and location of GI cancers ▪ organized new patients by disease group, then further organized GI group into groups determined by location of cancer. ▪ analyzed number for 2006 patient data. **Research Practicum** ▪ worked on Section II of Internship Practicum Report
Wednesday October 8, 2008	**Analysis of GI Clinic Patient Demographics** ▪ began organizing 2007 data by CPT codes and location of GI cancers ▪ organized new patients by disease group, then further organized GI group into groups determined by location of cancer. ▪ analyzed number for 2007 patient data. **Research Practicum** ▪ worked on Section II of Internship Practicum Report
Thursday October 9, 2008	**Analysis of GI Clinic Patient Demographics** ▪ began organizing 2008 data by CPT codes and location of GI cancers ▪ organized new patients by disease group, then further organized GI group into groups determined by location of cancer. ▪ analyzed number for 2008 patient data. **Research Practicum** ▪ worked on Section II of Internship Practicum Report
Friday October 10, 2008	**Research Practicum** ▪ worked on Section II of Internship Practicum Report **Internship Practicum Meeting** ▪ met with Lynn Baker to discuss progress of Section II of the Internship Practicum Report ▪ discussed finding of patient demographic analysis

Date	Daily Activities
WEEK 20	
Monday October 13, 2008	**Analysis of GI Clinic Patient Demographics** ▪ when reviewing the numbers of the patient demographic data, it was noted that there had been some hidden number with the excel spreadsheet which had been unhidden during the organization of groups into years. The new data which was uncovered was from other years, not the year the group was organized for. Had to begin to resort data into years and rerun data analysis. ▪ reorganized and analyzed patient demographic data for 2005 **Research Practicum** ▪ worked on Section II of Internship Practicum Report
Tuesday October 14, 2008	**Analysis of GI Clinic Patient Demographics** ▪ reorganized and analyzed patient demographic data for 2006 ▪ reorganized and analyzed patient demographic data for 2007
Wednesday October 15, 2008	**Analysis of GI Clinic Patient Demographics** ▪ reorganized and analyzed patient demographic data for 2008 **Internship Practicum Meeting** ▪ met with Lynn Baker to discuss new findings with resorted patient demographic numbers. **Research Practicum** ▪ began making changes to Section II of Research Practicum
Thursday October 16, 2008	**CRO Staff Meeting** ▪ discussed upcoming events ▪ discussed barriers to patient recruitment and issues faced by the different disease teams of the SSC CRO ▪ brainstormed ideas of how to work around barriers which where identified **Research Practicum** ▪ completed making changes to Section II of Research Practicum
Friday October 17, 2008	**GI Study Audit/Review of Financial Agreements & Budgets** ▪ began to analyze the profitability of ECOG study costs by comparing each studies estimated cost to the actual grant amount given to the site. **Research Practicum** ▪ started working on Section III of Internship Practicum Report

Date	Daily Activities
WEEK 21	
Monday October 21, 2008	**GI Study Audit/Review of Financial Agreements & Budgets** ▪ estimated cost of each ECOG SO600 study by identifying those costs which were standard of care and those which would have to be covered by grant. Completed comparison of cost to actual amount paid by grant. **Research Practicum** ▪ worked on Section III of Internship Practicum Report
Tuesday October 22, 2008	**GI Study Audit/Review of Financial Agreements & Budgets** ▪ estimated cost of each ECOG E3204 study by identifying those costs which were standard of care and those which would have to be covered by grant. Completed comparison of cost to actual amount paid by grant. **Research Practicum** ▪ completed Section III of Internship Practicum Report ▪ began to make corrections to Section I of Internship Practicum Report
Wednesday October 23, 2008	**GI Study Audit/Review of Financial Agreements & Budgets** ▪ estimated cost of each ECOG E5202 study by identifying those costs which were standard of care and those which would have to be covered by grant. Completed comparison of cost to actual amount paid by grant. **Research Practicum** ▪ began working on Section IV of Internship Practicum Report
Thursday October 24, 2008	**GI Study Audit/Review of Financial Agreements & Budgets** ▪ estimated cost of each ECOG E2204 study by identifying those costs which were standard of care and those which would have to be covered by grant. Completed comparison of cost to actual amount paid by grant. **Research Practicum** ▪ worked on Section IV of Internship Practicum Report
Friday October 25, 2008	**GI Study Audit/Review of Financial Agreements & Budgets** ▪ completed comparison of all ECOG studies to payments from sponsor **Internship Practicum Meeting** ▪ discussed changes to Section II and III of Internship Practicum Report ▪ discussed finding of patient demographic analysis

Date	Daily Activities
WEEK 22	
Monday October 27, 2008	**Research Practicum** ▪ made corrections to Section I of Internship Practicum Report ▪ made corrections to Section II of Internship Practicum Report
Tuesday October 28, 2008	**Research Practicum** ▪ made corrections to Section II of Internship Practicum Report ▪ rewrote Section III of Internship Practicum Report
Wednesday October 29, 2008	**Research Practicum** ▪ made corrections to Section III of Internship Practicum Report ▪ made corrections to Section IV of Internship Practicum Report ▪ developed Appendix contributions
Thursday October 30, 2008	**Research Practicum** ▪ proofread Internship Practicum Report ▪ began developing Power Point presentation
Friday October 31, 2008	**Internship Practicum Meeting** ▪ met with Lynn Baker to discuss changes to Internship Practicum Report ▪ discussed financial assessment and changes to Sections **Research Practicum** ▪ proofread Internship Practicum Report ▪ made changes to Practicum Report ▪ turned in final paper ▪ continued to work on Power Point Presentation

Date	Daily Activities
WEEK 23	
Monday November 3, 2008	**Research Practicum** ▪ worked on developing power point presentation for defense
Tuesday November 4, 2008	**Research Practicum** ▪ worked on developing power point presentation for defense
Wednesday November 5, 2008	**Research Practicum** ▪ worked on developing power point presentation for defense
Thursday November 6, 2008	**Research Practicum** ▪ worked on developing power point presentation for defense
Friday November 7, 2008	**Internship Practicum Meeting** ▪ met with Lynn Baker to discuss development of power point presentation ▪reviewed final changes to Internship Practicum paper **Research Practicum** ▪ finished slides for power point presentation for defense

Date	Daily Activities
WEEK 24	
Monday November 10, 2008	**Research Practicum** ▪ Meet with Dr. Gwirtz to review slides for Defense
Tuesday November 11, 2008	**Research Practicum** ▪ made corrections to slides ▪ practiced for defense
Wednesday November 12, 2008	**Research Practicum** ▪ practiced for defense
Thursday November 13, 2008	**Research Practicum** ▪ met with Lynn Baker to discuss slides and defense ▪ made additional corrections to slides ▪ practiced for defense
Friday November 14, 2008	**Clinical Research Internship Practicum Presentation** ▪ with Lynn Baker, MBA and Drs. Patricia Gwirtz and Rusty Reeves. ▪ located in LIB-110, starting at 1:00pm

Approved by:

Elisha Hatfield, MPAS, PA-C – Intern	November 14, 2008
Lynn Baker, MBA – Site Mentor	November 14, 2008

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