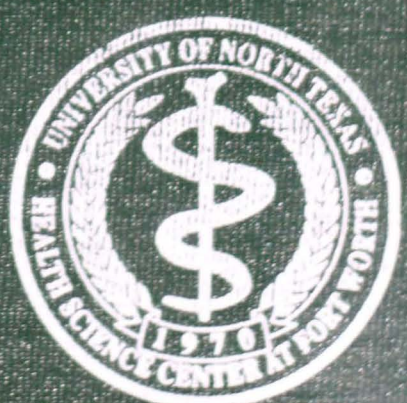
UNIVERSITY OF NORTH TEXAS
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ABSTRACT

The internship practicum requirement for my Masters degree was completed at Texas Pulmonary and Critical Care Consultants P.A., Research. I worked under the direction of John Burk, M.D., and Kathy Kwaak, RN CCRN. These were the principal investigator and study coordinator respectively. While at TPCCC, I learned about both the administrative and clinical aspects of clinical research. I also gained a great understanding of patient recruitment and retention. Along with this knowledge, I used current study data to complete my research project.

The primary focus of my practicum was to evaluate different aspects of patient compliance and retention as a result of the form of patient recruitment. Forms of recruitment in this study include TPCCC database and central advertising. I evaluated five studies. I collected information regarding the number of individuals contacted, enrolled, consented, screened, completed, and early terminations for each study. Furthermore, I determined the most effective form of recruitment at TPCCC. I also acquired data, via a questionnaire, regarding patients' feelings towards research.

CLINICAL RESEARCH PATIENT RECRUITMENT AND RETENTION

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MASTERS OF SCIENCE IN CLINICAL RESEARCH MANAGEMENT

By

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CHAPTER I

INTRODUCTION

While completing the internship practicum, my goal was to achieve an in depth understanding of the recruitment process as well as methods of obtaining good patient compliance and retention. The site at which this internship was performed was Texas Pulmonary & Critical Care Consultants, PA (TPCCC) Research, a private practice based research clinic. The TPCCC group is directed by Dr. John Burk and includes twenty-six other physicians. The clinics serve patients primarily with medical problems related to respiratory or sleep diseases and disorders. In addition to the clinical care that is provided, TPCCC has carried out research for many years and recently incorporated as TPCCC-Research as a clinical research laboratory dedicated to research on respiratory and sleep disorders.

During this internship, I worked closely with the lead research coordinator for TPCCC-Research, Kathy Kwaak, in supporting many of the activities related to several ongoing clinical trials. This provided an excellent environment in which to gain hands-on experience in the clinical research field. My experience and role in the clinical research included: 1) several site initiation visits by industry representatives, 2) monitoring visits and close out by company representatives, 3) management of the recruitment process, and 4) management and handling of the research data.

The specific work activities that were performed included maintaining regulatory binders, documenting drug receipt and accountability, completing case report forms, and aiding my study coordinator in any other duties assigned. I was trained in each of these areas including the use of electronic case report forms. I was also delegated the responsibility of patient recruitment for currently enrolling studies. The primary focus while completing the practicum included the assessment of clinical research patient recruitment and retention methods. The experience gained through this practicum has lead to the collection of this report.

CHAPTER II

SECTION I: BACKGROUND

Clinical research involving pharmacologic agents is continually growing, as evidenced by investigational drug applications now approaching 4,000 per year[1]. The number of subjects per new drug application currently exceeds 5,300, and approximately 80,000 clinical trials are ongoing in the United States alone[1]. Consequently, the need for subject or patient recruitment into these trials is quite large and this represents a significant challenge to the success of many clinical trials. While many efforts are being made to evaluate the problems associated with low patient recruitment, there is still great room for improvement. Patient recruitment is the single most difficult problem to overcome in conducting pediatric trials; it is the most common cause of delays, increased costs, and failure to complete drug trials[10]. Negative aspects of clinical research that may contribute to the difficulty of recruiting include denial of insurance coverage for any clinical trial treatment, the negative guinea pig perception and the inconvenience including time, travel, and discomfort[10]. In order to overcome this negative outlook on research, it is the research clinicians' responsibility to first identify the problems and then to make necessary changes to overcome these barriers. Furthermore, clinicians must help patients to realize that when involved in a clinical study, treatment is not compromised; it is simply another available treatment option[4].

Accrual rates for participation in studies of adult cancers are extremely low. This, in part, is due to the way the clinical trial system operates[3]. In particular, Collyar notes the problems associated with recruitment of women with breast cancer. If a woman is not approached with caution, fear and misunderstanding can develop as a result of the manner in which the patient is approached [3]. Furthermore, study coordinators must ensure that they take the time to explain the importance of clinical trails and reassure the subject that he or she is in control. Other barriers in clinical research may include physician attitude, knowledge of clinical trials, access to clinical trial care, insurance coverage, and informed consent[3]. For example, aside from the principal investigator there are 26 practicing physicians at TPCCC. It is important as research staff to inform these physicians about current clinical trials. With an awareness of current research, the TPCCC physicians are at a better place to refer patients to a study. Additionally, many individuals are excluded from research, because clinical trial procedures are not covered in their healthcare plan. The informed consent process is also an obstacle in research. Although these documents are written at an eighth grade reading level, language barriers continue to exist. Thus, without a bilingual employee, it can be difficult to convey the issues addressed in an informed consent to a patient.

Another angle to assess patient recruitment and compliance is to look at the attitudes towards clinical research amongst participants and non-participants. One particular study evaluated the attitudes of research participants as well as non-participants in response to clinical research. Overall, attitudes towards research participation were positive among the participants, but were less positive among the non-participants. Those with a positive response towards research felt both personal and altruistic motives were key influencing factors. The negative responses were primarily a result of the fear of the unknown and unease with the idea of randomization. Those who were research participants had negative feelings due to the frustration of seeing too many physicians. A great number of participants and non-participants have the misconception that medical research is primarily conducted to promote physicians' careers[9]. Thus, an important challenge is to allay this misconception when prospective patients are being recruited.

Challenges to Patient Recruitment

Recruiting patients for clinical trials has become progressively more complex and complicated. Due to the 15 percent annual increase in need for patient enrollment, sponsors have reevaluated recruitment budgets[2]. Until recently, a separate budget for patient recruitment was rare. Patient recruitment can be a long and tedious process. Some sponsors allot more money for recruitment than others. This could be based on the sites previous dealings with the sponsor, the size of the research site, or possibly even the success of other studies conducted at the research site. Thus, some research sites are

able to staff personnel specifically for recruitment, whereas smaller research centers may be limited in their personnel because they receive minimal funds for recruitment. Sponsors may assume that because a site is smaller, it does not have as many active studies. Subsequently, the site would have more time to focus on recruitment and would not need the aid. Being a smaller site, however, the research staff may not have as large of a patient database as larger research sites. Thus, the smaller sites are in need of more funds aimed towards recruitment. The drug sponsor and research site develop a study budget that is approved by both parties before a final agreement is made for the site's participation in the study. This budget includes items such as consent signing, conducting physicals, vitals, and other items collected at each visit. Also included in this budget should be pre-study tasks such as chart reviews and other related pre-screening tasks.

In a book by Diana Anderson[1], she discusses several issues of patient recruitment and retention including HIPAA rules, standard operating procedures, ethics, call centers, and budgeting all being areas to improve upon for successful recruitment. This book identifies the challenges associated with recruitment and retention and discusses approaches in overcoming and avoiding these obstacles.

Another study evaluated the importance of the physician's attitude towards research. The primary reasons for physician participation were the research topic (59%) and the involvement of an academic research group in the study (63%)[6]. Other physicians felt a moral obligation to participate in research[6]. Special attention must be

given to the patient and family, the treating physician and team, and the research team to improve patient recruitment[7].

Challenges of Patient Retention and Compliance

Patient recruitment, however, is only part of the battle; the success of a clinical trial also depends on patient compliance and retention. Patients may be lost to follow-up, terminated due to non-compliance, withdrawn due to protocol violations, or terminated for other various reasons. Poor compliance of research patients may be attributed to a lack of symptoms, terminal illness, forgetfulness, anger or dissatisfaction with staff, or medicine regimens that can be confusing or complex[5]. It is important that the research staff have an understanding of areas in clinical research that have a negative effect on compliance and be prepared to take extra steps to minimize these potential causes of poor patient retention and compliance. One study claims that there is no consensus as to which methods or instruments can provide the best compliance[8]. With improved knowledge of compliance, however, research staff would improve patient retention. The success of a study highly depends on the levels of compliance and retention of the enrolled subjects. Thus, it is imperative that research staff is aware of the issues associated with poor compliance, loss to follow up, and protocol violations to be able to take steps toward improving these matters.

CHAPTER II

SECTION II: SPECIFIC AIMS

The specific aims of my internship project were as follows:

1) Obtain a thorough understanding of the patient recruitment process.
    a. Understand the various forms of recruitment available.
    b. Understand the difference in the recruitment process as a result of the patient source.

2) Develop a more efficient method to recruit patients at TPCCC.
    a. Evaluate the current methods of recruitment
    b. Compile an ongoing patient database as a recruitment source

3) Analyze the data gathered from current and previous studies conducted at TPCCC as well as Baylor Research Institute
    a. Determine if there was a difference in the level of study drug compliance of the patients based on the form of recruitment.
    b. Determine if there was any correlation between type of study recruitment and study completion.
    c. Determine which patient source yields the most efficient recruitment.

4) Assess the patients' outlook on research

   a. Administer patient questionnaire on attitudes about research.

   b. Assess areas of patient recruitment that can be changed to help enhance successful recruitment in future studies.

CHAPTER II

SECTION III: PATIENT RECRUITMENT PROCESS AT TPCCC

Current methods of clinical research subject recruitment include sponsor-supplied central advertising, physician database, print advertisement including brochures and posters, generic advertising, and physician referral. TPCCC primarily depends on central advertising provided by the sponsor as well as its own pool of patients as a source of recruitment for clinical trials. TPCCC also runs a generic advertisement in the Fort Worth Weekly as another source of recruitment. Different steps are taken to screen and recruit patients from these different sources.

Review of TPCCC Patient Database

The process of recruiting TPCCC patients began with a search through the practice's database. A receptionist in the main office printed a monthly schedule report that included the patient's name, age, and purpose of visit. We were primarily looking for individuals who were seen for a follow-up spirometry, and who met the age criteria of the particular study. If the individual met these criteria, then we referenced the TPCCC patient file server for more information about the patient including a documented diagnosis of the disease at hand. The server was a collaboration of letters, consults, and follow-up visits for all of the TPCCC patients. Any medications, co-morbidities, or any other aspect of the patient's file that may include or exclude them from the study were noted as well. Following this phase an email or phone call was made to the patient's

pulmonologist or primary physician to receive confirmation that the patient may enter the research study. Once this was cleared a generic letter was sent to the patient to inform them of a research opportunity. See Appendix Section IV.

Sponsor-Based Central Advertising

Central advertising provided by the sponsor was another source of subject recruitment for the TPCCC Research Center. In this case, the sponsor paid to run a television or radio advertisement, and provided a number for any interested persons to call. The caller was connected to a central screening center where the screener ran through a series of questions. These questions were specific to each study, but very vague. A Chronic Obstructive Pulmonary Disease (COPD) study may have asked questions such as: when were you diagnosed with COPD, have you ever been diagnosed with asthma, or what medications are you currently taking. The screening center then sent reports of the subjects that pass the initial screening, based on the questions asked, to the nearest site of the caller. It was then the research staff's job to further pursue the potential subject. The screening center provided an online site where the investigator could view all subjects that passed the initial screening. The sites were asked to contact the person within 24-48 hours of receiving the report, and to go on line and document the status of the potential subject. In other words, the site must show that it has tried to make contact with the individual. The research staff contacted the individuals to further evaluate the subject's interest as well as to ensure that the subject does meet the inclusion and exclusion criteria. During the phone call the site generally asked more specific

questions. For example, during the initial screening phase, the subject may have informed the screener that he or she was on oxygen supply. One study conducted at TPCCC allowed subjects to use supplemental oxygen for no longer than 12 hours a day. The subject was asked a more specific question such as the amount of time the patient used oxygen when contacted. Additionally, several studies excluded subjects who were taking prednisone unless they agreed to come off of the medication. Even then the subject was required to meet a certain washout period. Furthermore, when TPCCC research staff contacted a subject supplementary questions were asked to get a feel for the availability of the subject. Some of the studies included 12-hour post dose spirometry maneuvers. This meant that the subject was required to arrive at the site at approximately 8 am, take study medication at 9:30 am, and complete the last pulmonary function test at approximately 9:30 pm. With requirements such as these, it was difficult to schedule a subject who worked from 8am-5pm. Then, if the site determined that the individual was a qualified candidate, an appointment was made to have the person come and give informed consent to participate in the study. Only after the subject had given consent could they be asked to come off of any current medication. If the subject was taking any medication listed in the exclusion criteria, he or she was required to enter a washout period. The length of the washout period differed for every study. After consent a screening visit was scheduled, and the date of the appointment was dependent on the washout period. If the individual was on certain medications, he or she may have been required to withhold the medication for a period of time before the screening could occur. Next, the subject was further evaluated at the screening visit to determine severity of the

disease. If the standards were met, then he or she was randomized to the study drug and began treatment.

Generic Advertising

As an additional means of advertisement TPCCC ran a generic advertisement in the Fort Worth Weekly every other week. It stated who we are and that we were seeking to enroll individuals with a documented diagnosis of COPD, chronic bronchitis, asthma, or emphysema. Kathy estimated that we have received approximately 100 calls from the advertisement in Fort Worth Weekly in the past year. When a phone call was received, the individual was first asked if he or she had a document diagnosis of asthma, bronchitis, COPD or emphysema. Most of the individuals that called did not have a documented diagnosis of COPD, chronic bronchitis, asthma, or emphysema. The majority of calls received were from smokers looking for help with smoking cessation. If the individual did have a documented diagnosis the research staff proceeded to tell the individual more about the study as well as ask the patient about concomitant medications, other diagnoses, or any additional questions that may have included or excluded them from the study. If the individual met the criteria, then he or she was scheduled for a consent visit

CHAPTER II

SECTION IV: PATIENT COMPLIANCE AND RETENTION

Good subject compliance is necessary to produce accurate data for the drug sponsor to evaluate. Good compliance encompasses taking study medication at the time directed as well as taking it as often as instructed. The goal of this study was to evaluate the compliance shown by study patients, and identify areas of improvement. The subject's compliance was documented throughout the study. That included both study medication compliance as well as study diary completion. The subject was reminded of an upcoming visit 1 to 3 days prior to the visit, and was also reminded to bring study medication and the subject diary. The subject was also reminded to withhold use of beta anticholinergics at least 6 hours before the visit. Part of each visit included documenting the subject's compliance, which consisted of counting the used and returned study drug. The diary was also evaluated to determine the subject's level of obedience in daily diary completion. Other factors were considered when a subject's compliance level was determined. This included receipt of medical records or return of a signed informed consent. These factors helped to determine whether the subject would have been compliant throughout the study.

Retention was based on study completion. The subject must have completed every visit listed in the study protocol to be considered a study completion. The subject was considered an early withdrawal if he or she was discontinued from the study for any reason. This may have included but was not limited to a protocol violation, exacerbation, or withdrawal by the PI.

CHAPTER II

SECTION V: CURRENT CLINICAL TRIALS AT TPCCC

The information collected from several studies conducted during my internship was used in the assessment of recruitment practices as well as subject compliance and retention. TPCCC has three active COPD studies, one active asthma study, one closed COPD study, and one closed asthma study. COPD trial #1 currently has one subject that is active in the study. COPD trial #2 has no active subjects in the study. The last individual completed the end visit on April 8, 2008. Two subjects are currently active in the COPD trial #3. There are no active subjects in COPD trial #4, and therefore the study monitor has closed out the study. Asthma trial #1 has no active subjects in the study. The study monitor has closed this trial. Asthma trial #2 is open for subject enrollment.

CHAPTER II

SECTION VI: MATERIAL AND METHODS

This section describes the steps taken to organize and evaluate the recruitment methods, compliance data, and retention data from current and previous studies in order to determine the most successful form of recruitment as well as the methods that led to the best compliance and retention. The initial step involved creating a patient database from the information obtained from previous studies. The screening files were reviewed, and previous recruitment letters were obtained that distinguished subjects who were identified through the screening center versus those who were patients of TPCCC. Versys, a scheduling database used by TPCCC, was also used to verify whether the individual was a patient of TPCCC. An account was created in Versys for every patient that has been seen by one of the physicians. The patient name was also searched in the sleep server, a compilation of patient files that included follow up letters, consults, and study results. After the recruitment source of each individual was determined, the information was entered into an Excel spreadsheet that was sorted according to recruitment source.Other identifying characteristics listed in the spreadsheet included address, telephone number, diagnosis, medications, and pack years where applicable. Any previous date of contact made by the study coordinator was entered into the spreadsheet. If available, the individual's response was included in the spreadsheet as

well as the study in which the subject was recruited. The spreadsheet contained approximately 200 individuals for possible contact in future studies.

TPCCC saw a large number of individuals with COPD and/ or asthma. Many of these patients had never been informed of the research opportunities at TPCCC, Research. Thus, they supplied a great addition to the research patient database. Versys served as means of acquiring individuals for the patient database. The clinical recall analysis feature on Versys was used to search for patients based on age, gender, diagnosis, service dates, and provider. The results were numerous and were displayed in a Notepad© document. The results of the search could not be narrowed down to include specifics for the inclusion and exclusion criteria for particular studies. For example, several studies aimed to treat COPD are conducted at TPCCC, Research, and the protocol for these studies required that the patient have a diagnosis of COPD but have no history of asthma. The Versys system retrieved every patient that had a documented diagnosis of COPD, but these patients often had other noted diagnoses. This may have included asthma, which was listed in the exclusion criteria for several of the COPD studies. There was no way to locate patients diagnosed with COPD but with no history of asthma. There was also difficulty in combining the list retrieved from Versys with the list compiled from the patient database. The two programs were not compatible, so more time and work will be required to complete this task.

Another goal of this internship was to retrieve data from previous studies in order to evaluate clinical research subject recruitment and retention and compliance. A list was made of all known individuals that were contacted regarding any of the research studies from research patient database. The studies included COPD Trial 1, COPD Trial 2, COPD Trial 3, COPD Trial 4 and Asthma Trial 1. The regulatory binders from each study also served as a valuable source of information. Every regulatory binder included a subject screening/enrollment log. The log listed every subject that signed consent, was screened, screen failed, and/or randomized. The list of all contacted subjects was double checked against the list in the regulatory binder to ensure that all individuals had been included. Also noted in the patient contact list was the form of recruitment in which each subject was informed about the study. After a subject was screened, a folder called the source was made containing all of the subject's relevant study information. All research individuals who performed visit assessments wrote a note regarding each visit and filed it in the subject's source. The notes included dates of contact with the subject; this could have included a visit, telephone call, or letter. If a subject was terminated, withdrawn, or was a screen failed, the detailed notes of this event were found in annotated notes in the subject's chart. Furthermore, these findings were noted on the list of subjects that were contacted for each study. Thus, the number of individuals contacted, number consented, number screened, number of screen fails, number randomized, number active, number of early terminations, and number of completed subjects was easily determined for each study.

Dr. Delbert Johns, OBGYN conducted a study at Baylor Research Institute (BRI), Fort Worth that was also used in the evaluation of subject recruitment methods. Vicki Duvall, director of clinical research at Baylor Research Institute Fort Worth recommended this particular study conducted by Dr. Johns, because it was a study in which he used a significant amount of advertising, and had the highest loss to follow up in any study that he had conducted.

Additionally, a goal of this study was to evaluate the level of retention based on the form of recruitment. Retention was graded in two areas: study drug compliance and study completion. Each subject's compliance with study drug was determined based on the subject diary as well as the study drug log kept in the subject's source documents. Each study required the subject to complete a daily diary. The subject was asked to provide a daily peak expiratory volume (PEV), answer various questions, and record study medication dosage time. Diaries came in either paper or electronic form. The electronic diaries were downloaded at each visit onto the study computer. A print out listing the subject's compliance in both diary completion and compliance in taking study medication was obtained from the download. The paper diaries were reviewed and collected as stated in the protocol. Generally, the diaries were reviewed every visit and turned in every other visit. When reviewing the diary the research staff was to ensure that the subject had made a daily entry and had recorded a daily PEV. The diary also asked questions regarding sputum production, rescue medication usage, and cough activity. Due to the large difference in paper and electronic diaries, no comparison in diary compliance between subjects was attempted.

A study drug compliance sheet was also kept in the source folder of each subject. The research staff was required to record the dispensing and return of medication on this log. The COPD Trial 1 study drug compliance was kept based on inhalations. As noted previously, the compliance percentages of the subjects in the study were obtained from the download print out. Each of the other studies used dry powder inhalation study medication. A certain number of capsules were dispensed to each subject, and the number of capsules remaining as well as the number of used capsules was recorded in the subject's source documents as per the protocol. Drug compliance was reviewed and recorded at every visit, but the sponsor only required that the information be documented when study medication was dispensed or returned.

Manual computation was required to determine the compliance in each of the studies that used a dry inhaler. Subjects participating in the COPD Trial 2 study used a once daily inhaler. A new box of capsules was dispensed to the subject at various visits according to the protocol. The number of capsules dispensed was noted; the number of returned capsules was also recorded. The subject's compliance percentage was determined by comparing the number of capsules that should have been used to the actual number of capsules used. The first phase of COPD Trial 3 dispensed three different capsules to the subjects. Individual compliance was kept for each of the blue, yellow, and white capsules. An average was taken of the three compliances at each compliance check.

After the compliance percentage was determined for each subject, the groups could be compared to determine whether one form of recruitment yielded higher compliance. The groups were patients of the TPCCC practice and subjects recruited via advertising. A one way Analysis of Variance (ANOVA) test was used to compare the group means. The SPSS program was used to perform the statistical analyses.

Using the list created, (number of individuals contacted via each recruitment method, number of individuals screened, number of study completions, etc) study completion was compared among the subjects enrolled in each of the trials. There was no differentiation between studies. The comparison was between TPCCC patients and subjects recruited via advertisement. A Chi-squared test was performed on the data to determine independence.

Another goal was to determine the most efficient form of recruitment. This task was simply a comparison of numbers. Using the data gathered from the spreadsheet, regulatory binders, and subject folders the number of individuals contacted via each form of recruitment were determined. This included individuals found through advertising as well as patients of TPCCC. The number of subjects that were actually enrolled in a study was also calculated. The efficiency percentage was determined by dividing the number individuals contacted by the actual number of enrolled subjects.

A questionnaire was sent out in an effort to learn of research subjects' opinions about research. See Appendix Section II. The survey was designed to send out to all individuals that were at one time contacted about a study, and included questions such as: why do you feel research is conducted, why are you interested in research, or how would you rate your compliance if you received study medication. Multiple-choice answers were given for each question, and a space was provided at the bottom of the survey welcoming any additional comments. The UNTHSC Institutional Review Board (IRB) gave approval before any of the questionnaires were sent out. See Appendix Section III. The IRB determined that the survey and protocol were exempt from full IRB review. Also included in the packet was a letter to the individual that stated the purpose and instruction for completing the questionnaire. The individuals were asked not to include a name on the return envelope or anywhere on the survey.

CHAPTER II

SECTION VII: RESULTS

The results from the research patient database and the list of all individuals contacted for each of the studies is displayed in Table 1.

Table 1: Patient Recruitment Numbers from TPCCC & Call Center

	Contacted	Consent	Screened	Screen fail	Randomized	Active	Early Termination	Completed	Call Center	TPCCC	Other
COPD Trial 1	30	14	14	7	7	1	2	3	7	23	1 (lost to follow up)
COPD Trial 2	50	11	9	4	5	0	2	3	34	16	0
COPD Trial 3	50	14	14	8	6	5	0	1	41	9	0
COPD Trial 4	20	3	3	0	3	0	1	2	0	18	2
Asthma Trial 1	99	9	7	5	2	0	2	0	83	16	0

Thirty persons were contacted concerning COPD Trial 1. Of these people, 23 were TPCCC patients; the remaining 7 were recruited from advertisement. Consent was given from 14 of those contacted. Ten individuals were either not interested or gave no response. Four individuals did not meet the criteria for the study. Two persons were no shows to the consent visit. Seven of the consented subjects were screen fails with six not meeting the severity criteria. One individual that signed consented decided not to go any

further in the study. Seven subjects were randomized. Three of these subjects have completed the study. Two individuals were discontinued prematurely due to exacerbation. One subject was lost to follow up, and another is still active in the study.

The sponsor of COPD Trial 2 did provide central advertising. Roughly 34 screened subjects were received from the central advertising company. Another 16 individuals were patients of TPCCC. Letters were sent to the patients of TPCCC. Approximately 20 people were not interested in participating. Eleven subjects were consented. The remaining 19 individuals did not qualify for the study or did not show up for a scheduled consent. Nine of the 11 individuals that were screened signed consent. Two individuals gave consent but dropped before screening due to exacerbation and family issues. There were 4 screen fails and 5 subjects randomized to study medication. In this case, the 4 screen fails were due to reason other than lack of severity of the disease. One subject died during the screening period of the visit. It was determined that her death was not related to the study. Another subject was determined to be a screen fail because he had not been diagnosed with COPD for an appropriate amount of time. Furthermore, one subject was discovered to have Alph-1 Anti-Trypsin Deficiency. The fourth individual was terminated due to non-compliance in study diary completion as well as missing scheduled visits. Three of the randomized subjects completed the entire study. Two of the randomized subjects did not feel to be benefiting from the medication and were withdrawn early.

Approximately fifty individuals were contacted regarding COPD Trial 3 study. Of these fifty, 20 individuals were not interested. This category included anyone who directly spoke of disinterest to the staff or who did not respond to our letters or phone calls. Another ten persons did not qualify for the study. This could have been due to several factors, including but not limited to, concomitant medications, co morbidities, or smoking status. Furthermore, six additional people did not give consent for various reasons. For example, the individual did not want to come off of current treatment or was afraid of receiving placebo. Fourteen of the individuals gave informed consent with 8 of those resulting in screen fails. The most common reason for the screen fails was that the subject did not meet the necessary severity of the disease. The remaining 6 subjects were randomized to study medication. There were 2 active subjects in the study. One subject completed the study. The sponsor discontinued two subjects; this was due to changes in the protocol at the second stage of the study. One subject was discontinued from the study because of a protocol violation.

The sponsor did not provide central advertising for COPD Trial 4. Thus, all subjects were recruited from the practice or previous studies. Approximately 20 persons were contacted by letter concerning this study. One letter was returned, and another individual was interested in participating in the study until he learned of the possibility of receiving placebo. One individual showed interest in taking part in the study, but had an exacerbation; this prevented her from being enrolled. Part of the exclusion criteria of the study included an exacerbation within 6 weeks of beginning the study. An exacerbation occurrence during the study would also have forced the subject to be withdrawn from the

study. No reply was received from the remainder of the subjects. Eighteen of the individuals were patients of TPCCC and two individuals were discovered from the patient database. Three individuals were consented, screened and randomized. Two of the subjects completed the study. The remaining subject was withdrawn from the study due to an exacerbation.

The Asthmas Trial 1, by far, received the most potential subjects via central advertising. Eighty-three persons were recruited through advertisement, and roughly 16 others were patients of TPCCC. Nine individuals signed consent, but only 7 subjects were screened. One subject gave consent, but was discovered to be using corticosteroids. This was listed in the protocol as study exclusion. Another subject did not undergo screening because of an issue with medications. Five of the 7 subjects screened were screen fails. Only 2 subjects were randomized. One of the randomized subjects was discontinued due to a miscalculation of reversibility. The other subject was discontinued because of inaccurate information regarding concomitant medication.

Dr. Johns' study at Baylor used radio advertising as well patients from his private practice to recruit subjects. Baylor ran advertising about the study for three months on three different radio stations. The site received 81 phone calls in response to the radio advertisement. Forty-three of these 81 were excluded during the phone screening process due to inclusion/exclusion criteria. Age and not currently in a monogamous relationship were the two most common reasons for exclusion. Thus, 38 women recruited via advertising were brought in to screen. Thirty-two women were brought in from Dr.

Johns' practice. All together 70 women signed informed consent; nine of these women withdrew consent.

Furthermore, the compliance level was evaluated of the subjects that were randomized to each study. Subjects in the COPD Trial 1 study received electronic diaries to record a daily peak expiratory volume (PEV) and study medication dosage time. Seven individuals were randomized to the COPD Trial 1 study. The compliance percentages are shown below in Table 2.

Table 2: COPD Trial 1 Subject Drug Compliance

	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	VE
Subject 1	100	100	100	96	100	100	98	100	100	N/A	N/A
Subject 2	100	100	100	100	100	100	100	98	98	98	N/A
Subject 3	100	100	100	100	100	100	98	100	100	98	N/A
Subject 4	N/A	100	100	100	100	89	100	100	98	98	N/A
Subject 5	100	100	100	100	100	92	96	88	100	N/A	N/A
Subject 6	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	100
Subject 7	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	100

Hand calculation was done to determine the subject drug compliance percentages for each of the other studies. Again, this number was determined by dividing the number of capsules that each subject should have used by the actual number of capsules used. The results are shown in the following tables.

Table 3: COPD Trial 2 Subject Drug Compliance

	V2	V3	V4	V5	V6	V7	V8	V9	V10
Subject 1	100	100	100	100	100	100	100	84	N/A
Subject 2	100	100	100	100	100	98	98	100	100
Subject 3	100	96	100	93	100	100	100	100	100
Subject 4	93	86	82	96	N/A	N/A	N/A	N/A	N/A

Table 4: COPD Trial 3 Subject Drug Compliance

	V7	V8	V10	V11	V12	V14
Subject 1	100	100	99	N/A	N/A	N/A
Subject 2	100	91	93	100	100	100
Subject 3	82	89	93	100	90	N/A
Subject 4	100	97	82	N/A	N/A	N/A
Subject 5	100	99	N/A	N/A	N/A	N/A

Table 5: COPD Trial 4 Subject Drug Compliance

	V5	V6
Subject 1	**93**	**93**
Subject 2	**86**	**100**

After the compliance percentages were obtained for each subject, a one-way ANOVA test was run to determine any significant difference in subject compliance based on the type of study recruitment. The null hypothesis was described as follows: There is no difference in the population means of the two groups. The two groups were subjects recruited via advertising and subjects recruited from TPCCC. The F critical value statistic was 3.92. The experimental F value was .086. Thus, we failed to reject the null hypothesis and said that there was no difference between the two population means. In other words, there was no difference in the level of compliance based on type of recruitment.

A chi-square test was used to determine if study completion was independent of recruitment group. The null hypothesis was as follows: Study completion does not depend on recruitment group. Twenty-three subjects have been randomized. Subjects that were still active in a study were not considered in this analysis. The results are shown in Table 6. Seven of the 11 patients recruited from TPCCC completed the study. The remaining 4 individuals did not participate in the entire study. Eight individuals found through central advertising were randomized. Five of these subjects completed the study, while 3 were terminated early. The chi-square test statistic was 0.0023. The chi square critical value was 3.841. Thus, we failed to reject the null hypothesis and said that study completion was independent of recruitment type.

Table 6: Chi-square Test of Independence

	Completed Study-Yes	Completed Study-No	Total
TPCCC	7	4	11
Central Advertising	5	3	8
Total	12	7	19

Another aim of this practicum was to determine the most efficient recruitment method. It was determined that out of the individuals contacted regarding the COPD Trial 2 study, 34 were done so through advertising means. Three of these individuals were actually consented resulting in a 9% success rate. Sixteen subjects were patients of TPCCC; eight of these individuals signed consent demonstrating a 50% success rate. The research staff contacted 23 TPCCC patients in an effort to recruit for the COPD Trial 1 study. Approximately 9 of these individuals were consented giving a 39% success rate. Five of the 7 individuals recruited by means of advertising signed consent; this lead to a 71% efficiency rate. Nine TPCCC patients were contacted regarding COPD Trial 3; six of these subjects signed consent demonstrating a 67% efficiency rate. Forty-one individuals were found via advertising. Eight signed consent giving a 20% success rate. Only one of the 18 TPCCC patients contacted regarding the COPD Trial 4 signed consent. Thus, a success rate of 6% was achieved. This study did not offer central advertising, so no individuals were contacted via this means. In the Asthma Trial 1, six of the 16 TPCCC patients contacted signed consent. This gave a 38% success rate. Only 3 of the 83 individuals found through advertising means gave consent. The success rate was 4%. Thus, four out of the five studies had higher success rates in consenting subjects from the TPCCC database. Insufficient information was obtained regarding Dr. Johns' study. Thus, only the recruitment efficiency for recruitment via advertising was

provided. Thirty-eight of the 81 women who contacted the screening center were brought in for consent. This yielded a 47% recruitment success rate.

Ninety-two questionnaires were sent to individuals that were contacted regarding any of the studies. Nine of the letters were marked return to sender. Sixteen questionnaires were answered and returned. In response to the first question regarding why the individual felt that research was conducted, nine people thought it was to benefit a patient suffering from a disease. The second most common answer was to further scientific discoveries. The second question asked why the individual became involved in research (if they responded to any form of study recruitment). Nine of twelve individuals answered that they had a genuine interest in research. Two others conveyed that they were interested in research because no other treatment has helped. One individual claimed that they could not afford the medication otherwise. Question three surveyed the individuals about their choice to not become involved in research. Five people did not qualify for the study. Another three individuals said that they were afraid to take a medication that was not approved by the FDA. Two people answered that they did not have the time to participate in the study. One person was afraid to come off of current treatment. Another individual was concerned about being randomized to placebo. Furthermore, one person claimed to benefit more from natural treatment such as exercise. A fourth question asked the subjects about the form of recruitment in which they learned about the study. Six individuals found out about the study from a television advertisement. Three subjects were informed of the study by their physician. The TPCCC research staff contacted two people regarding a study. Additionally, two

individuals learned of the research opportunity from a newspaper advertisement. Questions 5, 6, and 7 surveyed the individuals about compliance. There were very limited answers to these questions. Some individuals answered the questions although they did not receive study medication. Consequently, these questions and answers were not included in the results or discussion.

CHAPTER II

SECTION VIII: DISCUSSION

Based on the data and statistical analysis, there was no difference in compliance of the study subjects as a result of the form of recruitment into the trial. Approximately 100 recorded compliance percentages were taken into consideration for this test. These numbers ranged from 82% to 100%. On a whole, the values all demonstrated good compliance. Most subjects that entered into a study were taking medications to treat the disease at hand. We also find that most subjects are taking numerous concomitant medications. It is likely that there was no difference in compliance level during the study because these individuals are already disciplined in this area. They may possibly have a set medication schedule. Another possibility is that the individuals are determined to find a better treatment for the disease they suffer from. Therefore, based on these results, research staff should focus equally on recruiting from both private practice as well as the general public.

There also seemed to be a slight difference in compliance of the subjects based on length of the study. No tests were performed to determine if the difference was significant; there is, however, a difference. The subjects participating in the 52-week studies had on average a higher compliance rate than the individuals enrolled in the shorter duration studies. Again, this could possibly be due to routine. Further evaluation is needed to determine if there is truly any significant difference in study drug compliance based on duration of the study. The research staff at TPCCC reinforces the

importance of study compliance to our trial participants. Subjects should be reminded of this issue at every visit.

The chi-square test revealed no difference in study completion between the two groups. Again, the two groups are defined as subjects recruited through a form of central advertising and subjects found from the TPCCC practice. Although the analysis proved to be insignificant, a larger population to evaluate may show some difference in study completion. Unfortunately, the number of studies, and thus subject information was limited. Individuals that did not complete the study were terminated early due to the following reasons: exacerbation, personal issues, did not feel to be benefiting from the medication, received an intramuscular steroid (protocol violation), and lost to follow up. None of the randomized subjects were terminated due to non-compliance. At TPCCC, only one subject was lost to follow up. This subject was a participant in the COPD Trial 1 study, a 52-week study. We are not currently conducting any studies with duration longer than 52 weeks. Study length is something that needs to be considered when writing a protocol. Anything longer than 12 to 24 months would pose a potential risk of large loss to follow up. This is something that also could be further evaluated; the results would be extremely valuable and useful in achieving and maintaining higher compliance and study completion levels.

In general, non-compliance does not seem to be a significant issue at TPCCC Research. Although this study did not show any significant difference in study compliance or study completion as a result of recruitment type it is extremely important that research staff continues to reiterate the significance of subject compliance. When a

sponsor states in the protocol that the subject is to take study medication before 10 a.m. it is imperative that the individual follow the protocol. Some of the drugs in clinical trials are being tested based on the length of therapeutic window. Thus, taking the study drug as advised is very important in the analysis of the data.

Further efforts to learn of ways to improve upon patient recruitment included sending out a survey with questions related to recruitment. Question one asked the subjects why they felt that research was conducted. The majority felt that research is conducted to benefit patients suffering from a disease. About one third of the individuals replied that they felt research was conducted to further scientific discovery. The majority of these individuals also said that they inquired about a study because they had a genuine interest in research and the field of medicine. Thus, it doesn't seem that these individuals have a negative outlook on research. They do not feel that research is conducted merely for science. This is justified by responding that they have a genuine interest in research. It is important that the individuals we contact to participate in a study do not have the negative guinea pig perception of research. It is our duty as research staff to make the subject feel that research is conducted to benefit people suffering from a disease. Science and medicine are the foundation for developing these medications, but the primary focus should be on the subjects.

The majority of the individuals who responded to the questionnaire learned of a research opportunity through a television advertisement. The media allows us to reach a larger wave of people than does searching through our database and sending letters to potential subjects. The issue with recruitment through advertising lies in its inefficiency.

Although a greater number of individuals can be reached via a television or radio advertisement, the majority does not qualify for a study. COPD Trial 3 produced the following numbers: the call center received 5,379 calls from individuals inquiring about the study; 3,629 (67%) were disqualified at the center; 1,770 referrals were sent to 134 sites. Of the 1,770 referrals, 954 were determined to be unqualified or uninterested. Thus leaving a possible 816 individuals to be consented and screened. Overall, this is only 15% of the original callers. The recruitment efficiency for our site was also determined for each of the studies. In all but one of the studies, our site was more successful in recruiting patients of TPCCC than recruiting from advertising. Asthma Trial 1 yielded a very unsuccessful recruitment rate. This could be attributed, however, to the protocol. The protocol was very specific and detailed in the inclusion and exclusion criteria. The protocol is also something to take into consideration when determining the number of subjects that a research site will enroll.

We attempted to contact more individuals found via advertising, but were not able to enroll a large number of these subjects due to concomitant medication and co-morbidities. The employees conducting the phone screens do not generally have a medical background. The have not read and do not have a copy of the protocol. They are simply asking questions from a list created by the sponsors. The sponsors should supply a list of more relevant questions, or should require the screeners to have a more of a background in medicine. Advertising via print could be improved by making the advertisement more specific.

Possibly, we are more successful at recruiting from our own pool of patients because we are able to view a chart on these individuals. Instead of calling each individual or waiting for them to contact us, we are able to perform the chart research ourselves. Thus, we are to obtain information about concomitant medications and co-morbidities before contacting the individuals. This does take more time from our research staff, but yields a more successful recruitment rate. After taking into consideration the time that it takes to contact a great number of individuals recruited via advertising, the cost benefit ratio leans more in favor of recruiting from patient database.

CHAPTER II

SECTION IX: SUMMARY

COPD and asthma can significantly reduce the quality of life of the individual affected by the disease. The studies conducted at TPCCC, as well as studies taking place elsewhere, are all to better the quality of life of these individuals. Subject recruitment and retention are both big factors in the success of any clinical trial. Thus, it is important that all research and clinical staff are aware of the significance of these issues. The staff should review the protocol for each study and be aware of the inclusion and exclusion criteria as well as any difficulties with the protocol. It is imperative that we spend the time to look at the recruitment numbers. By doing this, we can decide where to put most of our time and effort. It serves a study no benefit to spend a significant amount of time recruiting via a particular means that proves to be inefficient.

When recruiting for a study, it is important to remind the subject that he or is she is always in control. These clinical trials are necessary to develop improved drugs. Patient retention and compliance are equally important. As a research site, the staff should discuss the methods that have proved to yield high retention. This may include phoning the subject to remind him of a visit the next day. Keeping track of study drug compliance and discussing this with the subjects can also lead to better compliance. The staff should also remind the subjects of the importance of compliance.

CHAPTER III

INTERSHIP EXPERIENCE

While at TPCCC I was fortunate to participate in a number of research opportunities. I have been to two Institution Review Board (IRB) meetings and have participated in several site initiation visits. I was also able to attend an investigator's meeting in Atlanta for the current asthma study at our site. As time progressed I was given more detailed responsibilities. This included query resolutions, answering site questionnaires, and completing study initiation requirements. Some of the requirements were preparing the Clinical Trial Agreement for new studies and sending CVs and budgets to the sponsors.

Dr. Burk has approximately 20 years experience in research. Kathy has served as the study coordinator for almost two years. The sub-investigator, Sandy Knaur APRN, also has several years experience with conducting research. With such a highly qualified and experienced staff, I was able to see research at its best. I not only learned the importance of documentation and GCP, but I also learned about the importance of communication and teamwork. As a research coordinator, one has to deal with a large number of people. This includes subjects, study monitors, the PI, sub PI, nursing staff, and number of regulatory administrative persons. It is important that the coordinator have a complete understanding of the responsibilities of all of these individuals. With the

knowledge and experience gained from this internship, I feel that I have a better insight into the field of research and what makes a study successful.

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SECTION I

ACRONYMS/ABBREVIATIONS

AE:	Adverse Event
ANOVA:	Analysis of Variance
APRN:	Advanced Practice Registered Nurse
CCRN:	Critical Care Registered Nurse
COPD:	Chronic Obstructive Pulmonary Disease
CRF:	Case Report Form
FDA:	Food and Drug Administration
GCP:	Good Clinical Practice
HIPAA:	Health Insurance Portability and Accountability Act
ICS:	Inhaled Corticosteroid
IRB:	Institutional Review Board
OBGYN:	Obstetrics & Gynecology
PFT:	Pulmonary Function Test
PFV:	Peak Expiratory Volume
RN:	Registered Nurse
TPCCC:	Texas Pulmonary and Critical Care Consultants

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SECTION II

QUESTIONNAIRE PACKET

I am a graduate student at the University of North Texas Health Science Center in Fort Worth, and am working towards a master's degree in Clinical Research Management. Clinical research trials greatly depend on the success of the recruitment and retention rate for any given study. I have compiled this survey in order to evaluate the success and efficiency of current recruitment procedures.

Any current health care or clinical research study that you are involved in is not directly related to this survey. Your participation in this study will have no affect on the current health care or clinical treatment that you receive, and there will be no direct benefit to you. If you choose not to participate, this will in no way impact your current form of treatment. I will perform statistical analyses on the data obtained from this study. Your name, address, nor any other personal information will be included in any document that I submit in my thesis. There are no potential risks involved in completing this questionnaire. The possible benefits include more efficient and successful recruitment in clinical research studies resulting in expediting new pharmaceuticals to market.

I have provided a return stamped envelope for you to return the survey. Please do not include your name on the survey or on the return stamped envelope. I would greatly appreciate your participation and feedback.

Sincerely,

Jessica Chandler
Graduate School of Biomedical Sciences
University of North Texas Health Science Center

Research Study Questionnaire

1. What do you feel is the most import reason that research is conducted?
    a. To benefit patients suffering from a disease
    b. To boost physician's careers
    c. To make money for drug companies
    d. To further scientific discoveries
    e. Other_____

2. Why did you become involved in research? Answer only if you responded to any form of advertisement for the study; answer even if you did not qualify for the study.
    a. Could not afford the medication otherwise
    b. No other treatment has helped me
    c. I have a genuine interest in research and the field of medicine
    d. Monetary compensation
    e. Other_____

3. Why did you choose not to become involved in research? Answer only if you did not respond to any form of advertisement.
    a. Did not have the time
    b. Simply not interested
    c. Afraid of taking a drug not approved by the Food and Drug Administration
    d. Negative guinea pig perception
    e. Did not have a good feel for what the study entails
    f. Other_____

4. Through which method did you learn of this research opportunity?
    a. Radio advertisement
    b. Newspaper advertisement
    c. Flyer or other form of poster or brochure
    d. Through my physician
    e. I was contacted by the research staff
    f. Television advertisement
    g. Other_____

5. If you participated in a research study (i.e. received study medication), what level of compliance do you feel you have displayed as a research study patient? (i.e. you took medication as directed; you recorded information in the study diary as instructed, you attended all of your visits)------5 being the most compliant and 1 being the least compliant

a. 1
b. 2
c. 3
d. 4
e. 5

6. If you participated in a research study (i.e. received study medication) and feel that you have achieved a compliance level of 3 or higher, what do you attribute this success to? (If not please skip to next question)

a. Reminders from the study coordinator.
b. You feel that the medication is helping
c. Monetary compensation
d. Other_____

7. If you participated in a research study (i.e. received study medication) and feel that you have achieved a compliance level of 2 or below, why do you feel that you were hindered? (If not please skip to next question)

a. Could not remember to complete tasks
b. Had several other things going on while involved in the study
c. The study medication did not seem to be helping
d. Other_____

Additional comments: Please make any suggestions that you feel would help to better clinical research patient recruitment and retention.

_____
_____
_____
_____
_____
_____
_____

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SECTION III

IRB EXEMPTION LETTER

UNIVERSITY of NORTH TEXAS
HEALTH SCIENCE CENTER at Fort Worth
★
Education, Research,
Patient Care and Service

DATE: **22, January 2008**

Office for the Protection of Human Subjects
3500 Camp Bowie Boulevard
Fort Worth, Texas 76107-2699

TO: **John R. Burk, MD (with student Jessica Chandler)**
Graduate School of Biomedical Sciences/Clinical Research Management

PROTOCOL: #2007-144

"Clinical Research Patient Recruitment and Retention"

IRB BOARD ACTION AND NOTICE OF APPROVAL

The Institutional Review Board (IRB) of the University of North Texas Health Science Center (UNTHSC) has reviewed your protocol and has granted approval for EXEMPT status (as specified in Federal Regulations 45 CFR 46 101(b), category (2).

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

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

If you have any questions, please contact Ms. Jill Kurschner, IRB Compliance Coordinator, at phone (817) 735-0424 in the Office for the Protection of Human Subjects, or send email to her at jkurschn@hsc.unt.edu .

Sincerely,

Brian Gladue, PhD
Chairman, UNTHSC Institutional Review Board

cc: **J. Kurschner, OPHS**

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SECTION IV

PATIENT RECRUITMENT LETTER

TEXAS PULMONARY & CRITICAL CARE CONSULTANTS, P.A.

Pulmonary and Critical Care Specialists

SLEEP CONSULTANTS, INC.

Comprehensive Care of Sleep Disorders
Diagnosis, Treatment, Follow-up, Education

Arlington - North
Joseph Austin, Jr., M.D., FCCP
Jack G. Gilbey, Jr., M.D., FCCP
Luis F. Guerra, M.D., FCCP
Mitchell C. Kupplnger, M.D., FCCP
David B. Plump, M.D., FCCP
Tony H. Su, M.D., FCCP
911C Medical Centre Drive
Arlington, Texas 76012
(817) 461-0201 (Metro)

Arlington - South
E. Duane Dilley, M.D., FCCP
Phan Nguyen, M.D.
Southpark Medical Building
601 Omega Drive, Suite 206
Arlington, Texas 76014
(817) 465-5881

Bedford
Gary L. Jones, M.D., FCCP
James T. Simonds, M.D., FCCP
Donald L. Washington, Jr., M.D.
1604 Hospital Parkway, Suite 403
Bedford, Texas 76022
(817) 354-9545

Burleson - Huguley
Henry S. Cunningham, M.D., FCCP
11797 S. Freeway, Suite 222
Burleson, Texas 76028
(817) 293-1900

Fort Worth - Medical District 1
John R. Burk, M.D., FACP
G. Ryan Gilligan, M.D.
Stuart D. McDonald, M.D., FCCP
Karim F. Rasack, M.D., FCCP
1521 Cooper Street
Fort Worth, Texas 76104
(817) 336-5864

Fort Worth - Medical District 2
Roger Gleason, M.D., FCCP
David S. Hernandez, M.D.
John T. Pender Jr., M.D., FCCP
Indra V. Singh, M.D.
1201 Fairmount Avenue
Fort Worth, Texas 76104
(817) 335-5288

Fort Worth - Southwest
Kevin G. Connelly, M.D., FCCP
Huy X. Duong, D.O.
6100 Harris Parkway, Suite 285
Fort Worth, Texas 76132
(817) 263-5864

Grapevine
R. L. "Lin" Cash, Jr., M.D., FCCP
Timothy G. Schroeder, M.D., FCCP
1600 West College, Suite 470
Grapevine, Texas 76051
(817) 424-5959 (Metro)

North Richland Hills
David R. Herrmann, M.D., FCCP
4351 Booth Calloway, Suite 210
North Richland Hills, Texas 76180
(817) 284-4343

Sleep Consultants, Inc.
Donald E. Watenpaugh, Ph.D., *Director*
Diplomate, American Board of Sleep Medicine
John R. Burk, M.D., FACP, *Medical Director*
Huy X. Duong, D.O.
Sandra Knaur, APRN, BC
John T. Pender, Jr., M.D., FCCP
Karim F. Rasack, M.D., FCCP
D. Heath Roberts, D.D.S.
1521 Cooper Street
Fort Worth, Texas 76104
(817) 332-7433
infocenter@sleepconsultants.com
http://www.sleepconsultants.com

April 09, 2008

Dear,

I wanted to inform you of an exciting opportunity in the Fort Worth area. Our Cooper street office (located in the hospital district) has been involved in clinical research, but now has created a research center. Our research center is located at ***909 Eighth Avenue, Fort Worth.*** We are participating in several studies for the treatment of chronic obstructive pulmonary disease (COPD). The center is looking for individuals interested in assisting in these studies.

A brief review of you records indicate you might be a candidate for one of the studies. In order to determine if you meet the criteria for a study you will need to come to the office. As a research client, your participation is completely voluntary and at anytime during study should you choose to withdraw you may do so. Your primary care physician and/or pulmonologist will still care for your medical/pulmonary needs. The research study will be explained to you very carefully and any decision made to participate occurs only after you have the opportunity to discuss with us, in detail the study and have your questions answered. Often the studies require changes in medications you are currently taking, but these changes are discussed with you and you are closely monitored at all times.

If you are interested in learning more about the possibilities of participating in our studies, I would like the opportunity to meet with you. Please call the office,(817) 332-5599, or my research cellular, (817-223-0061). I will ask you a few questions concerning your disease and medications. If you appear to meet the criteria for the study, an appointment will be scheduled for you to discuss the study and obtain your consent in writing. Enrollment into a research study allows for closer follow-up visits at no cost to you during the study period. Additionally all the procedures of the study and the study medication is of no cost to you. It is also possible you will be paid for your time and travel while participating in the study. Thank you for your consideration in our research.

Sincerely,

Kathy Kwaak RN CCRN
Clinical Research Coordinator

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SECTION V

DAILY JOURNAL

Monday Aug 13th-

- Met everybody over at the Cooper office.
- Spoke with Dr. Burk about what to expect from this internship.
- Kathy showed me around the research lab and told me a little about each of the studies.

Tuesday Aug 14th-

- Saw a patient for visit one-consent.
- Watched Kathy throughout the day.

Wednesday Aug 15th-

- Saw a patient for visit 2.
- Sat in with the COPD Trial 1 monitor and helped her conduct drug accountability.
- She also trained me a little on drug accountability and other areas of the regulatory binder.

Thursday Aug 16th-

- Saw two patients with Kathy.
- Worked on the COPD Trial 1 regulatory binder and made suggestions as to how I thought the binder should be organized.

Friday Aug 17th-

- Finished modifying the regulatory binder.
- Saw patient with Kathy.
- Friday was a half-day.

Monday Aug 20th-

- Organized the COPD Trial 2 binder.
- I watched/learned patient recruitment.
- Also did some filing in the patient CRF.
- We prepared for the next days visit.

Tuesday Aug 21st-

- Worked on table of contents for the COPD Trial 1 study.
- Saw patient for a randomization visit.

Wednesday Aug 22nd-

- Finished table of contents.
- Learned a little more about patient recruiting.
- We also had another patient visit.

Thursday Aug 23rd-

- Had my committee meeting where we discussed a few ideas for my thesis title.
- Kathy and I discussed budgets for studies.
- Thursday was a half-day.

Friday Aug 24th-

- No work

Monday Aug 27th-

- Kathy trained me on drug accountability and case report form transcription.
- We also signed all of the signature logs and designated my responsibilities in each of the studies.
- We faxed a form to the IRB of each study letting them know that I was going to be involved in the studies.
- We prepared for the next days visit.

Tuesday Aug 28th-

- Transcribed information into CRF for patient in the COPD Trial 2 study.
- Watched Kathy do a randomization visit.

Wednesday Aug 29th-

- Had two patient visits today.
- Transcribed source information into the CRF.
- Also transcribed some source information into an electronic CRF.
- Developed an invoice to one of the drug companies to reimburse a patient.
- Date and filled out patient information on the patient diaries to help prepare for next week when Kathy is on vacation.

Thursday Aug 30th-

- Had patient visit in the morning.
- Transcribed some source information into an electronic CRF.
- Helped Kathy prepare source documents and everything that we will need for our three visits next week.
- Confirmed drug shipment with IVRS.

Friday Aug 31st-

- Filed source documents.
- Began working on patient recruitment.

Tuesday Sep 4th-

- Helped Sandy with patient visits.
- Worked on patient recruitment and did literature searches.
- Temperature log.

Wednesday Sep 5th-

- Helped with visit.
- Filed paper work.
- Worked on patient recruitment and did literature searches.

Thursday Sep 6th-

- Went with Dr. Burk to IRB meeting.
- Did rounds with Dr. Burk.

Friday Sep 7th-

- Filed paperwork for visits this week and completed CRF.
- Literature searches.

Monday Sep 10th-

- Helped Kathy with visit.
- Filed paperwork from last week.
- I entered information into the EDC.
- I also sat in on a site initiation visit.

Tuesday Sep 11th-

- Helped Kathy with a patient visit in the morning.
- Then, we worked on ECD for the three studies last week.
- Worked on patient recruitment.

Wednesday Sep 12th-

- Sent out patient recruitment letters.

Thursday Sep 13th-

- Went over to Baylor Research Institute with Kathy and we discussed possible studies for the pulmonary center.
- I also got to visit with Vicki about possible data that she could release to me for my thesis.

Friday Sep 14th-

- No work!!

Monday Sep 17th-

- Filed paperwork.

Tuesday Sep 18th-

- I was out sick

Wednesday Sep 19th-

- We had a monitor visit today.
- I helped the monitor find what she needed, filed paperwork for her, and made copies.
- I also filed other paperwork as necessary.

Thursday Sep 20th-

- Had patient visit.
- Prepared paperwork for visit on Monday.

Friday Sep 21st-

- No work.

Monday Sep 24th-

- We had a monitor visit today.
- Worked on patient recruitment.
- I received EDC training from another monitor
- Prepared paperwork for visit on Tuesday.
- Filed paperwork that had been signed by Dr. Burk.

Tuesday Sep 25th-

- We had a monitor visit today and two patient visits.
- I entered both of the patient visits into the EDC.
- Kathy and I also worked on requests that had been made from the monitor the day before.
- I made the necessary changes in the drug accountability. Filed paperwork.

Wednesday Sep 26th-

- We had a patient follow-up visit.
- I entered the information into EDC.
- Then we went to a staff meeting.
- I received and recorded drug shipment.
- At lunch we went to Baylor for a Focus on Research presentation about current research on HIV drugs.
- Kathy and I went through some patient files together and sent out a few letters to recruit more patients into one of our studies.

Thursday Sep 27th-

- Had a patient visit today.
- Worked on rescue medication accountability for COPD Trial 2 study.
- Did some patient recruitment for the insomnia study.

Friday Sep 28th-

- Had patient visit and entered information into EDC.

Monday Oct 1st-

- Finished rescue medication accountability for COPD Trial 2 study.
- Helped Kathy prepare for the visit tomorrow.
- Sent laptop to sponsor for maintenance.
- Sent out recruitment letters.

Tuesday Oct 2nd-

- Filed signed paperwork.
- Sent out a recruitment letter.
- Received and documented receipt of study drug.

Wednesday Oct 3rd-

- Worked on patient recruitment.
- Went and visited with Reta about the Versys system, the scheduling and billing system.
- I did this so that I could better develop a more efficient method of recruitment.
- Started working on the spreadsheet.

Thursday Oct 4th-

- Attended an IRB meeting with Dr. Burk.
- Came back and worked on patient recruitment database.

Friday Oct 5th-

- Worked on patient recruitment database and proposal.
- Entered information into the eCRF.

Monday Oct 8th-

- Patient visit
- Worked on patient recruitment database
- Filed lots of paperwork that Dr. Burk signed and answered queries.

Tuesday Oct 9th-

- Worked on patient recruitment and database.
- I worked on queries and entered new information into the eCRF.

Wednesday Oct 10th-

- Worked on patient recruitment.
- I answered queries because they are trying to lock the database this Friday.
- I also helped Kathy prepare for tomorrow's visits.

Thursday Oct 11th-

- Worked on queries. Helped Kathy prepare for Monday's visit.
- Finished up proposal and worked on patient recruitment.

Friday Oct 12th-

- Worked on queries and patient recruitment.

Monday Oct 15th-

- Filed paperwork
- Transferred information from the source to the CRF and eCRF
- Patient visit
- Worked on patient recruitment

Tuesday Oct 16th-

- Patient recruitment
- Helped Kathy prepare for this months visits

Wednesday Oct 17th-

- Patient recruitment
- Talked with Dr. Watenpaugh about the possibility of a new project
- Worked on patient database

Thursday Oct 18th-

- Worked on queries.
- Worked on patient database.

Friday Oct 19th-

- Transferred information from the source to the eCRF.
- Had two patient visits.
- Worked on queries.
- Spoke with Dr. Burk about proposal and other possible project.
- Filed paperwork

Monday Oct 22nd-

- Worked on recruitment database.
- Filed paperwork

Tuesday Oct 23rd-

- Made new charts for patients
- Had patient visits
- Entered information into the CRF and eCRF
- Patient recruitment
- Worked on survey for thesis

Wednesday Oct 24th-

- Had two patient visits
- Staff meeting
- Patient recruitment

Thursday Oct 25th-

- Patient visit
- Had monitor visit
- Patient recruitment
- Worked on thesis material

Friday Oct 26th- No work

Monday Oct 29th-

- Entered information into eCRF.
- Filed paperwork.
- Patient recruitment
- Worked on referral project

Tuesday Oct 30th-

- Sent out recruitment letters
- Patient visit

Wednesday Oct 31st-

- Site initiation visit
- Two patient visits
- Entered information into eCRF
- Helped prepare for site initiation visit

Thursday Nov 1st-

- Working on patient recruitment
- Finished up the site initiation visit
- Had a web conference for advertising

Monday Nov 5th-

- Filed paperwork
- Answered queries for COPD Trial 4 study
- Drug shipment receipt
- Prepared documents for tomorrow's visit

Tuesday Nov 6th-

- Patient visit
- Monitor visit
- Worked on research survey
- Worked on patient database

Wednesday Nov 7th-

- Monitor visit
- Answered queries
- Entered information into the eCRF.

Thursday Nov 8th-

- Organized investigational drug for COPD Trial 1 study
- Filled out the informed consent log for COPD Trial 1 study
- Web conference computer test

Friday Nov 9th- No work

Monday Nov 12th-

- Worked on questionnaire and gathering information for my thesis

Tuesday Nov 13th-

- Worked on gathering information for my thesis

Wednesday Nov 14th-

- Filed paperwork signed by Dr. Burk
- Worked on database of patients that have been contacted by our office
- Answered queries

Thursday Nov 15th-

- Morning web conference
- Patient consents
- Worked on database of patients that have been contacted by our office

Monday Nov 19th-

- Worked on database of patients that have been contacted by our office
- Answered queries
- Worked on gathering information for my thesis

Tuesday Nov 20th thru Friday Nov 23rd- No Work

Monday Nov 26th-

- Filed paperwork
- Answered queries
- Completed eCRF
- Worked on database and thesis information

Tuesday Nov 27th-

- Filed paperwork
- Worked on database and thesis information
- Made new patient charts

Wednesday Nov 28th-

- Filed paperwork
- Worked on database and thesis information
- Worked on finding a record storage and estimating cost for research budget
- Made holiday party flier
- Made new patient charts
- Registered drug receipt

Thursday Nov 29th-

- Met with Dr. Watenpaugh about referral project
- Worked on referral project
- Worked on database
- Helped monitor with drug accountability

Friday Nov 30th-

- Worked on retrieving documents for the monitor
- Filed paperwork
- Answered queries on eCRF

Monday Dec 3rd-

- Filed paperwork
- Entered patient information into patient database
- Worked on queries

Tuesday Dec 4th-Out sick

Wednesday Dec 5th-

- Staff meeting
- Drug receipt
- Entered information into eCRF and CRF
- Worked on database

Thursday Dec 6th- No work

Friday Dec 7th- No work

Monday Dec 10th-

- Worked on database and survey
- Filed paperwork
- Worked on queries
- Entered information into CRF
- Drug accountability

Tuesday Dec 11th-

- Drug shipment receipt
- Organized study drugs
- Entered information into CRF
- Filed Paperwork
- Put new study binders together
- Monitor visit

Wednesday Dec 12th-

- Staff meeting
- Finished putting new study binders together
- Filed paperwork
- Answered queries

Thursday Dec 13th-

- Worked on information for the web site
- Worked on exemption form for survey
- Filed paper work

Friday Dec 14th-

- Entered information into eCRF
- Worked on exemption form for survey
- Worked on survey
- Holiday party with Landmark

Monday Dec 17th-

- Finished paperwork for survey exemption
- Filed paperwork

Tuesday Dec 18th-

- Filed paperwork
- Finished patient database
- Query inquiry

Wednesday Dec 19th-

- Office Holiday Party

Wednesday Jan 2nd-

- Staff meeting
- Filed paperwork
- Entered information into the CRF
- Sent computer back to sponsor for repair

Thursday Jan 3rd-

- Worked on CITI training
- Worked on thesis
- Made charts and got paperwork ready for Monday's visit

Friday Jan 4th- No Work

Monday Jan 7th-

- Filed paperwork
- Registered drug receipt

Tuesday Jan 8th-

- Monitor visit
- Got paperwork ready for Wednesday's visits

Wednesday Jan 9th-

- Staff meeting
- Worked on CITI training
- Worked on thesis
- Answered queries

Thursday Jan 10th-

- Completed CITI training
- Completed drug accountability
- Worked on thesis

Friday Jan 11th- no work

Monday Jan 14th-

- Entered information into eCRF
- Worked on thesis

Tuesday Jan 15th-

- Entered information into eCRF
- Worked on thesis

Wednesday Jan 16th-

- Answered queries
- Filed paperwork

Thursday Jan 17th-

- Filed answered queries in CRF
- Worked on thesis

Friday Jan 18th- No work

Monday Jan 21st-

- Answered queries
- Worked on thesis
- Filed paperwork
- Put away study supplies

Tuesday Jan 22nd-

- Entered information into CRF
- Drug accountability
- Trained research assistant
- Worked on thesis
- Worked on patient database

Wednesday Jan 23-

- Worked on thesis
- Worked on patient database
- Research speaker at BRI
- Filed paperwork

Thursday Jan 24th-

- Worked on thesis
- Worked on patient database

Friday Jan 25th- No work

Monday Jan 28th-

- Worked on thesis
- Filed paperwork
- Answered queries

Tuesday Jan 29th-

- Worked on thesis
- Monitor visit
- Filed paperwork

Wednesday Jan 30th-

- Staff meeting
- Worked on Source Documents for new study

Thursday Jan 31st-

- Finished source documents for new study
- Worked on budget for new study
- Filled out Clinical Trial Agreement for new study
- Filed paperwork

Friday Feb 1st- No work

Monday Feb 4th-

- Finished budget for new study and visited with Dr. Burk about it
- Filled out Protocol deviation form and sent it to IRB and sponsor
- Talked with Dr. Burk and Kathy about taking the role as Clinical Research Associate
- Filed paperwork

Tuesday Feb 5th-

- Completed study questionnaire for OSA/depression study
- Sent in CV's and licenses for all staff that would possible be working with the OSA/depression study

Wednesday Feb 6th-

- Entered patient visit information into the eCRF
- Answered queries for COPD Trial 2 study and sent to Data Management; also compiled a query list of all queries and tracking numbers that have already been sent to Data Management per our CRA.
- Answered queries regarding COPD Trial 3 study
- Filed paperwork

Thursday Feb 7th-

- Prepared for investigator's meeting
- Answered queries
- Filed paperwork

Monday Feb 11th- In Atlanta for Investigator's Meeting

Tuesday Feb 12th- In Atlanta for Investigator's Meeting

Wednesday Feb 13th-

- Web, investigator's meeting for the new COPD study
- Filed paperwork

Thursday Feb 14th-

- Site visit
- Answered queries
- CRM Internship Practicum Report

CRM Internship Practicum Report

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