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An open label, randomized, comparative, parallel, phase III multicenter study will be the main focus in the surgery department at the University of North Texas Health Science Center Patient Care Center. The study will evaluate the safety and efficacy of the fentanyl patient-controlled transdermal system (PCTS) versus an intravenous patient controlled anesthesia morphine pump (PCA pump) for abdominal surgery postoperative pain management. Patient enrollment is essential. Slow patient enrollment in clinical trials will lead to a delay in the sponsor's submission of the investigational product for review and approval from the FDA. The barriers and facilitators to the accrual and retention of patients in this study will be covered.

IMPLEMENTATION OF A PAIN MANAGEMENT PROTOCOL IN ABDOMINAL SURGERY PATIENTS INVOLVING AN INVESTIGATIONAL FENTANYL PATIENT-CONTROLLED TRANSDERMAL SYSTEM

ISSUES INVOLVING PATIENT ENROLLMENT

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THESIS

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CHAPTER I

INTRODUCTION

A clinical trial is a research study involving human volunteers used to find the safest treatments to improve the health of individuals (Clinical Trials, 2005). The objective of clinical research is to develop knowledge to improve health and increase the understanding of human biology (Emanuel, et al, 2000). In 1925, American medical educator, Abraham Flexner wrote, "...research can no more be divorced from medical education than can medical education be divorced from research" (Gallin, 2002). He felt that clinical research is a major component needed in the teaching of medicine (Gallin, 2002). A randomized clinical trial is a study in which participants are randomly assigned (by chance) to one of the two treatment groups in the clinical trial (Clinical Trials.Gov, 2005). An open label study is a study in which the subject, physician, coordinator, pharmacist, and nursing staff are all informed of the drug and dose being administered. In open label studies none of the subjects are given placebos (Center Watch, 2005). The concept of randomization was first introduced by Fisher in 1926 and applied to agricultural research (Friedman et al, 1998). The first clinical trial to use a form of random assignment was reported by Anderson, et al in 1931, in which a flip of a coin was used to determine which of the 24 subjects with pulmonary tuberculosis would receive sanocrysin, a gold compound commonly used during that time. It was not until 1948, that

the first use of random numbers to determine which subjects received which treatment was used by the British Medical Research Council (Friedman et al 1998). Most clinical trials are multicenter studies used to recruit an adequate number of subjects for the study in a reasonable amount of time, have a more representative sample of the study population, and enable investigators with similar interests and skills to work together on a common problem (Friedman et al, 1998). Within phase III trials, parallel and comparative studies test the effectiveness of a new study product which is similar to a type of medication or device already available to the public.

All clinical trials have specific inclusion and exclusion criteria which are guidelines on who can participate in the trial. Five different types of clinical trials exist in which subjects may be involved. These include treatment trials which test experimental treatments, prevention trials which looks for better ways to prevent disease in people, diagnostic trials which are conducted to find betters tests for diagnosing a particular disease, screening trials which test the best way to detect certain diseases, and quality of life trials which explore ways to improve the quality of life for individuals with a chronic illness (Clinical Trials, 2005). Being involved in clinical trials can allow subjects to play an active role in their own health care, gain access to new research treatments, obtain expert medical advice, and help others by contributing to medical research (Clinical Trials, 2005).

Currently, clinical drug trials are conducted in phases. Phase I trials allow researchers the opportunity to test the safety, determine a safe dosage, and identify the side effects of an experimental medication in a small group of healthy volunteers (20-80).

Phase II trials evaluate the effectiveness and safety of the study medication utilizing a slighter larger study population (100-300) who actually have the disease or condition for which the drug is being indicated. In phase III trials, the study medication is given to an even larger group of subjects (1000-3000) to confirm the effectiveness, further monitor side effects, and compare it to commonly used treatments (Clinical Trials, 2005), as well as to gain the information needed to write the instructions (label) for its particular indication (Gallin, 2002). If needed, a phase IV trial is conducted after the drug is available to the public to continue to evaluate the drug's risks, benefits, and optimal use (Clinical Trials, 2005).

In 1938, Congress passed the Federal Food Drug and Cosmetic Act which extended its control not only to include food and drugs but also cosmetics and devices. This meant that new drugs were required to be tested for safety before they could be marketed. Soon after, the Kefauver-Harris amendments were passed which required drug manufactures to also prove the effectiveness of their product before it was marketed for public use (Gallin, 2002).

Currently an open label, randomized, comparative, parallel, Phase III multicenter study is being conducted in the department of surgery at the University of North Texas Health Science Center Patient Care Center. The study evaluates the safety and efficacy of the fentanyl patient-controlled transdermal system (PCTS) versus an intravenous patient-controlled anesthesia (PCA pump) for postoperative pain management in lower abdominal and pelvic surgery subjects. Effective postoperative pain management is paramount to the care and recovery of an individual. If postoperative pain is not

managed, medical complications can occur which can increase the length of stay, rehospitilization rates, and more outpatient visits. Pain is also costly in terms of lost productivity and income and is the leading cause of medically related work absenteeism and results in more than 50 million lost work days per year in the United States (American Pain Society, 2004).

Fentanyl PCTS is currently in phase III of clinical trial testing. In previous clinical trial phases (I and II), fentanyl (PCTS) was found to be superior to a placebo and equivalent to the PCA pump in the management of postoperative pain in abdominal, orthopedic, and thoracic surgery subjects (Viscusi and Reynolds, 2004). The continued testing of the fentanyl PCTS and approval by the Food and Drug Administration (FDA) may provide physicians and subjects a safer and more effective drug delivery option.

The testing of the fentanyl PCTS requires enrollment of 250 pelvic surgery subjects and 250 abdominal surgery subjects. Any delays in meeting the sponsor's enrollment deadlines can lead to an increase in the amount of money the sponsor spends and delays their ability to submit required documentation to the FDA for approval. A delay in approval from the FDA will also affect millions of people who will not be able to obtain a potentially beneficial drug. For this reason, my internship focus was to analyze the varying barriers and facilitators that affect subject enrollment in the abdominal fentanyl PCTS study and to implement new ideas to increase subject enrollment.

CHAPTER II

INTERNSHIP SUBJECT

Significance

Subject enrollment and retention in clinical trials is essential for the discovery of new drugs and treatment plans and they are two of the major challenges that face sponsors of clinical trials (Integrated Trials, 2004). Ninety percent of all clinical trial sites fail to complete the subject enrollment requirement within the sponsor's projected timeline. This is due to the fact that less than one out of every four potential clinical trial volunteers learns about clinical trials through their primary care physician or nurse (Integrated Trials, 2004). Delays in meeting subject enrollment figures in a timely manner can often lead sponsors to extend their original enrollment period by six or more months. Often this time extension will lead to an increase in the amount of money spent by the sponsor to fund the clinical trial. If there is a delay in subject enrollment at clinical trial sites, it may cause a delay in the sponsor's ability to timely submit the appropriate documentation necessary to request review and approval of the investigational product to the Food and Drug Administration (FDA).

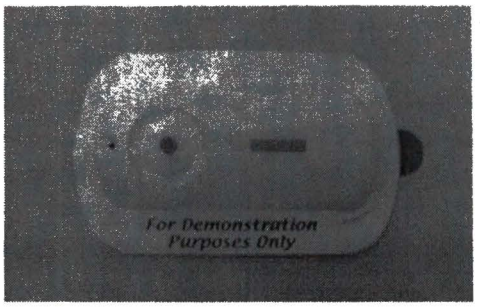
Effective postoperative pain management is a continuous issue faced by health care professionals on a daily basis. Dr. Schweitzer, a French medical missionary in 1931, wrote, "Pain is a more terrible lord of mankind than even death itself" (National Institute of Neurological Disorders and Stroke, 2004). Over time pain has become a common

disorder among subjects often being described as a fiery burning sensation, a sharp piercing or a dull throbbing sensation that makes human beings suffer leading to the hindrance of productive and active lives. Currently in the United States, approximately 20 million people per year require injectable opioids for the treatment of acute pain (Alza Corporation, 2003). If postoperative pain is allowed to persist for a long period of time, it can lead to medical complications such as pneumonia, blood clots, infection, and shock (American Pain Society, 2004). For example a patient having undergone thoracic surgery whose pain is not adequately controlled runs the risk of developing pneumonia due to shallow breathing and retained expiratory excretions. This in turn can prolong hospitalization and increase outpatient visits. Traditionally, opioids are given intravenously to help relieve pain (National Institute of Neurological Disorders and Stroke, 2004), and new advances in pain relief systems and additional opioids have been added to the list of pain management drugs. One of the major advancements in the delivery of drugs is the PCA pump which allows a subject to control their medication but requires the technical expertise of a nursing staff and intravenous access of the subject (National Institute of Neurological Disorders and Stroke, 2004). The PCA pump provides better pain control because it allows subjects continuous access to pain medication within predetermined limits and its economic advantages include lower cost due to less medical intervention needed and earlier release from the hospital (Gupta, et al, 1999). However, programming errors, uncontrolled delivery of syringe contents, and pump failure have often been reported (Viscusi and Reynolds, 2004). To overcome these problems, the fentanyl PCTS is being developed as an alternative method for drug

delivery. Its design combines the advantages of the PCA pump while also including the passive transdermal method of pain control (Gupta et al, 1999). Compared to the morphine pump, the new fentanyl PCTS does not require intravenous cannulation thus saving nursing staff the time of setting up an IV and allowing nurses to devote more of their time and attention to the subject (Biotech Week, 2004). Other benefits include subject mobility, decreased programming errors, and fewer subject tampering, compared to the morphine pump. The fentanyl PCTS delivers a set dose of 4μg/minute over a 10 minute period, decreasing the possibility of subjects developing respiratory depression from an overdose often seen with the fentanyl transdermal patch (not patient-controlled). A case involving opioid overdose with the transdermal patch was published in the *Anesthesia Analogs* in 2001 (Frolich and Giannotti, 2001). A 57-year-old woman wearing a fentanyl transdermal patch was given a warming blanket after her nasopharyngeal temperature dropped to 34.9° C (Frolich and Giannotti, 2001). The warming blanket caused an increase in drug delivery which ultimately led to increased systemic absorption of the fentanyl causing respiratory depression (Frolich and Giannoti, 2001).

The fentanyl PCTS is housed in a hard plastic cover to protect the medication from the external environment, and helps to eliminate events like this.

Illustration 1: Fentanyl PCTS



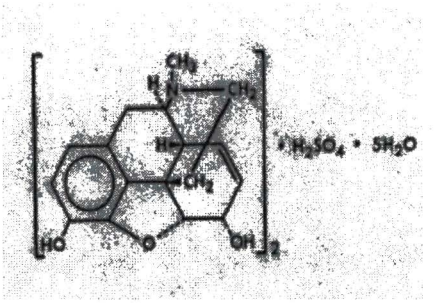
*Alza Corporation, 2004

The system contains an internal electronic circuit, a battery, anode and cathode hydrogels, and an external button to activate delivery of the fentanyl (Gupta et al, 1999). The PCTS delivers drug ions through the tissue by means of an electrical current during a 10 minute dosing interval instead of having medication continuously absorbed through the skin as seen with the non-controllable fentanyl transdermal patch (Ortho-McNeil Clinical Protocol, 2004).

Background

Morphine is a common narcotic analgesic used in hospitals. It was first isolated from opium in 1803 by German pharmacist, F.W.A. Serturner, who named it ***Morpheus,*** after the god of dreams. Given intravenously, it is still considered the most effective drug for pain relief (Columbia Encyclopedia, 2005).

Illustration II: Morphine Structure



*Physcians' Desk Reference, 2002

Having a molecular weight of 285.37 and chemical structure $C_{17}H_{19}NO_3$, morphine is very similar to fentanyl. However, fentanyl is 50-100 times more potent on a weight basis (Hardwick and King, 1997). Morphine can be administered intravenously, intramuscularly, and subcutaneously and has the same habit-forming properties as fentanyl. Side effects produced from both fentanyl and morphine are dizziness, light headedness, respiratory depression, nausea and vomiting, shortness of breath, and cold clammy skin (Mayo Clinic, 2004).

In 1968, the first patient controlled analgesic system (PCA) appeared in hospitals to be used in the management of postoperative pain (Lebovits and Zenetos, 2001). The clinical trials that took place in the 1970's and 1980's supported the safety, efficacy, and the advantages of the PCA pump. Such advantages included improved pain relief, shorter hospital stay, less anxiety, and lower level of analgesic consumption (Lebovits and Zenetos, 2001). The PCA pump delivers the drug into an intravenous access site on the subject through microbore tubing and has a visual display which provides information on a subject's drug consumption (Gupta et al, 1999).

Illustration III: PCA Pump

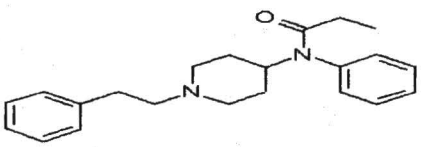
*Abbott Laboratories, 2004

Even though the PCA pump is very popular as the standard of care in hospitals, subject safety during use remains an issue. Dr. Michael Cohen said, "The PCA pump provides a measure of safety for patients because the morphine is delivered at doses lower than what is needed for sedation and an oversedated patient will not push the PCA pump button to give more opiate" (Sentinel Event Alert, 2004). However, the design of this pump affords family members or health care individuals the ability to push the button which bypasses the built-in safety feature making the situation potentially dangerous (Sentinel Event Alert, 2004). Another subject safety concern published in the *Biomedical Safety and Standards Journal* in November 2002, recounted the near death experience of a teenage boy in Cleveland prescribed a PCA pump for his postoperative pain (Biomedical Safety and Standards, 2002). A pulse oximeter which alerts nurses to decreased blood oxygen levels due to depressed respiratory rate was not placed on the boy's finger (Biomedical Safety and Standards, 2002). Nurses were alerted by the boy's mother who fortunately was at his bedside when he stopped breathing (Biomedical Safety and Standards, 2002). After this incident, the Cleveland hospital implemented a policy

requiring pulse oximeters with PCA pumps. The FDA and the Institute of Safe Medication Practices have also published warning articles about the potential problems of the PCA pump (Biomedical Safety and Standards, 2002). This led physicians to continue researching other narcotic analgesic delivery systems that would be comparable to the PCA pump. One such narcotic analgesic currently undergoing research is fentanyl.

Since the 1960's, fentanyl has been used during surgery to assist in sedation. However, its use for pain control using new and easier fentanyl delivery methods is a new topic in medical research. Fentanyl was first created by Dr. Paul Jannsen, a Belgian chemist, in the 1960's and was first introduced to the public as an intravenous anesthetic in 1963 (Mayo Clinic, 2004). Dr. Janssen synthesized fentanyl by reacting n-phenethyl-piperidone with aniline which produced 4-anilino-n-phenethyl-piperidine which he then reacted with propionyl chloride to produce pure fentanyl.

ILLUSTRATION IV: Fentanyl Structure



Fentanyl

*Chemistry Education, 2004

With a chemical structure makeup of C_{22}, H_{28}, N_2, and O_1 and a molecular weight of 336.5 (Medline, 2004), fentanyl in its pure form is toxic and therefore must be diluted (Mayo Clinic, 2004). Like morphine and oxycontin it is a controlled substance and is regulated by the Drug Enforcement Administration and can only be prescribed by a physician (Integrated Trials, 2004). Since the 1970's, illegal use of fentanyl has become

more common, because it possesses the same effects as heroin (Mayo Clinic, 2004). When used over a long period of time, individuals have been known to develop a physical dependency to the narcotic and show symptoms of withdrawal if treatment is stopped too quickly (Drugs, 2004). Fentanyl can be delivered to the body intravenously, transdermally, and transmucosally (WebMd, 2004). Its mechanism of action is by interacting with μ-opioid receptors as a pure agonist in the brain and spinal cord which causes a decrease in the feeling of pain. It is most effective in treating moderate to severe acute or chronic pain (WebMd, 2004).

Currently, fentanyl is used intravenously as a sedative prior to surgery, but it can also be administered as a transmucosal "lollipop" or transdermal patch for management of chronic pain (US Drug Enforcement, 2004). Fentanyl nasal spray is another form of delivery being investigated. Both the nasal spray bottle and the transdermal patch were created as an alternative delivery method of pain control that allows for greater subject mobility since there is no intravenous line attachment (Toussaint and Maidl, 2002). Nasal spray bottles allow subjects to self medicate without having to rely on a nurse for administration (US Drug Enforcement, 2004). A randomized double blind study published in the *Canadian Journal of Anesthesia*, involving 48 subjects who were given intranasal fentanyl or PCA pump looked at the efficacy of fentanyl nasal spray compared to the PCA pump in the management of pain (Toussaint and Maidl, 2002). Of the 23 subjects given the fentanyl intranasal sprays, 21 reached subject satisfaction, while 24 of the 25 subjects on PCA pump reached subject satisfaction (Toussaint and Maidl, 2002). This study determined that fentanyl is absorbed just as effectively and quickly in the nose

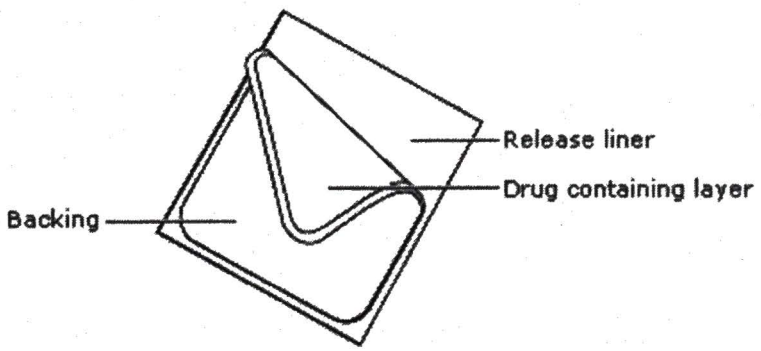
as the current intravenous forms of medication (Toussaint and Maidl, 2002). Subject satisfaction, side effects, pain relief, and speed of onset of the drug were all comparable (US Drug and Enforcement, 2004), leading to the conclusion that the results from the study were promising and will continue to be studied in future clinical trials (Toussaint and Maidl, 2002).

Another alternative to intravenous pain medication is transmucosal fentanyl which resembles a "lollipop" is shaped into a small grape-flavored cone on a stick (WebMd, 2004). The medicine should be placed in the mouth between the cheek and lower gum area and sucked for 15 minutes (Kramer, 2004). Because fentanyl is a lipid soluble opioid, a reaction takes place between the saliva and the lollipop creating a fentanyl solution (Kramer, 2004). Twenty-five percent of the fentanyl solution is absorbed in the mucous glands in the mouth which is then passed into the bloodstream allowing for pain relief within 3-5 minutes. The "lollipop" doses are given in increments of 200 μg starting from 200 μg and continuing upward to1600 μg (WebMd, 2004). The dosage of the transmucosal fentanyl is printed on the cone, the handle of the stick, and on the individual foil package (WebMd, 2004). Fentanyl in the transmucosal form allows subjects to be independent and mobile, although two major drawbacks with this type of fentanyl delivery is that the lollipop shape is attractive to children making them think it is candy. One lollipop contains enough fentanyl to be fatal to a child (Medline Plus, 2004) and this method of fentanyl delivery is not safe for postoperative subjects. It is best used by chronic cancer subjects who need continued extra pain control.

The transdermal patch is a third type of fentanyl delivery system approved by the Food and Drug Administration in 1990 as the first narcotic transdermal system used to control severe pain for a long period of time (Salmon and Lin, 2002). The patch should only be used if the subject is already using morphine or another opioid therapy treatment (WebMd, 2004). A 2003 publication of *Current Medical Research and Opinions*, comparing the fentanyl transdermal patch versus sustained release morphine, supported the theory that the transdermal patch was just as effective as and better tolerated than sustained release of morphine (Van Seventer and Smit, 2003). This study also proved the safety of the patch as none of the subjects in the study developed respiratory depression. The findings showed that 59% of the subjects on the sustained release oral morphine dropped out of the study compared to only 27% of those on the fentanyl transdermal patch (Van Seventer and Smit, 2003). These findings were statistically significant with a $p<0.001$ (Van Seventer and Smit, 2003).

The transdermal patch is in the shape of a rectangle with a transparent unit composed of a protective peel strip and four functional layers (Lehmann and Zech, 1992).

Illustration V: Transdermal Patch



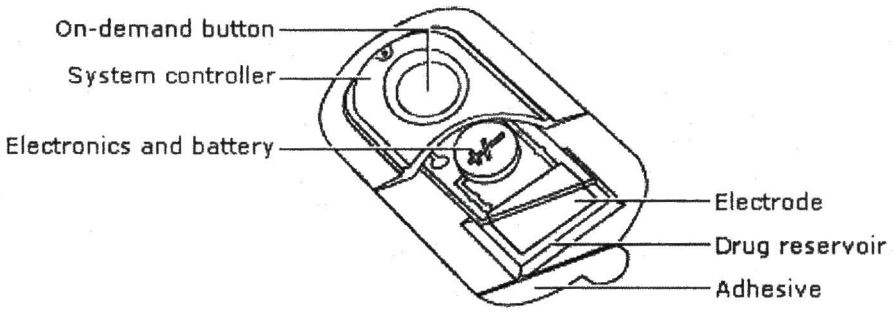
*Alza Corporation, 2003

The patch is applied directly to a flat dry area on either the chest, back, or arm where it can be left for 72 hours to give a continuous dose of fentanyl through the skin (Drugs, 2004). After application, the fentanyl is absorbed through the skin and then diffuses into systemic circulation (Hardwick and King, 1997). Individual patches are available that deliver 25, 50, 75, or 100 μg of fentanyl over one hour and even after their use and removal, the patch can still contain 28% to 84% fentanyl which can be lethal to a 154 lb person (Hardwick and King, 1997). Drawbacks to this delivery method are that it can not be used for acute or postoperative pain, or on children younger than 12 years old and heat may increase the amount of fentanyl released. A physical dependency may also develop if used for long periods of time (Hardwick and King, 1997). Respiratory depression during primary or secondary exposure to the fentanyl is another disadvantage (Chelly and Grass, 2004). The *Southern Medical Journal* in September 1997 reported a case of secondary exposure (Hardwick and King, 1997), when a two-year-old boy was found unresponsive after sleeping in bed with his grandmother. The grandmother's patch found on the boy's back was the cause of his respiratory depression (Hardwick and King, 1997). The grandmother, who had been wearing the patch to help relieve her chronic ovarian cancer pain, transferred the patch to the boy when she gave him a hug the night before (Hardwick and King, 1997). Due to this case and other reports of adverse events, the FDA released warnings regarding the fentanyl patch and relabeled subject instructions (Hardwick and King, 1997). As of April 5, 2004, 75 μg/hour patches were recalled because it was determined that some of these patches may be leaking medication along their edges (Fentanyl Transdermal System, 2004).

Even with all of these various systems of fentanyl delivery, there are still too many disadvantages to make them the perfect method of delivering fentanyl to an individual. The most recent fentanyl delivery method under investigation is the fentanyl patient-controlled transdermal system (PCTS). It has been designed to provide a drug delivery system that could effectively prevent unintentional dosing during use by having the features of a recessed dosing button, double push activation, electronic lockout, and disablement features (Viscusi and Reynolds, 2004). A subject can initiate dosing by pressing the button on the system twice within 3 seconds. This will activate the PCTS and allow for 4μg/minute of fentanyl to be delivered over a 10 minute period for a total dose of 40 μg into the subject's tissue by means of an electrical current (Viscusi and Reynolds, 2004).

Preliminary trials were conducted to determine the correct amount of fentanyl for the study (Chelly and Grass, 2004). A dose ranging clinical trial showed that 20 μg of fentanyl did not adequately control pain, 60 μg controlled pain better, but caused more adverse respiratory effects than the 40 μg doses (Chelly and Grass, 2004). In 2004, the *Anesthesia Analogs* published the results of a phase I clinical trail comparing the (PCTS) to placebo in postoperative pain management at multiple centers. The purpose of the single dose randomized double-blind study was to determine the efficacy and safety of 40 μg fentanyl PCTS in 205 subjects for management of their postoperative pain in the first 24 hours. The PCTS is the size of a credit card and adheres to the skin in the same manner as the transdermal patch.

Illustration VI: Fentanyl PCTS



* Alza Corporation, 2003

The electromechanical assembly (top housing) is made of a molded plastic component that protects the electronics and a printed circuit board assembly (PCBA). This PCBA controls the systems function and contains an integrated circuit, a transducer, a transistor, capacitors, resistors, inductors, a switch, a diode, a lithium battery, and a light emitting diode (LED). Thermal foam plastic with two recessed cavities for hydrogels, one containing a fentanyl hydrogel (the anode), and the other holding a pharmacologically inactive hydrogel (the cathode) comprises the bottom housing assembly. Each cavity also contains an electrode. An adhesive covers the bottom of the lower housing and allows the system to be attached to the patient's skin. (Alza, 2003). Drug delivery begins when the dosing button is pushed twice within 3 seconds (Viscusi and Reynolds, 2004). Pressing the button activates the PCTS which causes an electrical current to flow from the anode to the cathode hydrogel to deliver fentanyl to the skin. The system will beep and flash a red light indicating that a dosing period has begun, which is fixed to not exceed 40 μg of fentanyl over a 10- minute period (Viscusi and Reynolds, 2004). Using a low electrical current instead of an intravenous line the PCTS can deliver a maximum of six 10-minute doses per hour and can operate for 24 hours or release up to

80 doses (Chelly and Grass, 2004). Of the 205 subjects in the fentanyl PCTS and placebo study only 189 were considered valuable for efficacy (Chelly and Grass, 2004). Of these subjects, 25% on the fentanyl PCTS withdrew because of inadequate analgesia compared to the withdrawal of 40% subjects in the placebo group (Chelly and Grass, 2004). The mean global assessment score on the method of pain control judged by subjects and investigators was significantly higher with the 40 μg PCTS subjects than those on placebo. These results showed that 40 μg PCTS was effective and superior to placebo (Chelly and Grass, 2004). The superiority of the 40 μg PCTS was seen by the significantly fewer PCTS subjects withdrawing and a lower final mean pain intensity score. In addition, both subjects and investigators rated greater satisfaction with the PCTS.

A phase II clinical trial was performed after the first study to compare the fentanyl PCTS to the PCA pump. This study was lead by Eugene R. Viscusi, M.D. from Jefferson Medical College of Thomas Jefferson University and published in the 2004 issue of the *Journal of American Medical Association.* Six hundred and thirty six subjects who had undergone major surgery between September 2000 and March 2001 at 33 U.S. Hospitals comprised the study population (Viscusi and Reynolds, 2004). Subjects were randomly assigned to either the PCA pump (n=320) or fentanyl PCTS (n=316) in the post anesthesia care units (Viscusi and Reynolds, 2004). A rating of good or excellent on the subject global assessment of pain at 24 hours was reported by 74% of subjects who received the fentanyl PCTS and 77% who received the PCA pump (Biotech Week, 2004). Eighty percent of the subjects in both groups gave a good or excellent assessment for

their pain management after 48 and 72 hours (Viscusi and Reynolds, 2004). Dr. Viscusi and other researchers concluded that the fentanyl PCTS' effectiveness in pain management during the first 24 hours was equivalent to that of the PCA pump (Viscusi and Reynolds, 2004). As well as being effective in controlling pain, the fentanyl PCTS did not have higher opioid-related adverse events when compared to the morphine (Viscusi and Reynolds, 2004). The most common adverse events related to the study medication included nausea, general itching, vomiting, headache, and erythema at the anode site (Gupta et al, 1999). Currently, the fentanyl PCTS is in phase III clinical trials being evaluated on its safety and efficacy to provide more information to the FDA and sponsor.

Materials and Methods

This study will be testing the safety and efficacy of the fentanyl PCTS in management of postoperative pain in abdominal and pelvic surgery subjects. Subjects are identified in the clinic by the principal investigator or sub-investigators prior to the subject's surgery. The principal investigator will explain the risks and benefits of the study, and if the subject agrees to volunteer, the clinical research coordinator is informed. The research coordinator again reviews all study protocol with the subject, answers all questions, and if the subject meets all the inclusion and exclusion criteria, an informed consent is obtained. Subjects have to meet all specific inclusion and exclusion criteria stated in the protocol before they can be enrolled in the study. Inclusion criteria for a subject enrolling in this study include the following: subjects must be 18 years of age or older, American Society of Anesthesiology physical status I, II, or III, (see Table 1), and

will be admitted to the post anesthesia care unit (PACU) after general, spinal/epidural anesthesia with surgical time of up to 4 hours after non emergent abdominal or pelvic surgery.

Table 1: American Society of Anesthesiologists (ASA)

Physical Status Classification System

PI	A normal healthy patient
PII	A patient with mild systemic disease
PIII	A patient with severe systemic disease
PIV	A patient with severe systemic disease that is a constant threat to life
PV	A moribund patient who is not expected to survive without the operation
PVI	A declared brain-dead patient whose organs are being removed for donor purposes

*American Society of Anesthesiologists. ASA Relative Value Guide. January 21, 2005

Allowable abdominal surgeries include small and large bowel resections with anastomosis, colectomy, enterolysis, sigmoidectomy, closure of enteric fistulae, and repair of cecal or sigmoid volvuls, lower anterior resection, stoma closure, bariatric surgery, liver resection, splenectomy, gastrectomy, and fundoplication. Postoperatively,

subjects must be awake and breathing spontaneously, arousable, able to answer questions, and follow commands for at least 30 minute in the PACU, subjects who have been titrated with class IV opioids and state they are comfortable or report pain is less than or equal to 4 on a scale from 0 (no pain) to 10 (intense pain) for at least 30 minutes, and subjects who are expected to remain hospitalized for at least 24 hours post-operatively. Female subjects must be postmenopausal for at least one year, surgically sterile, or be practicing an effective method of birth control. Subjects must be capable of understanding and cooperating with the requirements of the study, can understand and communicate in English, and must have signed an informed consent document indicating that they understand the purpose and procedure of the study. Exclusion criteria for the study include the following: subjects whose postoperative pain would normally be managed with oral or non-opioid analgesia, receive long acting spinal or epidural anesthesia, receive local anesthetics in the surgical area, have taken steroids within one month prior to surgery, are opioid tolerant, will require additional surgical procedures within 72 hours, have active systemic skin disease, have had more than one previous surgery to the surgical site, subjects who are pregnant, and employees of the investigator or study center. Once these criteria are met, the subject will be provided with education regarding postoperative pain, pain assessments, and goals for pain management. This education information will include the subject watching an instructional video on how to use the fentanyl PCTS as well as receiving Patient Education Bedside material (Ortho-McNeil Clinical Protocol, 2004). After all protocol requirements have been met and informed consent signed, a medical history and physical examination is performed. A

copy of the informed consent will be given to the subject as well as a copy being placed in their source document and medical record chart.

At the time of surgery admission, the clinical research coordinator verifies that the subject still meets the criteria obtained during the screening phase. During this time the subject will fill out a Brief Pain Inventory (Appendix B) which assesses their pain prior to their surgery. Following surgery, subjects must be able to answer commands in the PACU and have a pain score of 4 or less before they are randomized to either the PCA pump or the fentanyl PCTS system. In the first three hours of randomization the subject can receive "rescue" pain medication, either intravenous fentanyl or morphine. After the first three hours, if a subject requires "rescue" pain medication the subject will be withdrawn from the study and will be given the appropriate pain medication. Throughout the study, assessments are taken 30 minutes after application of the PCTS, then every hour for four hours, then every two hours for four hours, and then every four hours for the duration of the study. Vital signs taken during the assessment include the following blood pressure, pulse, temperature, oxygen saturation, respiration rate, and pain intensity rating. Table II indicates the specific assessments required and when they are to be taken to follow study protocol (Ortho-McNeil Clinical Protocol, 2004).

Table II: Time and Events Schedule

Procedure	Screening		Baseline	Period 1		Period 2	Period 3
	PreOp: Up to Day 21	Post Op	Hour 0 Initiation of Study Medication	0-3 Hours	3-24 Hours	24-48 Hours	48-72 Hours or Early Termination
Informed Consent	X						
Inclusion/Exclusion Criteria	X	X		X			
Medical and Medication History	X						
Physical Examination	X						
Pre-operative education	X						
Determination of Pain Management Goal	X						
Provide subject with Patient Beside Education Material	X						
E-Trans & IV PCA Instruction	X		X	X			
Vital Signs	X		X	X	X	X	X
Oxygen Saturation			X	X	X	X	X
Application of Study Medication			X	X	X	X	X
Assessment of Adherence					X	X	X
Brief Pain Inventory	X						
Pregnancy Test	X						
Pain Intensity Rating			X	X	X	X	X
Ramsay Sedation Scale			X	X	X	X	X

Table II (cont.): Time and Events Schedule

Procedure	Screening		Baseline	Period 1		Period 2	Period 3
	PreOp: Up to Day 21	Post Op	Hour 0 Initiation of Study Medication	0-3 Hours	3-24 Hours	24-48 Hours	48-72 Hours or Early Termination
Subject Global Assessment					X	X	X
Subject Ease of Care Questionnaire							X
Investigator/ Surgeon Global Assessment							X
Record Number of On Demand Doses Delivered				X	X	X	X
Non-Routing Checklist				X	X	X	X
Adverse Events		X		X	X	X	X
Concomitant Medication		X		X	X	X	X
Nurse Ease of Care Questionnaire							X

*Ortho Mc-Neil Clinical Protocol, 2004

Throughout the study the subject will also be asked to assess his or her pain based on the 0-10 scale that was discussed during the screening period. If at anytime during the study the subject does not feel that their postoperative pain is being managed, they will be withdrawn from the study and given appropriate pain medication prescribed by their physician. Each fentanyl PCTS will inactivate after 80 doses or 24 hours after the first dose is given and subjects will be given a new PCTS unit every 24 hours while on the study. Subjects randomized to the PCA morphine will receive 1 mg morphine bolus

doses with a lock out period of 5 minutes and up to 10 doses/hour or a maximum of 240 doses/24 hours. A subject may continue in the study for up to 72 hours or until oral medication is taken. At the completion of the study or withdrawal from the study, subjects complete a Subject Ease of Care Questionnaire (Appendix C) and overall Global Assessment Form (Appendix D). The efficacy of the fentanyl PCTS is then assessed by the Subject Global Assessment Method of Pain Questionnaire which the subject answers at the end of each 24 hour period. If the response by the subject is good or excellent the efficacy of the fentanyl PCTS will be defined as a success. The investigator, surgeon and nurse will also be given Ease of Care Questionnaires (Appendix E and F) to complete (Ortho-McNeil Clinical Protocol, 2004).

My internship focus was to analyze the varying barriers and facilitators that affect subject enrollment in the abdominal fentanyl PCTS study. *According to the Annuals of Internal Medicine*, physicians have important roles as advisors and potential referral sources for their subjects who are considering volunteering for clinical research (Chen et al, 2003). The *Journal of Clinical Oncology* recently reported they are finding subjects are becoming more knowledgeable about clinical trials and are more willing to participate (Ellis and Tattersall, 2001). Some of the barriers reported in literature involving subject enrollment include physicians' decisions, logistics factors, attitudinal factors, language, growing complexity of trials, and time lines of studies (Chen et al, 2003). Physicians may be a barrier to accrual of subjects, because they are seen as playing the role of "gatekeeper" meaning that it is the physician who decides whether or not to offer participation in a trial to a subject they are treating (Chen, et al, 2003). A physician

should always emphasize that research participation is optional and that a decision not to participate will not affect the quality of clinical care they will receive (Chen et al, 2003). Finding a subject unsuitable for a clinical trial may include anticipated logistic problems for subjects, concerns regarding long-term survival for elderly subjects, and subject comprehension of trial information (Chen et al, 2003). Logistical factors may be another barrier to accrual of subjects which may include subjects not wanting the burden of taking extra tests or submitting questionnaires and a subject's personal view towards clinical trials. Many times subjects do not want to be "experimented on" or be "guinea pigs" (Chen et al, 2003). According to the *Controlled Clinical Trials Journal,* the study protocol itself may also be a barrier to increase subject enrollment (Penn and Steer, 1990). As clinical trials have become more complex with greater requirements and shorter timelines it has become harder for clinical research coordinators to accrue subjects for enrollment in clinical trials. However some important facilitators of subject enrollment found in the literature, include subject's belief that the trial will be beneficial to them, involvement may result in a potential cure, they will receive extra monitoring from physicians, nurses, and staff, and subjects realize their involvement in clinical trials will benefit future generations (Chen et al, 2003). The internet has become a major facilitator in clinical trials allowing for an increase in subject awareness about new trials and drugs that are being researched making subjects more knowledgeable and wanting to volunteer for trials they believe will benefit them the most (Chen et al, 2003).

At the beginning of my internship, I hypothesized that our site would not meet the enrollment of ten subjects in six months that we had committed to for the abdominal

fentanyl PCTS study. Throughout my internship, the sponsor of the clinical trial, *Ortho-McNeil,* would continually send subject enrollment status reports for both the pelvic and abdominal surgery trial. As of August 24, 2004, only 3 abdominal subjects were enrolled from the 35 sites compared to 98 pelvic subjects for a total enrollment of 101 total subjects. This data showed that the sites that enrolled only pelvic subjects in the study had an easier time than the sites that enrolled lower abdominal surgery subjects. I hypothesized that the low accrual of subjects is protocol related. The study protocol did not allow surgical procedure areas above the umbilicus which eliminated splenectomy, pancreatectomy, and gastrectomy surgeries, thus lowering subject enrollment. Appendectomies were also once totally eliminated because such cases are emergent and not planned. In October 2004, sites were given the opportunity to ask the sponsor for exemptions for potential subjects. For appendectomies to be exempt from the exclusion criteria, the subject undergoing the surgery must be stabilized, coherent, not in great pain, admitted to a hospital room before undergoing surgery the next morning, and must be expected to require a PCA pump for at least 24 hours after surgery to be accepted into the study, subjects have to be alert for at least 30 minutes and have a pain score of 4 or less on a scale from 0-10 (with 0 being the least amount of pain and 10 is the greatest) before they can be randomized to either the fentanyl PCTS or the PCA pump proved to be another limiting factor that makes it difficult to increase subject enrollment following surgery (Ortho Mc-Neil Clinical Protocol, 2004).

Lower abdominal surgeries are invasive, serious procedures, and often times involve removal of a portion of a cancerous organ and can directly affect obtaining

informed consent from a subject due to their concerns about the outcome of their upcoming surgery. An example of subject concern about their surgery affecting study participation and obtaining informed consent involved a man scheduled for a hemicolectomy for a colon mass . After the study protocol was explained to him, he was encouraged to ask any questions and express any concerns. He was told he would be moved to the VIP suite and monitored twenty four hours around the clock by study personnel at which time he agreed to be a volunteer. However, the next day he said he did not want to participate, because it required him being moved to another room and floor for monitoring involving a change in the nursing staff that he had become accustomed to. The clinical research coordinator and I felt that the subject's concern about his cancer and upcoming surgery were the major factors for him not wanting to participate, and not the move to another room.

Sending email reminders to the physicians about the study, posting flyers with a synopsis of the fentanyl PCTS study around the hospital and clinic, actively talking to the physicians and nurses about the study every day, checking the clinic and surgical schedule, and coordinating meetings with the physicians and nurses about the study have positively affected subject enrollment. Prospective subjects for lower abdominal surgeries can be missed if this collaboration is not pursued by the research coordinator.

Informing the subject that dedicated nurses and qualified clinical personnel will stay with them overnight for the duration of the study to check the subject's vital signs is an incentive for the subject's participation in the study. Spending their postoperative time in the hospital VIP suite at no extra charge and receiving a monetary amount for

their participation in the study is another incentive. Since nurses know that there is a monetary incentive, they are actively pursuing prospective qualified subjects for the study which helps to increase subject enrollment.

During a meeting with the sponsor, solutions to increase subject enrollment included reminding subjects they will receive 24 hour continuous nursing care and use of the VIP room at no extra charge. The continued collaboration between the clinical research coordinator, the nurses and physicians, as well as continuing to monitor the surgery schedules has helped to increase the subject enrollment. Hopefully the effort will allow the sponsor to meet its set subject enrollment goal in a timely fashion and allow for the New Drug Application (NDA) documents to be sent to the FDA for review and approval.

Results

During my internship, the clinical research coordinator and I were able to enroll three additional study subjects, mainly due to continued support from the principal investigator and sub-investigators as well as the synopsis flyers given to the nurses as reminders about the study. In November 2004, *Ortho-McNeil,* the sponsor, held a clinical research coordinator workshop to discuss slow subject enrollment in the abdominal surgery portion of the trial. At the meeting, the sponsor informed the coordinators that the pelvic portion of the trial had been closed to enrollment as the projected goal of 250 subjects had been met, but the abdominal portion would remain open to enrollment. The timeline *Ortho-McNeil* presented at the meeting showed their goal of having the last subject randomized to the abdominal fentanyl PCTS trial by

February 2005 and the closeout of the abdominal portion of the trial by May 2005. Since then the sponsor has not met their desired enrollment goal, and the abdominal fentanyl PCTS will remain open. Over the duration of the study, three different amendments have been added to the protocol in hopes of leading to an increase in subject enrollment. Amendment I was added in March 2004 which allowed for volvulus, lower anterior resections, and stoma closures to be allowable procedures (Ortho-McNeil Clinical Protocol, 2004). Amendment II was added on October 2004 which allowed subjects who had surgery performed exclusively with a laparoscopic surgery to participate in the study. At this time these two amendments have not had a huge impact on subject enrollment at the various abdominal sites involved in the study. Recently amendment III was added to include all abdominal surgeries. The title was revised to allow for procedures of both the upper and lower abdomen. This change meant that bariatric surgery, liver resection, splenectomy, gastrectomy, and fundoplication would be allowed and this same amendment also allowed subjects to receive epidural anesthesia as well as general and spinal anesthesia already allowed in the protocol (Ortho-McNeil Clinical Protocol, 2004). Our site has not been able to determine whether these two amendments to the protocol have helped increase subject enrollment due to the closing of the Osteopathic Medical Center of Texas on October 8, 2004, located across from the University of North Texas Health Science Center and was where all of the surgeons practiced. Since all clinical trials in the department of surgery are inpatient, the closing of the Osteopathic Medical Center of Texas has had a negative influence on subject enrollment. Specifically, the abdominal fentanyl PCTS trial has lost up to five eligible subjects. However, efforts have

been made to overcome the closing of the hospital by submitting all surgery study protocols to Plaza Medical Center of Fort Worth's Institutional Review Board (IRB) in mid October. Our site hoped to begin enrolling subjects for the trials by the middle of December.

Ortho-McNeil had a teleconference meeting on January 21, 2005 with all of the participating study sites. Dr. David Hewitt, Director of Analgesic Research, led the meeting which focused on FDA approval, amendment III IRB approval, drug shipment, total subject enrollment, and the study timeline. Since the beginning of the phase III study, the FDA has put even more focus on the data as this will determine whether or not the fentanyl PCTS will be approved. This has led to an expedited process of returning the case report forms and data clarification forms to the sponsor site for a more rigorous review of the data.

The sponsor hoped they would have IRB approval by February 13, 2005 for amendment III from all the sites. Unfortunately since this amendment will have to go through a full board review at both the University of North Texas Health Science Center and Plaza Hospital, the anticipated approval date is March 2005.

Also discussed was returning expired study product and making sure that only the new study product was dispensed and used. Dr. Hewitt made a point to remind all sites to notify *Ortho-McNeil* immediately of any pharmacy on-site failure or skin reactions that occur. The sponsor requests that a digital picture be taken and sent to them to help identify the exact type of skin reactions occurring from the study drug.

As of January 18, 2005, the total subject enrollment for both the pelvic and abdominal surgery subjects was 345 and only 84 of these being abdominal surgery subjects. One hundred sixty six subjects are still needed in the abdominal surgery branch of the study before it can be closed. Dr. Hewitt hopes that all of the sites will continue to work hard and would like for the last subject randomized in the abdominal fentanyl PCTS study by May 30, 2005. As of January 25, 2005 we received final approval for the four study protocols we submitted to Plaza Medical Center of Fort Worth's IRB which will allow for the initiation of surgery trials and recruitment of subjects to begin.

Discussion and Summary

My internship focused on the barriers and facilitators related to subject enrollment in the study and the safety and efficacy of the fentanyl patient-controlled transdermal system. I have been involved in all aspects of attempting to increase subject enrollment at the center in addition to obtaining a thorough understanding of the clinical research activities conducted at a surgical unit. At the close of my internship, the University of North Texas Health Science Center Patient Care Center did not meet the enrollment goal of ten subjects in six months for the fentanyl PCTS due to barriers such as the strict study protocol, subject's concern about their upcoming surgery, and subjects wanting the option to "chose" which drug delivery system they would be randomized to. The subjects that were enrolled during my participation with the study were excited to learn about the fentanyl PCTS in comparison to the PCA pump and often expressed the desire to be randomized to that branch of the study. Their main reason for wanting the fentanyl PCTS was that its application did not require any needles, was small, and not

cumbersome allowing them to move around freely. Of the two subjects that received the fentanyl PCTS, both were happy with the management of their postoperative pain.

The major limitation to the accrual of subjects was due to the closure of the Osteopathic Medical Center of Texas. Prior to the closure of the hospital, the study coordinator and I were able to enroll three study subjects with one being a screen failure of the four subjects enrolled. The department of surgery has submitted all study protocols, investigator brochures, serious adverse events, financial disclosures, 1572 Forms, and all surgeons' resumes and licenses to Plaza Medical Center of Fort Worth's Institutional Review Board (IRB) for expedited review. At the time of the submission of these materials in October, our site was expected to have approval from Plaza's IRB by the second week of November. As of January 25, 2005, the department of surgery has been notified that four of the studies, which include the fentanyl PCTS study, have been reviewed and approved by Plaza's IRB.

CHAPTER III

INTERNSHIP EXPERIENCE

Internship Site

The site where I completed my clinical research internship was located at the University of North Texas Health Science Center Patient Care Center in the Department of Surgery located at 855 Montgomery Street, Fort Worth, Texas. The Department of Surgery treats approximately 1200 subjects a month from the Dallas-Fort Worth metroplex and surrounding areas. There are four general surgeons, one cardio-thoracic surgeon, three vascular surgeons, and one ear, nose, throat (ENT) surgeon who performed the majority of their cases at the two-hundred bed Osteopathic Medical Center of Texas (OMCT) until its closing on October 8, 2004. The department of surgery has been affected more than other departments in the Patient Care Center, due to the fact that all of the surgery studies are inpatient clinical trials. Since closing, the surgeons are now practicing at Plaza Medical Center of Fort Worth, Harris Northwest in Azle, and Baylor All Saints. All of the surgery clinical trial protocols were submitted to the Plaza Medical Center of Fort Worth's Institutional Review Board for approval as all of the surgeons are on staff at that hospital. Plaza Medical Center of Fort Worth was opened in 1974 and is located in the medical district of Fort Worth. It holds three hundred and twenty beds and is investing $57 million dollars into its facility for expansion of research offices and teaching facilities.

The department of surgery is participating in 20 clinical trials to test new drugs and innovative procedures. Studies have included treatment of abdominal abscess, postoperative pain in coronary artery bypass graft (CABG) subjects, postoperative pain in hernia subjects, and several peripheral vascular disease studies. Currently the department has four studies that are open, with three being closed due to the Osteopathic Medical Center of Texas closing and subject enrollment goals being met. All of the studies are multi-center studies and either phase II or phase III studies which focus on the efficacy and safety of the study drugs. Each study has its own specific protocol which specifies the duration of the study, additional tests needed, lab draws, paper case report forms or electronic case report forms, and specific assessments required. For example, the abdominal fentanyl PCTS trial did not require subjects to have labs drawn whereas the postoperative pain in coronary artery bypass graft (CABG) trials did require labs drawn. Many of the surgery trials also differed in whether or not the presence of the clinical research coordinator was required in the operating room. For the fentanyl PCTS study, the clinical research coordinator was not required to be in the operating room, but was required to be present in the post anesthesia care unit. All data related to each study is maintained at the Patient Care Center in the storage room.

Journal Summary

During this internship, I learned the numerous aspects and activities of being involved in clinical research and feel that all of these activities are important in the coordination of clinical trials and essential in maintaining good clinical practice. Some of the activities I was involved in included obtaining informed consent, subject enrollment,

inputting data on the case report forms and verifying and correcting data during the monitoring visits, and change of principal investigators for the fentanyl PCTS.

Obtaining informed consent is the most important process required during clinical trials. According to the *Journal of American Medical Association*, the purpose of the informed consent is to ensure that individuals have control over whether or not they enroll in a clinical research study and that they only participate when the research is consistent with their values, interests, and preferences (Emanuel et al, 2000). In each case, the study was explained to the subject by the principal investigator or subinvestigator during an office visit. For the fentanyl PCTS study, the required informed consent was to be obtained preoperatively during the screening period. At this preoperative visit, the clinical research coordinator reviewed the inclusion and exclusion criteria, the informed consent, and answered any questions the subject might have about the study. After the subject signed and dated the informed consent, the clinical research coordinator signed and dated the informed consent verifying that they were present at the same time the subject gave their consent. After both signatures are obtained, the clinical research coordinator provided a copy for the subject to keep as well as placing a copy in the subject's medical charts and case report form.

For every subject enrolled in this study, the clinical research coordinator and I always met with the subject right before they went into surgery and were with them when they were brought into the post anesthesia care unit (PACU) to assure that the protocol was followed correctly. It was in the PACU, that the clinical research coordinator made sure that the subject was at a pain level of 4 on the scale from 0-10 before they were

allowed to be randomized in the study. After randomization the coordinator was responsible for obtaining the drug delivery system from the pharmacy. If the subject was randomized to the fentanyl PCTS, the coordinator was responsible for opening the pouch the system was stored in, removing the protective clear plastic liner, and applying the sticky side of the system to either the subject's chest or arm. While applying the system, the coordinator made sure to apply pressure to the whole system for 15 seconds, per protocol, to insure appropriate contact to the skin. The pouch the fentanyl PCTS came in is saved as it was used to store the protective plastic liner while the system was being used and then for storage of the fentanyl PCTS after its use. Throughout the subject's time in the PACU and hospital room, the clinical research coordinator and I monitored and recorded all of the subjects' vital signs after the first 30 minutes, every hour for the first four hours, every two hours for the next four hours, and then every four hours until the study was completed or the subject withdrew.

I was actively involved in the process of inputting data into each subject's case report form which included medical history, vitals, adverse events, concomitant medications, surgical medications, technical failure forms, and ease of care questionnaires. After discharge from the hospital, a copy of the subject's medical records was obtained which included medication records, progress notes, nurse's notes, and physicians' orders and were organized into a binder and called the subject's source document. The subject's source document was reviewed and all information required in the subject's case report form would be transferred from the source document. When the study monitor came to visit our site, a review of the data in the case report form was

performed to compare information found in their medical record. After reviewing the case report forms, the monitor would indicate any corrections that needed to be made to the case report form and if any corrections were made, the changes were initialed and dated by the coordinator. Once the case report forms were verified against the medical records and corrections had been made, the monitor would take a copy of the case report form pages and turn them into the data management team at the sponsor site. In January 2005, the clinical research coordinator received data clarification forms (DCF) from the sponsor. These forms asked specific questions corresponding to each subject's case report form that the sponsor was not clear about. Both the coordinator and I reviewed the data clarification form, source document, and case report form before answering the questions stated on the DCF. Once the DCF's had been filled out, signatures from the principal investigator were obtained and the pages faxed back to the sponsor.

Increasing subject enrollment was the major focus of my internship. Throughout my time at the Patient Care Center, I actively reminded both surgeons and nurses about the study twice a week and checked the surgery schedules daily. I also prepared a flyer synopsis on the study and distributed them to the nurses so that they would have a better understanding of the study. I feel that all of these activities would have helped subject enrollment continue to increase if the Osteopathic Hospital had not closed.

Finally, one major activity that I participated in during my internship was the change of principal investigator and the submission of study protocols to the new IRB at Plaza Hospital after the closing of OMCT. Because there was a change in principal investigator, the study monitor had to visit our site to closeout all of the four subjects

under the first principal investigator before transferring the study to the new principal investigator. The changes in principal investigator also led to a new 1572 Form, financial disclosures, and updated resumes and licenses. I was involved in obtaining signatures on the new 1572 Form and financial disclosures from the new principal investigator and subinvestigators of the study. Since the closing of the hospital, I was able to participate in obtaining all the necessary documents needed to submit clinical trials to the Plaza Medical Center's IRB. These documents included obtaining NIH certificates, updated resumes and licenses from all the physicians, 1572 forms, financial disclosure forms, copies of any serious adverse events, and copies of both the investigator brochures and study protocols. The clinical research coordinator also had to meet with Plaza's IRB and answer any lingering questions the hospital had about the study protocols submitted. In addition to submitting all of these materials to Plaza, *Ortho-McNeil*, the study sponsor, also required all of these documents to be submitted to them. These additional documents included the following: DEA 222's from all of the surgeons, the new pharmacist's resume, license, and DEA 223 form, resume of the Plaza lab director and medical directors, Plaza lab normal values, The College of American Pathologists (CAPS) and Clinical Laboratory Improvement Amendments (CLIA) certificates, and approval letters from both the Clinical Trials' IRB located on the university campus and Plaza's IRB before the sponsor would reinitiate the study at Plaza Medical Center of Fort Worth.

I am encouraged about the opportunity for clinical trials to continue with Plaza Medical Center of Fort Worth. New programs will be implemented at Plaza Hospital for

those subjects involved in clinical trials, such as different colored wrist bands as well having different screen color background when their medical records are brought up on the computer screen signifying study participation. As of January 25, 2005, the surgery department has received approval for four of the studies submitted to Plaza Hospital's IRB. A detailed day-to-day description of my activities is attached in the Appendix of this report.

APPENDIX A

DAILY JOURNAL

DAILY JOURNAL

Monday, August 16, 2004

Watched patient informational tape on the fentanyl transdermal patient controlled system

Read over the study protocol involving fentanyl and IV morphine PCA pump

Read study protocol on the DepoMorphine clinical trial

This clinical trial involved studying pain management in patients undergoing hip arthroplasty

Walked over to the Orthopedic Surgery building to deliver paperwork

Listened to the meeting between the site monitor, Dr. Berbel, and Chris

Showed the site monitor the osteopathic medical hospital, pharmacy, medical records, OR, PACU, and recovery rooms

Met all the staff on the 5th floor surgery department in the Patient Care Center

Tuesday, August 17, 2004

Arrived at the Patient Care Center

Went to the OR, with Chris to pick up Mrs. B. blood samples

Went to the lab and centrifuged the blood sample and then went to the RES-building to put them in a -70 degree C freezer

Came back to the Patient Care Center and filled out SAE reports from another site for a closed study

Went back to the hospital OR, and watched a fem-fem pop surgery for Mrs. B.

Followed study protocol; upon release of anastomosis, Dr. Yurvati applied the study drug, either placebo or human thrombin

Had anesthesiologist record the time bleeding stopped

Lunch

Continued work on the SAE reports

Two hours after surgery ended we visited Mrs. B and assessed her condition and obtained more blood samples

Then we took the blood to the lab and centrifuged at 3500 rpm for 10 minutes

We then placed the blood into the freezer

Walked back to the Patient Care Center and worked on the SAE

Wednesday, August 18, 2004

Arrived at the osteopathic hospital

Met Lisa and Raina (nurses) who showed me where to get hospital scrubs and change

Changed into scrubs and went into OR room and watched them prepare the room

Went with nurses to obtain patient Mr. L from the Pre-Op waiting room and into the OR

Watched the anesthesiologist give Mr. L. an epidural

Watched Dr. Buchanan, and residents, Dr. Frano and Dr. Carpenter perform a right inguinal hernia surgery

Came back to the Patient Care Center after watching the surgery

Talked to a prospective patient about participating in the fentanyl study

Said he would like to talk to Dr. DeLange before he made his decision

Went to see Mrs. B. to draw more blood

Copied Mrs. B. chart to be used in her source document

Processed Mrs. B. blood in the lab and then took them to the -70 degree C freezer

Mailed all the samples in the Zymogenetics box packed with dry ice
Put together Mrs. B. CRF document and filled it out using the information found in her source document

Put Mrs. B. information into the electronic CRF form on the computer

Researched the medication Mrs. B was on and found out the diagnosis for giving each medication

Thursday, August 19, 2004

Arrived at the Patient Care Center

Went to the hospital to see if one of Dr. DeLange's patients wanted to enroll in the fentanyl pain study

Patient declined because he did not want to move rooms.
Came back to the Patient Care Center and continued work on the electronic CRF

Went to the Pre-op admissions to visit with Mrs. Mc about participating in the fem-pop study

Went over the inclusion and exclusion criteria, side effects, and the informed consent

Had Mrs. Mc sign the informed consent

Made copies of the informed consent so she could have a copy

Had the nurses draw more blood from Mrs. Mc to be processed in the lab

Went to see Mrs. B and check how she was doing. She only said her back was bothering her but otherwise she felt fine

Lunch

Continued work on the electronic case report form for Mrs. B

Friday, August 20, 2004

Went to the hospital to see if Mrs. Mc had begun surgery

Dr. DeLange was running behind schedule so she had not gone into the OR yet

Worked on the electronic CRF until time to return to the hospital
Returned to the hospital where Chris went into the OR to obtain blood samples

Processed the blood samples in the lab

Went to the 4th floor of the hospital to copy the rest of Mrs. B. records making sure we copied her ER records this time

Took the processed blood to the freezer on the 3rd floor Patient Care Center

Continued and finished work on the SAE reports

Went to the hospital pharmacy to pick up the study drug for the Zymogenetics study

Went to Mrs. Mc surgery and had Dr. DeLange apply the study drug to the anastomosis site

Returned to the Patient Care Center where Dr. Buchanan's surprise baby shower was taking place

Worked with Chris on the Mr. V. fentanyl study CRF using the source document

Corrected the fentanyl study CRF using the monitors correction sheets.

Went back to the hospital two hours after Mrs. Mc's surgery to check on her status in the CCU. Mrs. Mc. seemed to be feeling well

Had Allen (nurse) draw more blood from her so that we could process it

After the blood was drawn, Chris made out an order for a blood draw of Mrs. Mc. on Saturday

We then took the blood and processed it in the lab and brought it over to the 3rd flood Patient Care Center to be frozen until we mailed

Monday, August 23, 2004

Arrived at the Patient Care Center

Met Della that morning and informed her on what I am working on with Chris

Worked on new electronic CRF for Mrs. Mc and finished Mrs. B electronic CRF

Went to the hospital to visit Mrs. Mc and she how she was doing
Mrs. Mc said that she was feeling well and glad that she had her surgery and was ready to go home with her daughter

Copied Mrs. Mc medical records to add to her source document

Came back to the Patient Care Center and continued work on Mrs. Mc. electronic CRF

Tuesday, August 24, 2004

Arrived at Patient Care Center

Called Dr. Bens to set up an appointment with her

Researched literature for my proposal on the computer

Lunch

After lunch, talked to Chris about the fentanyl system and how I would approach writing my outline for my proposal

Went to the library to continue research on the fentanyl system

Wednesday, August 25, 2004

Arrived at Patient Care Center

Met with Dr. Bens and asked her about my outline for my proposal

Came back to the Patient Care Center and read over the study manual for the fentanyl study

Went over the informed consent with Chris to see if there were any items that might be keeping patients from enrolling in the study

Chris informed me about the teleconference meeting that took place yesterday.

Tried to come up with ideas to increase patient enrollment

Went to Ground Rounds with Della and Chris to hear the speaker from Texas Cancer Center

Heard about the new developments in breast cancer

Came back to the Patient Care Center and went with Della to take blood vials to the hospital for the Zymogenetics study patient

Had Olivia, nurse, put the vials on the patient's chart so that blood would be drawn from Mrs. K before she had her surgery

Went to the freezer to get other blood samples out of the freezer and packaged them to be mailed by FedEx

Meet with the nurses in charge of scheduling surgery to see if they had any lower abdominal surgeries coming up

Helped Chris photocopy, staple, and hole punched SAE reports from a closed study so that we could turn them in to the IRB

Asked Dr. Berbel to sign the SAE that he had missed the first time so that we could turn them into the IRB

Continued to read the study manual on the fentanyl study and make notes to add information to my proposal

Thursday, August 26, 2004

Bought a new parking pass

Arrived at the Patient Care Center

Worked on my journal

Went with Xochitl and Della to the pre-surgery room where Mrs. K was getting ready for surgery

Obtained the blood samples and went to the laboratory to process the blood and then placed into the freezer in the 3rd floor EAD building

Came back to the Patient Care Center and filled out CRF reports for the central line infection study

Lunch

Made correction Sheila, monitor, had told us about on the ACL study CRF

Went to the library to research the fentanyl system

Came back to the Patient Care Center and helped Chris file away correspondence from different studies into their appropriate regulatory binders

Friday, August 27, 2004

Arrived at the Patient Care Center

Went with Xochitl to pick up Mrs. K.'s blood and went to the lab to centrifuge

Took the blood to the freezer on the 3rd floor EAD building

Went to visit with Dr. Rudick and meet the new associate dean of the graduate school

Worked on my outline for my research proposal

Helped Xochitl with the CRF for Mrs. K

Lunch

Continued work on the outline for the fentanyl system

Typed SAE reports for a closed study that had to be sent to the IRB

Continued research on fentanyl study for my proposal

Monday, August 30, 2004

Arrived at Patient Care Center

Helped Xochitl with patient narrative for Mrs. B and Mrs. K

Read over journal information on the fentanyl nasal spray and patch

Began writing proposal for my internship practicum

Lunch

Went with Xochitl to pick up Mrs. K. blood and mail the blood by FedEx

Obtain dry ice from the clinical trials building

Meeting with Mrs. G and her husband at the Patient Care Center

Informed her about the study and had her watch the educational video

Had Mrs. G. read over the informed consent and sign it

Talked with Della, Chris, and Xochitl about Mrs. G participating in the study

Called to the hospital to see if the VIP room would be available for Mrs. G

Worked on typing up a patient brochure about the fentanyl study for nurses to give to prospective patients and then if they were interested have them ask the doctor for more information about the study

Tuesday, August 31, 2004

Arrived at Patient Care Center

Talked to Breena about Mrs. G. and asked her what time Mrs. G surgery would be scheduled

Called over to the OR and talked to Kathy about the surgery schedule

Went to the pharmacy to see how the IV morphine PCA pump works

Visited the OR to see if they had posted the start time for Mrs. G's surgery

Lunch

Worked on the source document for Mrs. G

Went into the surgery to watch Dr. Berbel perform Mrs. G.'s surgery

Stayed with Mrs. G when she came into the PACU

Called Chris to let him know that the patient was out of surgery

Called to get Mrs. G randomized

Mrs. G was randomized to the IV PCA morphine pump so we attached that up for her

Took vitals of Mrs. G once she had been moved to the VIP suite

Wednesday, September 1, 2004

Arrived at the Patient Care Center

Copied the SAE report forms for Chris and took them over to the IRB office for Deb to sign them

Went to the hospital to see how Mrs. G was doing

Worked on filling out Mrs. G CRF using her source document

Visited with Mrs. G and took her vitals

Told us she was feeling a little better

Went to Ground Rounds for lunch and listed to the doctor talk about cardiovascular improvements

Went back to the hospital to check on Mrs. G. Told she was having fluttering in her chest

Talked to Dr. Berbel about Mrs. G. and he said to wait a little while and they would have an EKG done

Went to Dr. DeLange's office to have him sign the electronic CRF

Had Dr. Berbel sign the date clarification form

Talked with Mrs. B to she how she was feeling after having surgery

Asked her to come back in two weeks so that we could process her blood again

Opened the FedEx box which contained new lab kits

Arranged them in the laboratory

Look at the SAE from the IRB to see what corrections needed to be made

Went to the hospital to see if Mrs. G was feeling better and take her vitals
Mrs. G. said she was still feeling fluttering in her heart and was worried and wanted to be taken off the study

Talked to Dr. Berbel about Mrs. G. and what she was saying
Dr. Berbel said to take Mrs. G off the study

Went back to the hospital where Della wrote the orders per Dr. Berbel on what medication Mrs. G. was to receive

Took the pump off Mrs. G. and returned it to the pharmacy

Wrote down the models number, serial number, and manufacture's name so that we could add that information to Mrs. G. source document

Thursday, September 2, 2004

Arrived at Patient Care Center

Talked to Chris about Mrs. G and told him that we had taken her off the study

Worked on the Mrs. G. CRF to see what information we still needed to obtain from her medical records

Worked on my journal

Went to the hospital to see how Mrs. G was feeling with her new medication

Copied her medical records

Filled out queries (data clarification forms) for past studies

Left for Colorado

Friday, September 3, 2004

In Colorado

Monday, September 6, 2004

Labor Day

Tuesday, September 7, 2004

Arrived at the Patient Care Center

Worked on my journal

Worked on the CRF form for Mr. V from the bacterium study

Filled out concomitant medications using Mr. V. source document as a reference

Lunch

Continued work on my proposal

Wednesday, September 8, 2004

Arrived at the Patient Care Center

Worked on my journal

Helped Chris file papers

Invited by Dr. Buchanan to watch a right thyroid lobectomy surgery in the OR

Worked on proposal and literature review

Thursday, September 9, 2004

Arrived at the Patient Care Center

Checked with Chris to see if he needed anything to be filled out

Continued work on my proposal and literature search

Lunch

Put together a source document for Mrs. I. which included an informed consent for her to sign if she agreed to the study

Continued work on my proposal

Friday, September 10, 2004

Talked to Dr. Sheedlo about my proposal and medical school applications

Had him go over any corrections or questions he had about my proposal

Made corrections on the reference page so that it would look correctly

Arrived at the Patient Care Center

Worked on putting together Mrs. I. informed consent

Lunch

Visited Mrs. I. in pre-operative admissions

Talked to Mrs. I. about participating in the study and had her watch the educational video and sign the informed consent

Went by the pharmacy to let John, the pharmacist, know that we had a patient having surgery tomorrow that would be on the fentanyl study

Saturday, September 11, 2004

Went to the North Texas Association of Clinical Research Professionals' Meeting held at the University of North Texas Health Science Center

Listened to Phillip Waldron, consumer safety research officer from the FDA, speak about "FDA Bioresearch Monitoring: The facts versus what you think you know."

Took a test to see if we had understood the lecture

Listened to budget amendments and heard about what had taken place at last months meeting

Monday, September 13, 2004

Arrived at Patient Care Center

Called medical records to see if Mrs. G. chart was copied

Worked on my journal

Went to the hospital to see if Mrs. I. surgery was complete

Mrs. I. out of surgery and not quite awake yet
Waited for her to wake up some more

While waiting, worked on Mrs. I. source document using her medical records

Copied her medical records

Made sure Mrs. I.'s pain level was at a 4, before we went to get the fentanyl system from the pharmacy

Put the fentanyl system on Mrs. I. arm and checked her vitals

Continued work on Mrs. I. CRF

Checked Mrs. I.'s vitals which include: respiratory rate, oxygen saturation, heart rate, blood pressure, and pain intensity

Lunch

Went back to the hospital to take Mrs. I.'s vitals

Came back to the Patient Care Center to fill out Mrs. I.'s CRF

Cornelia gave me a prospective patient's work number to call and see if he would be interested in participating in the study

Go back to the hospital and check her vitals

Found her asleep and comfortable

Came back to the Patient Care Center and called Mr. Mc to see is he would be interested in participating in the study

Mr. Mc's work number did not work so called his home number and left a message with his son

Left the Patient Care Center when Chris was paged by Mr. I

Walked back to the Patient Care Center and called Mr. I back

Mr. I did not feel that his wife was getting enough pain relief from the fentanyl system and wanted to be taken out of the study

Walked back to the hospital where Chris took off the fentanyl system and had the nurses order an IV PCA morphine pump

Walked back to the Patient Care Center to obtain the fentanyl system's envelope so that we could put the used fentanyl system in it and returned it to the pharmacy

Left the Patient Care Center to help at a charity event

Tuesday, September 14, 2004

Arrived at the Patient Care Center

Called Mr. Mc at work and discussed the study with him

Mr. Mc said he was interested and agreed to meet with us before his pre-op admission on Friday

Went to get my edited proposal from Dr. Sheedlo and ask him what I needed to correct on my proposal

Talked to Dr. Reeves about medical school applications

Read over the Skypharm protocol for the upcoming IRB meeting

Obtained the patient's randomization number for Xochitl when she called from the hospital

Lunch

Made the necessary corrections on my proposal

Wednesday, September 15, 2004

Arrived at the Patient Care Center

Talked to Mrs. Mc about her legs in the clinic

Obtained more blood from her according to the protocol to close the study

Went to the hospital lab to centrifuge her blood

Went to medical records to see if Mrs. G. medical records were ready

Visited Mrs. I. to see how she was feeling after being taken off the study

Asker her to fill out a end of study questionnaire, but she was too tired from walking so she asked if we could come back

Put the blood into the freezer in EAD

Lunch

Filled out Mrs. B. and Mrs. Mc electronic CRF for their 28th day visit

Printed out their lab results from Meditech

Went back to the hospital to get a copy of Mrs. G. medical records from Brandy

Went to visit Mrs. I. to have her answer the end of study questionnaire

Researched Mrs. G. con meds and put them into her source document

Thursday, September 16, 2004

Arrived at the Patient Care Center

Worked on my journal and proposal

Went over the con medications with Chris to make sure I had written them correctly

Lunch

Started filling out Mrs. G. CRF

Called Mrs. G. to see how she was doing and asked her what date she began taking her antibiotics before the surgery

Went over Mrs. G.'s source document and CRF with Chris to make sure everything was filled out properly and spelled correctly

Compared the source document to the CRF to make sure they were identical

Friday, September 17, 2004

Arrived at the Patient Care Center

Worked on my journal and copied the informed consent and source document papers for Mr. Mc to sign

Went to visit with Dr. Peska about my proposal

Dropped my proposal paper off with Dr. Sheedlo

Went over my proposal with Chris and made necessary changes

Lunch

Continued making corrections on my proposal

Monday, September 20, 20004

Arrived at the Patient Care Center

Worked on my journal and called Dr. Reeves and Dr. Sheedlo to see if they would write me letters of recommendation

Edited my proposal with Chris, then reread it and printed it off

Lunch

Helped Xochitl with Mrs. K. electronic CRF because she had come into the clinical for her 28th day visit

Continued corrections on my proposal

Tuesday, September 21, 2004

Talked to Dr. Reeves about medical school applications, my internship, and letters of recommendation

Went to the Registrar's office to have official transcripts sent to the medical school application service

Walked to the post office to drop off a FedEx envelope for Chris

Went over to the hospital to talk to John, pharmacist, about a new patient that will be on the study.

Went to medical records to ask Candace to copy Mrs. I.'s chart

Lunch

Called Mr. Mc about coming early to his pre-op admissions appointment so that we could discuss the fentanyl study with him and have him sign the informed consent if he wanted to participate

Went to the hospital to pick up Mrs. I. chart from Candace

Worked on Mrs. I.'s CRF and source document

Had Dr. Smith sign the principal investigator end of study documents for both Mrs. G. and Mrs. I

Left to meet with Dr. Kinsey and "shadowed" her at Bluebonnet Pediatric Clinic

Wednesday, September 22, 2004

Visited with Dr. Sheedlo about my proposal and letters of recommendation

Had Dr. Sheedlo look at my proposal over the weekend

Talked to Chris about my conversation with Dr. Sheedlo

Emailed Dr. Bens and asked her if she would look over my proposal

Lunch

Asked Dr. Berbel to sign the surgeon end of study questionnaires for both Mrs. G. and Mrs. I

Filed the signed papers into Mrs. G and Mrs. I.'s source document and CRF

Finished putting together Mrs. I.'s CRF

Went to the registrar's office to fix transcript mistake

Thursday, September 23, 2004

Arrived at the Patient Care Center

Meet with a Sandy, monitor, for site initiation visit for the encapsulated morphine hip pain study

Went to the hospital to check for the missing boxes sent from the sponsor containing CRF worksheets.

Checked with Mr. Davis in central processing to see where he had put the boxes

Continued work on journal

Lunch

Filled correspondence documents with Chris in the storage room and organized a new depomorphine regulatory binder

Organized the fentanyl regulatory study binder with new correspondence from the sponsor

Went to "shadow" Dr. Kinsey at the Bluebonnet Pediatric Clinic

Friday, September 24, 2004

Talked to Dr. Reeves about letter of recommendation

Talked to Chris about what needed to be done while he was gone on trip

Had meeting with Dr. Bens where we went over my proposal and talked about the correction that needed to be added

Lunch

Went home, since Chris had left for his trip

Monday, September 27, 2004

Chris out of town

Tuesday, September 28, 2004

Arrived at Patient Care Center and talked to Chris about meeting with Mrs. G. and having her fill out the end of study patient questionnaire

Went to see Dr. Sheedlo to have him sign my proposal so that I could turn it into the graduate school

Helped Xochitl organize the Abott study binders, label them, and organize them numerically

Visited with Mrs. G. during her clinic visit

Asked her to fill out the end of study patient questionnaire for the fentanyl study she was involved in

Worked on my journal and added corrections to my proposal

Left to go to my medical school interview

Wednesday, September 29, 2004

Arrived at the Patient Care Center

Worked on my journal and proposal

Listened to the teleconference call between Dr. Hewitt from Ortho-McNiel, and the various sites involved in the fentanyl study

Talked about ways to improve patient enrollment in lower abdominal surgeries

Dr. Hewitt mentioned that they would probably allow for total laparoscopic surgeries that are nonemergent to be allowed

Also told that the pelvic study would be closed by the end of October since they were reaching the total patient enrollment needed by the sponsor

Talked to Chris about the teleconference meeting and also told the nurses that we may be allowed to have total laparoscopic surgeries allowed in the study

Lunch

Typed up journal on the computer and showed Chris

Had Chris look over journal entries

Talked to Chris about the prospective patient in the ER

Called the ER to see if Mrs. S. had been admitted

Told she was still in the room and had not been admitted to the hospital

Chris called the hospital to have Dr. Cole paged so we could see when Mrs. S. was going to have surgery

Left to go to the airport

Thursday, September 30, 2004

Arrived at the Patient Care Center

Talked to Chris about Mrs. S

Chris said that he had talked to Mrs. S. about the study last night and that she was interested, but we have to wait until we find out when she is having surgery and then we will talk to her about signing the informed consent

Went to see if Melva knew when Mrs. S.'s surgery would be, but she was on vacation

Chris said Dr. Fikkert said that they had not scheduled Mrs. S.'s surgery yet, but would probably be tomorrow

Worked on typing up my journal on the computer

Lunch

Continued typing up my journal

Went to see the associate dean of the graduate school and have him sign my proposal so that I could turn it in to the graduate school

Went to the hospital to see if Mrs. S.'s surgery had been scheduled yet

Talked to her about the study and showed her both the fentanyl patient-controlled system and the IV PCA morphine pump

Had Mrs. S. sign the informed consent

Made a copy of the informed consent for Mrs. S.'s records

Friday, October 1, 2004

Arrived at the Patient Care Center

Worked on typing up my journal

Went to the hospital to visit Mrs. S. and see how she was feeling and if there had been a decision as to what surgery would be performed

Talked to Dr. Buchanan about a prospective patient for the pain study that he had seen earlier in the day

Walked back to the Patient Care Center and continued work on my journal

Called over to the hospital to see if the residents knew anything about Mrs. S.'s surgery

Found out Mrs. S. would be having procedures done by Dr. Hey, urologist, and Dr. Fikkert, surgeon, later this afternoon

Chris left his pager number with the residents so that they could page him if the physicians need to perform a lower abdominal surgery on Mrs. S. later today

Monday, October 4, 2004

Arrived at the Patient Care Center

Talked with Chris about Mrs. S.'s prognosis and if anything had happened over the weekend

Chris said that he needed to call over to medical records to have past patient's medical records pulled so that Rachel, monitor, could look over them when she came to review the pain study CRF's

Went to the hospital and found out the Mrs. S. would be having a lower abdominal surgery sometime tomorrow

Continued typing my journal and working on secondary medical school applications

Called over to medical records to have patient's charts pulled so that Rachel, monitor, could look over them while checking the CRF's

Lunch

Went back to the hospital to see if Mrs. S was in her room after having x-rays earlier in the day, but she had not returned

Checked her medical records to see if the physicians had written any new orders

Came back to the Patient Care Center and used the typewriter to fill out the blind study questionnaire from the one Chris had filled out

Went back to visit Mrs. S. and see how she was feeling

Found out the physicians were just going to let the fistula heal on its own and not perform surgery on Mrs. S. until later

Waited for Dr. Buchanan to return from surgery so that I could meet with him and talk about medical school

Tuesday, October 5, 2004

Arrived at Patient Care Center

Worked on typing up journal
Met with Rachel, monitor, and took her over to medical records in the hospital

Reviewed practicum guide guidelines that Chris had received from his meeting with Dr. Bens and other on-site mentors

Went over to the hospital to make corrections on the CRF Rachel had checked

Lunch and presentation at Baylor All Saints Hospital
Presentation given by Lynn Palmer about adverse event reporting

Came back to the Patient Care Center and continued reviewing the practicum review guidelines for my thesis

Returned to the hospital to make corrections on the other two CRF's that Rachel had corrected

Brought back the CRF's, source documents, and extra forms to put into Chris's office

Wednesday, October 6, 2004

Arrived at the Patient Care Center

Talked to Chris about the corrections Rachel, monitor, had made yesterday on the CRF's

Corrected both source documents and CRF's with the extra corrections Rachel had left for us to complete

Documented reasons why ephedrine and benadryl had been given to a couple of our patients and had Dr. Berbel sign the letter

Made a binder for Kendle/Adolor correspondence and filled away the incoming letters in Chris's office

Went to Ground Rounds to hear about new legislative procedures.

Had Chris review the SAE reports I had typed earlier and had him correct them

Retyped the SAE reports and had Dr. Berbel sign them

Made copies of the SAE reports and put the copies into the SAE report binder and sent the originals to the IRB office
Called the medical school application service to see if they had received my completed application

Thursday, October 7, 2004

Arrived at Patient Care Center

Talked to Chris about the items that we would work on today

Chris talked to me about the Ortho-McNeil meeting in Florida and what I needed to write on the registration form

Walked to medical records with Xochitl and obtained medical charts for patient's involved in the Zymogenetics study

Copied the missing documents needed to fill out the source documents

Walked to Dr. Aschenbrenner's office and Dr. Sheedlo's office to talk to them about my internship and medical school applications

Returned to the Patient Care Center and typed SAE documents

Filled SAE documents into the Wyeth study binder and had the original documents sent to the IRB to be signed

Lunch

Met with Della and Chris about what needed to be done if the hospital closes

Friday, October 8, 2004

Talked to Chris about OMCT (Osteopathic Medical Center) closing and what we would do with the studies since the hospital is closing

Typed old SAE forms and typed new SAE forms for the Tigecycline study

Met with Della, Chris, and Xochitl to make a list of the items that needed to be done since the hospital is closed

Per Chris and Della and we are unable to continue some of the clinical trials at this time, but that Wendy in the IRB office is going to submit the studies for approval to Plaza Medical Hospital where all of the surgeons have staff privileges

Chris called and emailed monitors about OMCT closing and asked what needed to be done about shipping the drugs back

Walked to the clinical trials office and met with Wendy to see what the progress was with the IRB at Plaza

Dr. Clearfield told us he had talked to Dr. Buchanan about the clinical trials and that he would help us in any way with getting the studies over to Plaza Hospital

Met with Dr. Buchanan and the surgery department to discuss the hospital closing and what needed to be done at the clinic

Finished typing SAE forms and filled them in the Wyeth binder

Monday, October 11, 2004

Arrived at Patient Care Center

Talked to Chris about my flight reservation

Chris informed me that Larry would be here to closeout the study and pick up the drugs

Larry and Chris walked over to the OMCT

Went with Xochitl to the hospital rehab center

Talked to Ted, the pharmacist, to find out how long the pharmacy would stay open

Helped Xochitl with the electronic case report form for Mrs. L. and entered the necessary data

Larry, the microbiologist, brought study binders from the hospital lab for us to put in the storage room in the patient care center

Lunch

Worked on my journal and medical school application

Drove to Fort Worth Dialysis Center and obtained Mrs. O.'s 28th day blood sample

Came back to the Patient Care Center and centrifuged the blood
Called Maureen to about the Ortho-McNeil meeting and to see if she had received my fax

Faxed my registration form to Maureen again

Opened the centrifuge and pipetted out the correct amount of sample into research vials to be sent to Zymogenetics

Sent other samples to Quest Diagnostics to have labs done on Mrs. O.

Tuesday, October 12, 2004

Arrived at Patient Care Center

Talked to Dr. Aschenbrenner from 9:30-11:00 about medical school letters of recommendation

Went to the lab with Xochitl and Chris to count the number of Zymogenetics boxes left in storage that could be used to ship back the placebo and thrombin

Lunch

Went to the pharmacy to obtain papers from John to fill out the shipping form for shipping back the fentanyl

Had John fill out the DEA 222 form to be submitted to the sponsor verifying the shipping of the fentanyl from OMCT to the pharmaceutical company

Obtained a box from John to ship back the thrombin and placebo

Returned to the Patient Care Center and faxed the 15 shipping documents to Rachel

Went back to the hospital to wrap the thrombin in bubble wrap and zip lock bags and placed in the shipping box

Brought the box back to the Patient Care Center third floor to obtain ice packs to keep the drug cold during the shipment process

Taped up the box and filled out the form for FedEx to pickup

Went to the EAD to obtain Mrs. O.'s blood sample to be mailed

Shipped Mrs. O.'s blood sample and called FedEx for a pickup

Wednesday, October 13, 2004

Arrived at school and took Dr. Aschenbrenner my personal statement

Came to the Patient Care Center and asked Chris if he had heard anything from Wendy

Checked American Airlines to see if my flight was scheduled for the meeting

Chris talked to Rachel about the documents we faxed her about the pain study and that we had shipped the drug back to the pharmaceutical company

Went to the pharmacy to pick up the last 16 thrombin vials, study binders, and corrected the fentanyl accountability log

Came back to the Patient Care Center to look for a box to mail the thrombin vials

Walked to the FedEx store to pick a box to mail the vials

Packaged and weighed the FedEx box and called them to schedule a pick up

Checked email to see what Wendy had said about the IRB meeting

Per Wendy's instructions we photocopied all of the investigator brochures and protocols for the studies and sent them to Wendy

Had a meeting with Dr. Buchanan about medical school

Thursday, October 14, 2004

Arrived at Patient Care Center

Talked to Chris about the status of the IRB and implementation of the studies at Plaza

Received SAE reports from other sites for the Zymogenetics study over the fax

Typed out SAE forms for the Zymogenetics study

Had Chris check the SAE forms we had typed and make any necessary corrections

Had Dr. DeLange sign the typed SAE forms, make copies of the reports and the SAE forms, and mailed them to the IRB office

Went to the hospital to drop off employment information to Larry, the microbiologist, and picked up the box supplies for the Covance study

Went to the administration department in the hospital to have them put a label on the Covance box should that we could leave the hospital with the box

Worked on medical school applications

Friday, October 15, 2004

Arrived at the Patient Care Center

Worked on electronic case report form for Mrs. O.

Worked on typing up journal

Left at 11:30

Saturday, October 16, 2004

Arrived at the Texas Scottish Rite Hospital in Dallas for the North Texas Association of Clinical Research Professionals Meeting

Attended the conferences (8:00-3:00) given by Michael Smit of the FDA and Tamara Norton of Norton Auditing, Inc.

Discussed various protocol violations and compliance issues in clinical trials

Monday, October 18, 2004

Arrived at Patient Care Center

Met with Chris and discussed the corrections needed to made on the SAE forms the IRB had sent back

Told that the studies should be started at Plaza by the end of October

Walked over to the medical records department in OMCT to have the charts pulled fro Cynthia to review for the Zymogenetics study

Came back to the Patient Care Center and talked to Della about what had happened with OMCT and the studies while she had been gone last week

Continued to type up my journal

Lunch

Helped Sheila and Chris, store the medication for two of the clinical trials in the cabinet

Continued typing up journal on the computer

Helped Chris type up the SAE forms from Deb in the IRB office

Tuesday, October 19, 2004

Arrived at the Patient Care Center

Updated my journal

Talked to Chris about the correction made to the SAE 307 forms

Retyped SAE forms with the edited corrections Chris had mad on the forms

Made copies of the SAE forms and filed the copies into the 307 binder

Paper clipped the original 307 SAE forms so that Dr. Berbel could sign them on Monday

Lunch

Worked on corrections for the electronic case report form for 499C07 and 499C08 all afternoon

Met with Dr. Aschenbrenner in his office and discussed medical school options

Wednesday, October 20, 2004

Arrived at the Patient Care Center

Corrected 499C08 SAE form and then copied and sent back to Deb in the IRB office

Walked to clinical trials to drop off the SAE forms to DEB

Picked up SAE 307 forms that had been approved by the IRB board

Filled the Wyeth 307 SAE forms in the regulatory binder

Organized the Wyeth 307 binder to find out which SAE are missing IRB signatures.

Pulled out the missing IRB signature pages and numerically ordered them for Chris

Lunch

Went with Chris to drop off the SAE forms to Deb

Talked to Wendy to ask her how the study submission at Plaza Medical Center was going

Came back to the Patient Care Center and worked on my medical school essays

Looked for sponsor letters in the 307 binder to type SAE forms from other sites

Made copies of the sponsor letters and clipped them to the old SAE forms for Chris to review and edit

Thursday, October 21, 2004

Arrived at the Patient Care Center

Updated journal and checked email

Talked to Chris about the corrections made to the SAE forms

Retyped the SAE forms with the edited corrections Chris had made on them

Made copies of the SAE forms and filled the copies into the 307 binder

Paper clipped the original copies together so that Dr. Berbel could sign them on Monday

Lunch

Worked on corrections for the electronic case report form for the 499C07 and 499C08 all afternoon.

Met with Dr. Ashenbrenner in his office and discussed medical school options

Friday, October 22, 2004

Not here today, due to Chris and Della being in Florida for a Investigator's Meeting

Monday, October 25, 2004

Arrived at the Patient Care Center

Updated journal

Discussed with Chris about the investigator's meeting in Florida

Obtained physicians signatures for Form 1572 and Financial Disclosure forms from Dr. Buchanan, Dr. Martin, and Dr. Orr

Lunch

Obtained signatures from Dr. Yurvati

Met with Chris and Della to discuss the status of the trials at Plaza Medical Center

Gave Della the signed forms that the physicians had signed

Tuesday, October 26, 2004

Arrived at the Patient Care Center

Updated journal on the computer

Met with Chris to discuss the situation at Plaza and the progress of the IRB meeting

Lunch

Went to the Fireside Lodge Nursing Home to visit Mrs. L.

Obtained blood samples from Mrs. L. for the 28th day visit for the Zymogenetics study

Came back to the Patient Care Center to centrifuge Mrs. L.'s blood

Received the fax from Ortho-McNeil about my flight to the coordinator's meeting

Continued typing up my journal on the computer

Wednesday, October 27, 2004

Arrived at the Patient Care Center

Walked over to the EAD building to pick up Mrs. L. blood samples

Returned to the Patient Care Center to drop the blood to Quest Diagnostics on the 1st floor

Packaged frozen samples for shipping

Called Maureen to confirm the meeting in Orlando

Ground Rounds (12-1)

Worked on medical reports

Thursday, October 28, 2004

Met with Caroline from Adolar to discuss the site and protocol for the study

Asked Dr. Yurvati to go over the pre-op procedures at Plaza

Went to the Plaza Hospital to show Caroline the pharmacy, medical records, and the pre-op room

Met with Mirza Baig, RPh. in the pharmacy and discussed where the drugs would be stored

Returned to the Patient Care Center and turned in the financial disclosures to Chris

Worked on journal

Friday, October 29, 2004

Arrived at the Patient Care Center

Worked on my journal on the computer and medical school applications

Called Sharon to confirm the FedEx package would be delivered

Lunch with Xochitl

Met with Chris to discuss the fentanyl PCTS exclusion and inclusion criteria

Came up with new ideas to increase patient enrollment

Went over the study protocol and any other questions that would be asked at the study coordinator meeting

November 1-3, 2004

Worked on medical school applications and shadowed Dr. Kinsey due to Chris being out of town

Thursday, November 4, 2004

Arrived at Miami, Florida

Went to the study coordinator registration desk

Talked to Marilyn and Sharon about registering and obtaining a packet of information

Attended the coordinator dinner and met with various people from Ortho-McNeil, Pharmanet, and Quality Review Associates

Friday, November 5, 2004

Attended a coordinator breakfast

Attended the coordinator meeting at the Royal Palm Ballroom

Learned about Data Clarification Forms, regulatory audits, and editing CRF

Watched a video about audits and heard the presentation from Omega with Johnson and Johnson Pharmaceutical

Went over the closing dates for the lower abdominal study and how queries would be sent via email or by fax

Participated in workshops to learn how to correctly fill out CRF forms and how to adequately and completely fill out data clarification forms

End of meeting

Monday, November 8, 2004

Arrived at Patient Care Center

Talked with Della and Chris about what had gone on during the week

Gave Della and Chris the documents Dr. Buchanan had received from FedEx for the new thrombin study

Worked on my journal and updated it with the information I had gained from the trip to Miami

Discussed with Chris about the meeting in Florida and the new changes to the CRF and how to accurately incorporate the data in the forms

Reviewed data clarification forms and how to properly fill them out

Lunch

Made copies of the Wyeth 307 SAE reports after Dr. Berbel had signed them

Put the copies of the SAE reports in the Wyeth 307 binder

Sent the original SAE reports to Deb in clinical trials

Continued work on the medical school applications

Went to thank Dr. Phillips and give him the CT scans

Tuesday, November 9, 2004

Arrived at the Patient Care Center

Discussed with Chris about the IRB meeting at Plaza tomorrow at 12:00

Continued work on my medical school applications

Moved belongings to another area to work at a new station on the surgery floor

Met with Dr. Phillips to discuss the CT scan

Lunch

Rearranged equipment at new cubicle desk

Gave Della the screening log for the Rh thrombin study

Talked to Dr. Buchanan about having a work order placed to have the computer set up as well as the cabinet moved behind the desk

Continued work on my journal and applications

Talked to Chris about the Plaza IRB meeting

Wednesday, November 10, 2004

Arrived at the Patient Care Center

Worked on medical schools applications most of the morning

Discussed with Chris and Della about the IRB meeting they had had yesterday and asked if there had been any resolution

Tried putting the computer together at the new desk, but the keyboard did not work so Pam put in a work order to have the technology people fix it

Continued work on journal and medical school applications using Tonya's computer

Lunch

Helped Della organize the Zymogenetics materials that had to be moved from the old desk since Tonya was sitting there

Left the Patient Care Center to talk to Dr. Reeves about letters of recommendation

Thursday, November 11, 2004

Arrived at the Patient Care Center

Worked on updating my journal

Met with Chris and Della to listen to the teleconference about the DVT study

Read over the new study data that pharmanet had faxed over about the 370 study

The data showed the enrollment at various sites and the need for more patients to be enrolled for the lower abdominal portion of the study

Photocopied the data of the patient enrollment

Called Jennifer at Pharmanet to ask her to change the fax number to Chris's correct fax number

Lunch

Typed up SAE reports for the Wyeth 307 study

Matched the incoming IRB SAE reports with those already filled out in the Regulatory binder

Found that some were missing from the binder that we had sent to the IRB

Walked over with Chris to Clinical Trials to see if Deb was in her office to ask her about the missing IRB papers

Deb was not in the office so I returned to the Patient Care Center

Filled out the 22-96 SAE reports in the 301 Regulatory binder

Talked with Chris about Rachel's upcoming monitoring visit next week and talked about what needed to be done so that she could closeout the site since OMCT closed.

Left the Patient Care Center and went to talk to Dr. Ashchenbrenner and Dr. Sheedlo

Gave Dr. Ashchenbrenner the letters of recommendation to fill out

Friday, November 12, 2004

Arrived at the Patient Care Center

Updated journal in the notebook

Went over to Clinical Trials to see if Wendy was in her office

Per Sharon, Wendy was not feeling well, so we asked Sharon if we could look at the IRB reports since we were missing some copies to match the ones we had in the Wyeth 307 and 301 regulatory binders

Made copies of the missing SAE forms from the IRB binder so that we could have a copy to put in the regulatory binders

Came back to the Patient Care Center and filled out the appropriate papers in the binder so that each one had a copy of the IRB forms for each study (Wyeth 307 and 301)

Monday, November 15, 2004

Arrived at the Patient Care Center

Talked to Chris about my computer being set up

Chris called over to James in the technology office so that he could come set up my computer password

James helped me set up my computer password so that I could log into the computer

Began typing up my journal on the computer so that I could add it to the end of my thesis

Talked with Chris about Rachel's upcoming visit and asked him what we needed to have ready for her to look at when she arrived

Continued work on medical school applications the throughout the rest of the morning

Lunch

Discussed the status of the studies with Chris and asked him when he thought we would be able to initiate them

Continued to work on medical school applications

Tuesday, November 16, 2004

Arrived at Patient Care Center

Worked on medical school application on Excel

Went over to clinical trials to pick up the approved SAE forms from Deb

Helped Chris empty out the office next to Dr. Buchanan so that the monitor from the clinical trial studies would have a place to work

Moved the computer and speakers to the storage room

Lunch with Xochitl

Continued work on medical school applications

Organized the office for Rachel to work in when she came tomorrow

Filled the SAE reports in the regulatory binders for the 301 and 307 study and put them in the storage room

Wednesday, November 17, 2004

Arrived at Patient Care Center

Talked to Chris to see when Rachel would be arriving that morning

Rachel arrived and we informed her about the status of the studies with the Plaza hospital and answered the questions she had about the closing of the Osteopathic Medical Center

Dr. Yurvati came by and met with Rachel to introduce himself as the new Director of Clinical Trials

Took Rachel over to the OMCT so that she could review the patient's medical records and the CRF's

Made corrections on the CRF, which included changing the medication dosage to one time dose, or ongoing, changed the dates and made sure the source documents were in order

Walked Rachel back over to the Patient Care Center and then to Milano's for lunch

Returned to the Patient Care Center where Rachel continued to monitor the patient's CRF's, regulatory binder, pharmacy binder, and source documents

Made copies of the papers from the binders that Rachel needed to take back to Pharmanet

Made additional corrections on the CRF's

Made copies of the physician's new licenses to put in the regulatory binder

Had Cornelia fill out the nurse's end of study questionnaire

Had the physicians involved in the study also fill out the physician delegation log

Went over to Plaza so that Rachel could meet with Christine, administrative assistant

After meeting with Christine, we took Rachel to the pharmacy to meet Mirza Mirza showed us where each of the drugs would be stored

Talked to Mirza about obtaining a copy of his DEA 223, license, and CV and told him that we would be having a site initiation visit soon

Went to visit the surgery holding area where the patients are kept before entering the operating room for surgery

Took Rachel to visit the area where the medical records are kept

Left Plaza and returned to the Patient Care Center

Rachel continued to review the CRF and binders

Thursday, November 18, 2004

Arrived at the Patient Care Center

Made the needed corrections on the CRF that Rachel wanted us to change

Typed up a Note to File to explain that the OMCT had closed and that the final location of the medical charts was not known

Typed up another Note to File to discuss the change of Principal Investigator from Dr. Smith to Dr. Berbel

Typed up a Note to File to clarify that benadryl was not given to our study patients because of an adverse event, but that bendaryl is given as the standard of care in the PACU to prevent itching from fentanyl and morphine

Filled correspondence from Rachel, Pharmanet, and Ortho-McNeil in the regulatory binder

Dr. Smith came to the Patient Care Center to sign off on the patient's CRF's that had been in the study while he was the principal investigator

Talked to Dr. Berbel about meeting with Rachel to discuss him becoming the new Principal Investigator

Went over to clinical trials to talk with Wendy about having a new informed consent made up with Dr. Berbel as the Principal Investigator as well as new financial disclosures made up

Returned to the Patient Care Center, where Rachel finished reviewing all the patient's CRF and pulled the copies she needed to take with her to pharmanet

Had a meeting with Rachel and Chris at the end of visit to discuss what needed to be done after she left and what she needed us to mail to her

Friday, November 19, 2004

Arrived at the Patient Care Center

Talked to Chris about what we needed to obtain from the physicians

Talked to Dr. Berbel and asked him which sub investigators he wanted to include on the study

Also asked him for a revised copy of his CV with the listing of the hospitals he is affiliated with

Asked Dr. Martin, Peska, Buchanan, Fikkert, Delange, Knust, and Smith to update their CV

Went over to Clinical Trials to pick up the revised 1572 and financial disclosure from Wendy

Had Dr. Berbel sign the 1572 and Dr. Buchanan, Dr. Fikkert, Dr. Martin, Dr. DeLange sign the financial disclosures

Talked to the physicians about taking the NIH test, that Plaza was requesting

Obtained resumes from Dr. Berbel, Dr. Yurvati, Dr. Fikkert, Dr. Martin, Dr. Knust, Dr. DeLange, and Dr. Peska and made multiple copies and filled them in the filling cabinet

Monday, November 22, 2004

Arrived at the Patient Care Center

Walked over to clinical trials to remind Wendy to change and print out a new informed consent

Talked to her about what paperwork we needed to have to give to the IRB to let them know that there would be a principal investigator change

Drove to Dr. Smith's office to drop off financial disclosures for him to sign and fill out

Talked to Mrs. Smith about having Dr. Smith try to update his CV so that we could send a copy to Rachel

Took a tour of the new office building and exam rooms

Lunch

Made copies of the NIH certificates after the surgeons had completed their test

Put the NIH certificates into a folder for Wendy to take over to Christine at Plaza

Called Mirza at Plaza to see if he had put together a packet with his license, CV, and DEA 223.

Told us he would meet with us on Tuesday

Tuesday, November 23, 2004

Arrived at the Patient Care Center

Talked to Chris about taking the fentanyl PCTS and tape over to Plaza so that Mirza could look at it

Drove to Plaza and went to see Mirza in the pharmacy

Obtained Mirza's license, CV, and DEA 223

Talked to Mirza about the studies and showed him how the fentanyl PCTS worked on the patients

Went to the microbiology lab and met with the director of the laboratory, Jo-Anne

Went on a tour of the microbiology lab and was told per Jo-Anne, that since the closing of the OMCT, the histology lab went up 40% in workload

Obtained the CV of the medical director of the lab, Richard Hare

Drove to Dr. Smith's office to pick up the packet of signed papers and talked to him about being a sub investigator, and updating his CV

Returned to the Patient Care Center and had the surgeons sign their financial disclosures

Lunch

Went to Wendy's office to ask her about emailing Rachel to explain to Rachel, that it was not a closeout of the site but a change in principal investigators

Returned to the Patient Care Center and faxed Wendy a copy of Mirza's CV, license, and DEA 223.

Put all of the surgeons' licenses in a packet for Rachel

Wednesday-Friday, November 24-26, 2004

Thanksgiving Break

Monday, November 29, 2004

Arrived at the Patient Care Center

Updated my journal in the spiral and on the computer

Asked Chris if he had given Wendy the packet of financial disclosures last Wednesday

Helped Xochitl make copies of the licenses and CV of the surgeons for the internal audit for the Zymogenetics study

Lunch

Punched holes in the SAE reports and filled them in the Wyeth 307 binder in the storage room

Obtained a copy of Dr. Martin's updated license from Lynda so that we could send it to Monica with Adolar

Called the Plaza pharmacy to ask them their address, fax number, and telephone number

Talked to Mirza and asked him to update his CV so that it would include Plaza Hospital

Told him that we would come by his office tomorrow morning and pick it

Chris called over to Dr. Smith's office to see if he had his CV ready for us to pick up

Mrs. S. emailed the updated CV to Chris and we made copies of the CV

Called the pharmacy to determine which person was the lab director at the Plaza pharmacy

Emailed Rachel to ask her what we needed to send to her in the UPS mailer she left with us

Tuesday, November 30, 2004

Arrived at the Patient Care Center

Worked on organizing the filling cabinets with the surgeons CV and licenses

Took the NIH test on the computer for most of the morning

Went over to Plaza to have Mirza update his CV

Talked to Christine about the status of the studies and asked when we would receive approval letters

Lunch

Enclosed the resumes in the UPS mailer along with the surgeon's licenses and mailed to Rachel

Had Dr. Buchanan sign the investigator agreement for SkyPharma study

Asked him if he knew of any orthopedic surgeons that had privileges over at Plaza

Also talked to him if he knew of the anesthesiologists over at Plaza

Gave us the phone number of Dr. Clark and Dr. Million to talk to them about the protocol.

Wednesday, December 1, 2004

Arrived at the Patient Care Center

Worked on SAE Reports for the Wyeth 301 study. Put them into the regulatory binder

Printed out Zymogenetics protocol for Della

Also printed out the amendment for the upcoming internal audit

Went back to Plaza to pick up the corrected resume form Mirza

Lunch

Worked on updating my journal on the computer

Researched the PCA pump to use in my paper

Put together a file for the Theravance skin protocol and filed the appropriate documents

Had the documents add the new principal investigator and subinvestigator to the forms and had them sign

Faxed the forms to Dawn Kerlin

Went to Dr. Hahn's office to have him sign the contract, but were told we need to drop it off at the legal department first

Went to Wendy's office to drop of the contract so that it could be taken to the legal department

Thursday, December 2, 2004

Arrived at the Patient Care center

Went to the EAD building to listen to Xochitl's defense

Listened to her internship experience and Zymogenetics study

Came back to the Patient Care Center and talked to Chris about what needed to be added to my paper so that I could start working on my thesis
Helped Chris fill out the study information page for Adolor

Reprinted the study information page before faxing it back to the company

Lunch

Began working on my paper and researched information about fentanyl and the PCA pump

Went to Wendy's to see what else needed to be done and what we needed to do to complete the study for an initiation visit

Chris told me that Adolor would be coming for a site initiation visit on the 13th

Continued work on thesis paper for the rest of the afternoon

Friday, December 3, 2004

Arrived at the Patient Care Center

Talked to Chris about the blinding plan for Covance

Discussed what needed to be filled out on the blinding plan

Chris filled out the blinding plan in pencil and then I rewrote what he wrote in pen on a new piece of paper

Asked Dr. Berbel to sign the blinding plan

Made a copy of the blinding plan

Returned to the Patient Care Center and faxed the copy of the plan to Covance

Lunch

Called over to Plaza laboratory to talk to Jo-Anne

Asked Jo-Anne if we could obtain lab normals from her for WBC, RBC, et. so that we could send them to Monica Nations

Lunch

Received fax from Jo-Anne Beveridge, but the lab normals were not coming out clearly so we called her and told her we would come over to Plaza to pick up the lab normals

Monday, December 6, 2004

Arrived at the Patient Care Center

Asked Chris if Monica had received the information we had sent her. Per Chris he said that she had received the documents but also needed us to send her the CAPS and CLIA certificates

Went over to the Plaza laboratory to talk to Jo-Anne and obtained the lab normals from her and had her sign her resume, also obtained copies of the CAPS and CLIA forms

Returned to the Patient Care Center and talked with Dr. Berbel about medical schools

Lunch

Discussed with Chris what physicians we needed to talk to about getting their DEA 222 forms

Went to the post office to mail the documents to Monica Nations

Tuesday, December 7, 2004

Arrived at the Patient Care Center

Talked to Chris about my medical school interview

Medical school interview

Wednesday, December 8, 2004

Arrived at the Patient Care Center

Read the email Rachel had sent from Pharmanet which listed the documents she was still missing

Also read the email Rachel sent to Wendy regarding the missing documents Rachel had not received yet

Called Rachel to verify the exact documents she was missing. Per Rachel, she explained that we were still missing the principal investigators and subinvestigator's DEA 223 forms

Discussed with Chris about the missing documents

Chris called Jo-Anne to ask her if we could obtain the lab normal for pregnancy tests

Called Dr. Smith to ask for an updated resume with his signature on it

Send Rachel and updated copy of Mirza's resume

Lunch

Emailed Rachel to notify her that we were sending the documents that she had requested

Per Rachel, she asked to have Mirza fill out a DEA 222 form and send it to her so that she could look it over

Thursday, December 9, 2004

Arrived at the Patient Care Center

Discussed with Chris about what we needed to obtain while we were at Plaza

Copied the protocol for the Skypharma protocol for the anesthesiologists at Plaza that we would be meeting with

Went over to the Plaza laboratory and obtained the lab normals from Jo-Anne

Went to the OR are to talk to Dr. Clark about the encapsulated morphine protocol

Gave him a copy of the protocol and obtained Dr. Million's number from him

Went to the pharmacy to talk to Mirza about filling out the DEA 222 form and obtained a blank copy of the 222 form so that we could ask Rachel which areas we could fill out

Called Dr. Million and met with him on the 2nd floor and discussed with him about the protocol procedures and reimbursement

Gave him a copy of the protocol
Lunch

Returned to the Patient Care Center and faxed Rachel all of the DEA 223's, note to files, and lab normals for a pregnancy test

Emailed Rachel to let her know that we were sending the documents

Friday, December 10, 2004

Arrived at the Patient Care Center

Worked on updating my journal and medical school applications

Brought Chris the FedEx tracking number so that he could check to see whether or not Monica had received the documents

Made filling folders for Dr. G. Smith and Dr. Hull which included their CV, DEA 223

Lunch

Chris showed me the copy of the form Pharmanet had sent that instructed us on how to fill out the DEA 222 form when we take it over to Mirza

Continued work on my thesis

December 13, 2004-January 2, 2005

Christmas Break

Monday, January 3, 2004

Arrived at the Patient Care Center

Discussed with Chris about the email Wendy sent about missing SAE forms for multiple studies

Photocopied Adolor SAE's for Wendy and took them over to her

Told her that as of today we had not received any SAE's for either the Ortho-McNeil or Skypharma study

Picked up the 1572's and financial disclosure forms

Walked over to Dr. Gerhart Smith's office and dropped off the financial disclosure form for him to sign

Talked to Dr. Peska about setting up a time for my defense

Returned to the Patient Care Center and checked the files for the investigator agreement Dr. Buchanan had signed

Rechecked the files to confirm that now SAE's had been received from Ortho-McNeil or Skypharma

Lunch

Continued work on thesis defense

Discussed with Chris about Adolor calling to say that they did not want to participate in the study because the study had to be reviewed by two IRB boards

Dr. Yurvati said that he would talk to Christine at Plaza to discuss the options we could present to Adolor

Photocopied the informed consent for a study to enclose with the continuing review paper

Obtained the tutorial certificates from Della for Dr. Berbel, Della, and Chris to enclose with their continuing review paperwork

Made copies of the certificates and filled them

Wednesday, January 5, 2005

Arrived at the Patient Care Center

Checked email to determine whether or not my committee members were okay with the date of my defense

Filled out the room request form to reserve for my defense

Continued working on preparing my paper for review by Dr. Sheedlo.

Chris walked over to clinical trials to submit the 1572 to Wendy since we added Dr. Clark on the list

Emailed my committee members to let them know that I had reserved a room for my defense

Talked with Chris and Della about the post-op illeus study and whether or not the UNT IRB would defer since the sponsor company does not want to go through two IRB's

Thursday, January 6, 2005

Worked on thesis paper

Friday, January 7, 2005

Chris in Austin

Monday, January 10, 2005

Arrived at the Patient Care Center

Talked with Chris about the status of the study approvals at Plaza

Chris said that Randy would be here tomorrow to do a close out visit for the urokinase study

Worked on thesis paper

Called the Las Vegas medical school to schedule an interview

Went over to Plaza to obtain the contract from Christine

Asked her how the studies were doing and if we would be up and running soon

Per Christine, she said that the studies were going and that it was just taking awhile

Lunch

Continued work on thesis

Tuesday, January 11, 2005

Arrived at Patient Care Center

Talked with Chris about my upcoming medical school interview
Asked Dr. Peska to sign my intent to defend paper

Called the medical school to schedule my interview date and reserve plane tickets

Lunch

Randy arrived and began looking through the regulatory binder and case report forms

Obtained the study drug from the locked safe and had Randy check to make sure they were all there before they were sent to the sponsor.

Took Randy to see Dr. Peska so that they could go over the closeout visit study information and discuss any lingering questions

Took the package to the post office and mailed it

Wednesday, January 12, 2005

Researched journal articles in the library for my thesis

Picked up fiancé after his surgery was completed

Thursday, January 13, 2005

Job Interview in Las Colinas

Friday, January 14, 2005

Worked on thesis

Monday, January 17, 2005

Martin Luther King Jr. Holiday

Tuesday, January 18, 2005

Arrived at the Patient Care Center

Reviewed thesis before turning it in to Dr. Sheedlo and Dr. Bens

Chris notified me about the upcoming teleconference with Ortho-McNeil this Friday.
Worked on thesis for the rest of the afternoon

Wednesday, January 19, 2005

Arrived at the Patient Care Center

Printed out my thesis and made a copy to turn into Dr. Sheedlo.

Worked with Chris to fill out the data clarification forms for Mrs. G and Mrs. I

Compared the source document to the data we had inputted in the patient's CRF

Went to Ground Rounds to hear Dr. Singh discuss estrogen therapy

Returned to the Patient Care Center and faxed Donna the finished DCF's

Filled the original DCF's into each subject's CRF

Typed up an SAE for the Depodur study

Thursday, January 20, 2005

Arrived at the Patient Care Center

Worked on updating my journal

Called Carolyn to see when Dr. Vishwanatha would be in his office so that I could get him to sign my intent to defend

Per Carolyn, Dr. Vishwanatha would not be back until tomorrow

Had Dr. Buchanan sign the SAE for the Depodur study, made a copy of the SAE and put it into the regulatory binder and sent the original to Deb in the IRB office

Lunch

Went over thesis with Chris and made corrections

Friday, January 21, 2005

Arrived at the Patient Care Center

Worked on correcting my thesis paper
Went to Dr. Vishwanatha's office to ask him to sign my intent to defend

Went to the graduate school and paid my filling fees

Went back to the Patient Care Center and continued making edits on my thesis

Participated in the teleconference call with Ortho-McNeil, in which new ways were discussed to help increase patient enrollment

Lunch

Typed up a synopsis of the teleconference meeting to add to my thesis paper

Went over edits on my paper with Chris

Monday, January 24, 2005

Medical School Interview

Tuesday, January 25, 2005

Medical School Interview

Wednesday, January 26, 2005

Arrived at the Patient Care Center

Talked with Chris about my medical school interview

Made corrections on my thesis with Chris

Lunch

Typed up the ASA table for my thesis and edited my paper as well as added the teleconference information to my paper

Worked on PowerPoint presentation

Checked on medical school status

Thursday, January 27, 2005

Arrived at Patient Care Center

Worked on thesis all day

Friday, January 28, 2005

Arrived at Patient Care Center

Worked on thesis in the morning

Went over to Plaza to pick up Mirza's 222 form to have the fentanyl shipped back to the pharmacy

Picked up a list of the IRB members at Plaza and made copies at the Patient Care Center

Lunch

Mailed the DEA 222 form to the sponsor to have the drug shipped

Continued work on thesis

Monday, January 31, 2005

Arrived at Patient Care Center

Talked to Chris about the figures I tried to scan over the weekend, he helped me resize them so they would fit

Went to the library to scan the figures, and checked out the digital camera to take pictures of the fentanyl PCTS

Carried books over to Della's new office

Scanned the morphine structure and returned the camera

APPENDIX B

BRIEF PAIN INVENTORY

BRIEF PAIN INVENTORY-PRE-OP

Thinking about your **abdominal or pelvic pain**, please respond to each of the statements/questions below.

Date of Assessment					
month		day		year	

1. Please rate your pain by checking the one number that best describes your pain at its **worst** in the past week.

No pain ☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 Pain as bad as you can imagine

2. Please rate your pain by checking the one number that best describes your pain at its **least** in the past week.

No pain ☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 Pain as bad as you can imagine

3. Please rate your pain by checking the one number that best describes your pain on the **average** in the past week.

No pain ☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 Pain as bad as you can imagine

4. Please rate your pain by checking the one number that tells how much pain you have **right now**.

No pain ☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 Pain as bad as you can imagine

5. In the past 24 hours, how much **relief** have pain treatments or medications provided? Please check the one percentage that most shows how much relief you have received.

No relief ☐ 0% ☐ 10% ☐ 20% ☐ 30% ☐ 40% ☐ 50% ☐ 60% ☐ 70% ☐ 80% ☐ 90% ☐ 100% Complete Relief

6. Please check the one number that describes how, during the past week, **pain has interfered** with your:

A. General activity

Does not interfere											Completely interferes
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	
0	1	2	3	4	5	6	7	8	9	10	

B. Mood

Does not interfere											Completely interferes
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	
0	1	2	3	4	5	6	7	8	9	10	

C. Walking ability

Does not interfere											Completely interferes
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	
0	1	2	3	4	5	6	7	8	9	10	

D. Normal work (includes both work outside the home and housework)

Does not interfere											Completely interferes
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	
0	1	2	3	4	5	6	7	8	9	10	

E. Relations with other people

Does not interfere											Completely interferes
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	
0	1	2	3	4	5	6	7	8	9	10	

F. Sleep

Does not interfere											Completely interferes
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	
0	1	2	3	4	5	6	7	8	9	10	

G. Enjoyment of life

Does not interfere											Completely interferes
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	
0	1	2	3	4	5	6	7	8	9	10	

APPENDIX C

SUBEJCT EASE-OF-CARE QUESTIONNAIRE

SUBJECT EASE-OF-CARE QUESTIONNAIRE

	The statements below are about your experience with the device that delivered your pain medication. **For each item, please circle the best response.**	**Not at all**	**A little bit**	**Some-what**	**Quite a bit**	**A great deal**	**A very great deal**
1	I liked being in control of my pain medication.	0	1	2	3	4	5
2	I used less pain medication than if a nurse or doctor had provided it regularly.	0	1	2	3	4	5
3	My pain control was interrupted because of problems with the device.	0	1	2	3	4	5
4	I had soreness/irritation on my skin where the device was attached.	0	1	2	3	4	5
5	The device was easy to use.	0	1	2	3	4	5
6	I needed help from a nurse to use and/or adjust the device.	0	1	2	3	4	5
7	Because of the device, I had to be careful when I used my hands or arms (to eat, brush teeth, sit up in bed).	0	1	2	3	4	5
8	The device made it difficult for me to adjust my position in bed.	0	1	2	3	4	5
9	The device was difficult to use.	0	1	2	3	4	5
10	The device interfered with my ability to get out of bed and walk around (to chair in room, bathroom, hallway).	0	1	2	3	4	5
11	My pain went up and down (i.e, sometimes the pain was bad and other times it was under control).	0	1	2	3	4	5
12	Pain woke me up from sleep.	0	1	2	3	4	5
13	My pain level was controlled.	0	1	2	3	4	5

The statements below are about your experience with the device that delivered your pain medication. For each item, please circle the best response.		Not at all	A little bit	Some-what	Quite a bit	A great deal	A very great deal
14	I had problems pressing the button because I was drowsy and/or feeling weak.	0	1	2	3	4	5
15	I was comfortable giving myself pain medication.	0	1	2	3	4	5
16	I was worried that I might be taking more medication than I was supposed to.	0	1	2	3	4	5
17	The beeps from the device reassured me that it was working properly.	0	1	2	3	4	5
18	I was afraid of becoming addicted to the pain medication.	0	1	2	3	4	5
19	I was worried that a nurse or doctor was not monitoring how much pain medication I was taking.	0	1	2	3	4	5
20	The beeps from the device bothered/annoyed me.	0	1	2	3	4	5
21	I used more pain medication than if a nurse or doctor had provided it regularly.	0	1	2	3	4	5
22	I was worried that the device would run out of medication.	0	1	2	3	4	5
23	The beeps from the device made me worry that the device was <u>not</u> working properly.	0	1	2	3	4	5
24	I understood <u>how often</u> I could press the button to get my pain medication.	0	1	2	3	4	5
25	The instructions provided by the nurse were useful.	0	1	2	3	4	5
26	I understood <u>how much</u> pain medication I was getting when I pressed the button.	0	1	2	3	4	5

27	How satisfied were you with the level of your pain control? *Check one box*
	☐ Extremely satisfied ☐ Very satisfied ☐ Satisfied ☐ Dissatisfied ☐ Very dissatisfied ☐ Extremely dissatisfied
28	How satisfied were you with the way in which your pain medication was administered? *Check one box*
	☐ Extremely satisfied ☐ Very satisfied ☐ Satisfied ☐ Dissatisfied ☐ Very dissatisfied ☐ Extremely dissatisfied

APPENDIX D

SUBJECT GLOBAL ASSESSMENT

END OF STUDY PATIENT GLOBAL ASSESSMENT

"Overall, would you rate this method of pain control during the last 24 hours as being:"

Purpose of Assessment	Date/Time of Assessment	Subject Global Assessment
☐ 24 hour time point ☐ Withdrawal from study	(mm dd yy) (24 hr clock)	☐ Excellent ☐ Good ☐ Fair ☐ Poor
☐ 48 hour time point ☐ Withdrawal from study	(mm dd yy) (24 hr clock)	☐ Excellent ☐ Good ☐ Fair ☐ Poor
☐ 72 hour time point ☐ Withdrawal from study	(mm dd yy) (24 hr clock)	☐ Excellent ☐ Good ☐ Fair ☐ Poor

APPENDIX E

INVESTIGATOR AND SURGEON GLOBAL ASSESSMENT

END OF STUDY GLOBAL ASSESSMENT

Purpose of assessment:

☐ Study Completion

☐ Withdrawal from study

SURGEON GLOBAL ASSESSMENT
(Surgeon Who Performed Operation)

Date of Assessment: ☐☐☐☐☐☐ (mm dd yy) **Time of Assessment:** ☐☐:☐☐ (24 hr clock)

Surgeon ID Number: S U ☐☐☐☐

Was the surgeon who performed the operation also the principal investigator?

☐ No (Please answer the following and have principal investigator complete Investigator Global Assessment below.*)

☐ Yes

Please answer the following question:

"Overall, would you rate this method of pain control for this subject as being:"

☐ Excellent ☐ Good ☐ Fair ☐ Poor

*PRINCIPAL INVESTIGATOR GLOBAL ASSESSMENT

Date of Assessment: ☐☐☐☐☐☐ (mm dd yy) **Time of Assessment:** ☐☐:☐☐ (24 hr clock)

☐ General Surgeon ☐ Gynecologist ☐ Anesthesiologist ☐ Other, specify _____

Please answer the following question:

"Overall, would you rate this method of pain control for this subject as being:"

☐ Excellent ☐ Good ☐ Fair ☐ Poor

* To be completed only if the surgeon who performed the operation was not also the principal investigator.

APPENDIX F

NURSE EASE-OF-CARE QUESTIONNAIRE

NURSE EASE-OF-CARE-QUESTIONNAIRE

Nurse ID Number: | N | U | | | | |

Check One: ☐ Staff Nurse ☐ Study Coordinator ☐ Research Nurse

Date		
month	day	year

Check One: ☐ E-TRANS® fentanyl ☐ IV PCA morphine

To be completed by all floor nurses and research nurses who provided primary care for subjects during the study. One form should be completed for E-TRANS and one for IV PCA if care was provided to subjects in both groups.

Thinking about study subjects treated with the above checked method of pain control only, please circle the best response. *Check (X) "Not responsible for task" if someone else was responsible for a particular task during the course of the study.*

			Time-Consuming					
	Please rate how time-consuming the following tasks were:	**Not responsible for task**	**Not at all**	**A little bit**	**Some-what**	**Quite a bit**	**A great deal**	**A very great deal**
1	Accessing device-related supplies	☐	0	1	2	3	4	5
2	Initial set up of device	☐	0	1	2	3	4	5
3	Maintaining device function	☐	0	1	2	3	4	5
4	Changing or adjusting the device due to malfunction or dosing schedule	☐	0	1	2	3	4	5
5	Educating/re-instructing subject on how to use the device	☐	0	1	2	3	4	5
6	Positioning, moving, or transferring the subject with the device	☐	0	1	2	3	4	5
7	Managing breakthrough pain	☐	0	1	2	3	4	5
8	Treating subject problems related to the device (dosing, skin irritation, infiltration, etc.)	☐	0	1	2	3	4	5
9	Determining amount of medication provided to subject	☐	0	1	2	3	4	5
10	Removing or disposing of device, including medication	☐	0	1	2	3	4	5
			Bothersome					
	Please rate how bothersome the following tasks were:	**Not responsible for task**	**Not at all**	**A little bit**	**Some-what**	**Quite a bit**	**A great deal**	**A very great deal**
11	Accessing device-related supplies	☐	0	1	2	3	4	5
12	Initial set up of device	☐	0	1	2	3	4	5
13	Maintaining device function	☐	0	1	2	3	4	5
14	Changing or adjusting the device due to malfunction or dosing schedule	☐	0	1	2	3	4	5
15	Educating/re-instructing subject on how to use the device	☐	0	1	2	3	4	5
16	Positioning, moving, or transferring the subject with the device	☐	0	1	2	3	4	5
17	Managing breakthrough pain	☐	0	1	2	3	4	5
18	Treating subject problems related to the device (dosing, skin irritation, infiltration, etc.)	☐	0	1	2	3	4	5
19	Determining amount of medication provided to subject	☐	0	1	2	3	4	5
20	Removing or disposing of device, including medication	☐	0	1	2	3	4	5

21	How satisfied were you with the pain control provided by the device? *Check one box*
	☐ Extremely satisfied ☐ Very satisfied ☐ Satisfied ☐ Dissatisfied ☐ Very dissatisfied ☐ Extremely dissatisfied
22	Please rate your overall satisfaction with the device. *Check one box*
	☐ Extremely satisfied ☐ Very satisfied ☐ Satisfied ☐ Dissatisfied ☐ Very dissatisfied ☐ Extremely dissatisfied
23	How many E-TRANS® fentanyl subjects have you cared for during the course of this study? ____Subjects (If IV PCA only, please leave blank.)
24	How many years have you cared for patients using IV-PCA? _____Years

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