11-18-2012

An Organizational Diagnosis Of A Centralized Investigational New Drug Core Within A Large Academic Health Center

Kathleen M. Thomas
University of Pennsylvania, kathleen.thomas@uphs.upenn.edu

Submitted to the Program of Organizational Dynamics In the Graduate Division of the School of Arts and Sciences In Partial Fulfillment of the Requirements for the Degree of Master of Science in Organizational Dynamics at the University of Pennsylvania
Advisor: Dana Kaminstein

An Organizational Diagnosis Of A Centralized Investigational New Drug Core Within A Large Academic Health Center

Abstract

This capstone examines the root cause of the ineffectiveness of a centralized Investigational New Drug (IND) core within a research department of a large Academic Health Center (AHC). This capstone utilized an organizational diagnosis approach to collect data to determine what is and is not contributing to the success of the core.

The hypotheses of this study are: 1) The centralized model was set in place without clear objectives; 2) The IND core is not operating in the way it was structured to operate; 3) The IND core is understaffed and unable to fully carry out the level of responsibility associated with being a Sponsor; and 4) Future expansion was not included in the planning phase. Data was collected by interviewing staff members, and participant observations. Prior to conducting the current state interviews, I conducted background interviews with previous staff members to determine the rationale behind centralization.

The results supported the importance of learning an organization's history prior to implementing a change, as well as the need for group development prior to the implementation of a new model within an organization. The organizational diagnosis I conducted was able to confirm three of four of the hypotheses. I was able to uncover two variables that I did not consider before the diagnosis: role definition, and inter-group dynamics.

Comments

AN ORGANIZATIONAL DIAGNOSIS OF A CENTRALIZED

INVESTIGATIONAL NEW DRUG CORE WITHIN

A LARGE ACADEMIC HEALTH CENTER

by

Kathleen M. McCarthy-Thomas

Submitted to the Program of Organizational Dynamics
In the Graduate Division of the School of Arts and Sciences
In Partial Fulfillment of the Requirements for the Degree of
Master of Science in Organizational Dynamics at the
University of Pennsylvania

Philadelphia, Pennsylvania

AN ORGANIZATIONAL DIAGNOSIS OF A CENTRALIZED

INVESTIGATIONAL NEW DRUG CORE WITHIN

A LARGE ACADEMIC HEALTH CENTER

Approved by:

_____
Dana Kaminstein, Ph. D., Advisor

_____
John Pourdehnad, Ph. D., Reader

_____
Alice Laneader, Mbe,RAC, Reader

ABSTRACT

This capstone examines the root cause of the ineffectiveness of a centralized Investigational New Drug (IND) core within a research department of a large Academic Health Center (AHC). This capstone utilized an organizational diagnosis approach to collect data to determine what is and is not contributing to the success of the core.

The hypotheses of this study are: 1) The centralized model was set in place without clear objectives; 2) The IND core is not operating in the way it was structured to operate; 3) The IND core is understaffed and unable to fully carry out the level of responsibility associated with being a Sponsor; and 4) Future expansion was not included in the planning phase. Data was collected by interviewing staff members, and participant observations. Prior to conducting the current state interviews, I conducted background interviews with previous staff members to determine the rationale behind centralization.

The results supported the importance of learning an organization's history prior to implementing a change, as well as the need for group development prior to the implementation of a new model within an organization. The organizational diagnosis I conducted was able to confirm three of four of the hypotheses. I was able to uncover two variables that I did not consider before the diagnosis: role definition, and inter-group dynamics.

ACKNOWLEDGEMENTS

LIST OF TABLES

LIST OF FIGURES

TABLE OF CONTENTS

CHAPTER 1

INTRODUCTION

Clinical research overview

I have spent the past ten years working in the field of clinical research, growing (or expanding) my working knowledge and understanding of Good Clinical Practices (GCP) and regulatory requirements. Until recently, I have never explored the dynamics at play within this field, nor have I been able to locate much research on these dynamics. This is one reason that this capstone research had particular appeal to me as it allowed me to use my knowledge of research regulations and organizational dynamics to diagnose one of the current systems in my workplace.

This capstone will evaluate the effectiveness of a centralized IND core at an Academic Health Center (AHC). My interest in this topic began two years ago when I was asked to oversee the operations of the IND core. Since then I have struggled with providing the most effective processes for this core. My goal with this capstone is to determine if a centralized model is the most efficient and effective way of managing multiple INDs within the department.

History of clinical research regulations

Over the past one hundred years, significant events within the field of clinical research have led to the development and implementation of regulations. This section will present an overview of significant events that led to the development of guidelines centered on Protection of Human Subjects and Investigational New Drugs applications. The purpose of presenting this literature is to provide the reader with an understanding of

the crucial events leading to regulations and processes within the field of clinical research. These events led to (and continue to) regulations concerning protection of human subjects and drug-related research.

The first event of significance for this capstone is the passing of the Pure Food and Drug Act in 1906. This law mandated all new drugs be tested for safety before marketing. The test results were required to be submitted to the Food and Drug Administration (FDA) as a New Drug Application (NDA). Unfortunately, this law did not prevent tragic events from occurring. In 1937, a drug company manufactured a strep throat treatment drug. The solvent included in this drug was poisonous, killing nearly one hundred people. It was discovered that the drug had not been tested in animals or humans before being marketed. This event became known as the Elixir Sulfanilamide tragedy (White-Junod, 2012). The Elixir Sulfanilamide tragedy led to the passing of the Food, Drug and Cosmetic Act of 1938. This law required peer-market review of safety in an NDA, and labeling requirements. In addition, this law provided the FDA with the ability to audit manufacturing organizations (White-Junod, 2012). "A new provision in the act -- requiring drug sponsors to submit safety data to FDA officials for evaluation prior to marketing -- appeared with relatively little discussion following on the heels of the Elixir Sulfanilamide disaster" (White-Junod, 2012). This statement stood out to me because the article did not specify who was involved in the decision-making process. This raised some questions in my mind. Was there a thought out plan in place? Or was the act instituted as a knee jerk reaction? The government was liable because numerous deaths occurred and in order to demonstrate the problem was being fixed, a regulation was developed.

The Nuremberg Code is a regulation that was written in 1948 in response to the rights and welfare of human subject research participants and their mistreatment by Nazi Germany (Gordon & Prentice, 2000, p.1). "The origin of modern concern for the rights and welfare of human subjects participating in research is generally acknowledged to have occurred in December, 1946." (Gordon & Prentice, 2000, p.1) Twenty-three individuals (physicians and administrators) were charged with murder and torture of humans for medical science. Between 1942 and 1945, thirty-two experiments were conducted on concentration camp prisoners. This code (see the HHS.gov website, http://www.hhs.gov/ohrp/archive/nurcode.html) consists of ten standards that must be met when conducting human subject related research (Table 1).

Table 1. Nuremberg Code

Code number	Code
1	The voluntary consent of the human subject is absolutely essential.
2	The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.
3	The experiment should be so designed and based on the results of animal experimentation and knowledge of the natural history of the disease.
4	The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.
5	No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur.
6	The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.
7	Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.
8	The experiment should be conducted only by scientifically qualified persons.
9	During the course of the experiment the human subject should be at liberty to bring the

	experiment to an end.
10	During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

Following the implementation of the Nuremberg Code came strong regulations specific to the drug industry. "In 1961, a popular drug in Europe, a hypnotic known as thalidomide, was discovered to cause severe birth defects and even death in babies when their mothers took the drug early in their pregnancies. Because of the concerns of FDA drug reviewer Dr. Frances Kelsey, the drug was never approved for sale in the U.S. Nonetheless, the drug sponsor had sent samples of the drug to thousands of U.S. doctors who gave the samples to their patients without telling them that the drug was an experimental one, making their patients the unwitting subjects of human drug experimentation" (White-Junod, 2012). This event led to the Kefauver-Harris amendments of 1962, which mandated all drugs must be proven safe and effective before marketing. This was the underlying foundation for INDs.

In 1964, the World Medical Association (WMA) published the Declaration of Helsinki. This document describes ethical principles of conducting research involving humans. Gordon and Prentice (2000) state the document breaks medical research into two categories: clinical research combined with professional care, and non-therapeutic clinical research. This document was built upon the Nuremberg Codes as many American Physicians raised concerns about learning from "barbaric" events (Gordon & Prentice, 2000).

The Tuskegee Syphilis Study was conducted between 1932 and 1972. This is a widely publicized study, which led to further regulations within the field of clinical

research. In the mid-1920s, a health initiative was started within the black community for which the Rosenwald fund provided monetary support to investigate treatment options for the disease of syphilis. The standard treatments were salvarsan, mercurial and bismuth, which in turn showed minor advantages and high toxicity. The fall of the stock market and Great Depression caused the Rosenwald fund to cut support.

In 1932, the United States Public Health Service (PHS) sponsored a study at the Tuskegee Institute (and its affiliated hospitals) in southern Alabama. The goal was to investigate the stages of syphilis over the course of its lifetime. Two hundred and one healthy black males (controls) and three hundred and ninety-nine syphilitic black males were enrolled into the study. For the most part, these men were of low income and did not know the severity of the disease from which they suffered. At the time of enrollment, they were informed they were being treated for bad blood, and in actuality the doctor had no intention of treating the disease at all, due to the lack of "safe" treatment options (Center for Disease Control and Prevention).

The details of this study were revealed in 1972 leading to the National Research Act. Simultaneously the Department of Health, Education, and Welfare (DHEW) published regulations for the use of human subjects (Gordon and Prentice, 2000). These regulations -- known as 45 CFR 46 (Regulations for the Protection of Human Research Subjects) -- included the mandate of an Institutional Review Board (IRB) to oversee, review studies for safety and established criteria for Informed Consent.

These events led the United States to develop regulations for the conduct of clinical research. "It should be recognized that the system for protection of the rights of human subjects of research, which evolved painfully from the horrors of Nazi Germany,

itself continues to evolve" (Gordon and Prentice, 2000, p.7). Clinical research is continuing to evolve, and the regulations will need to evolve as well.

<u>Background</u>

The field of clinical research has been evolving over the past century and has led to the development of regulations and infrastructure to support the research. Clinical research (human subject research/clinical investigation) is defined as "any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that must meet the provisions of part 58, regarding nonclinical laboratory studies (21 CFR 56.102)." This definition is taken directly from the Code of Federal Regulations (CFR).

AHCs have a vested interest in the conduct of clinical research protocols. Some protocols involve the use of investigational drug therapies, which in turn require the submission of an IND application to the FDA, an agency of the US Department of Health and Human Services. The FDA is responsible for overseeing the safety of all FDA regulated products and overseeing the protection of human research participants for clinical investigations. There are numerous centers under its structure with two specific to INDs: The Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research. A process for submitting an IND is clearly defined in 21 CFR

312 and is mapped out in the flowchart below (see Figure 1). The process for submitting

an IND involves numerous working parts and a high level of expertise for the personnel

involved.

Figure 1. IND application process
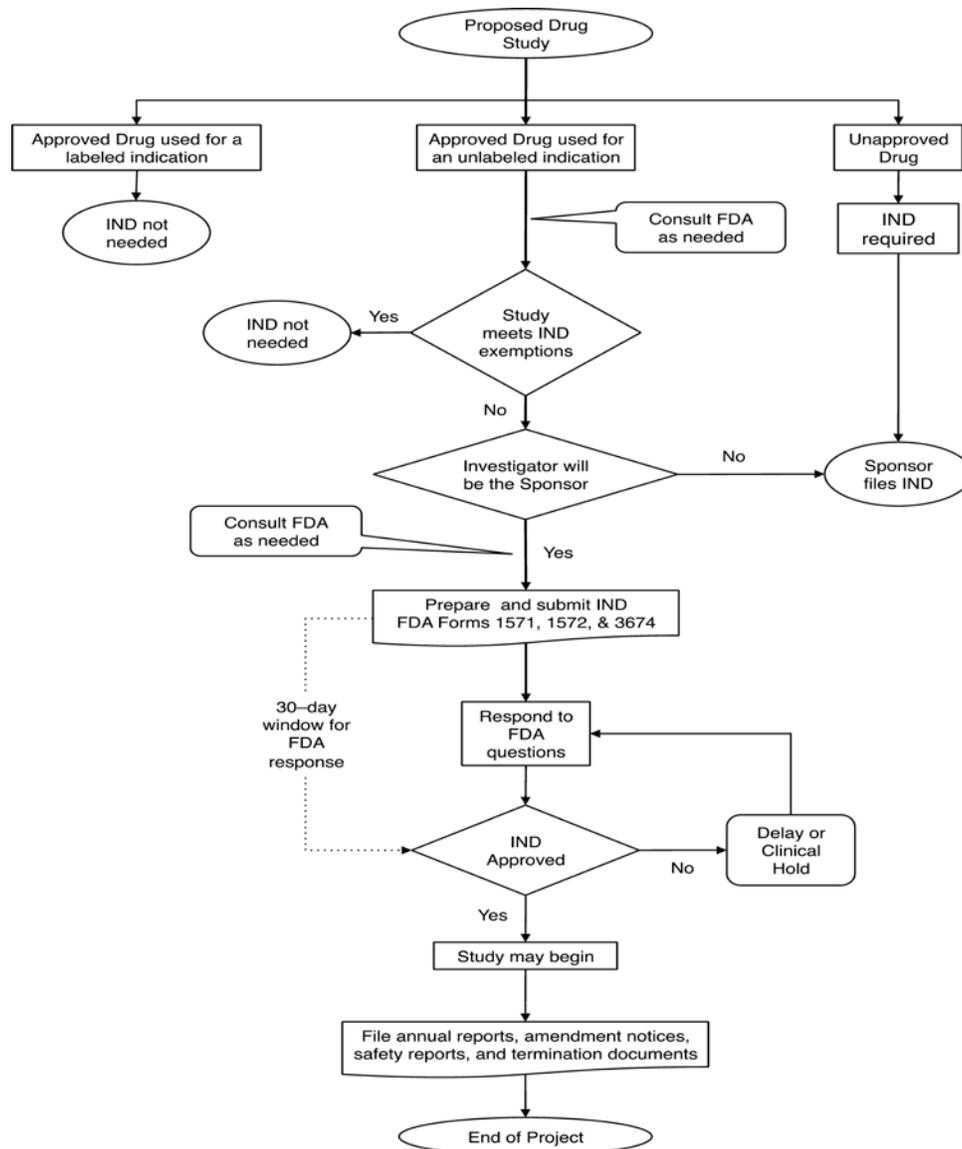
Figure 1. Holbein, M. E. Blair, 2009

The process of conducting clinical research involves several stakeholders. Two of the primary stakeholders are the Investigator, an individual responsible for the conduct of the clinical research (see Table 1) and Sponsor (see Table 2). The standards for Investigators are very high, and Investigators are expected to undergo proper training before conducting a clinical research protocol (Berro, Marlene, Burnett, Bruce, Fromell, Gregg, Hartman, Karen, Rubinstein, Eric, Schuff, Kathryn, & Speicher, L. (2011).

Table 2. Responsibilities of investigators under an IND (21 CFR 312) Regulations

(http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.60)

Ensuring that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations; for protecting the rights, safety, and welfare of subjects under the investigator's care; and for the control of drugs under investigation
Obtain the informed consent of each human subject to whom the drug is administered
Record keeping and record retention
Assurance of IRB review
Reporting: progress, safety and final report

Investigators wishing to conduct research utilizing an investigation drug must meet regulatory requirements above those mandated for Investigators of non-drug related research. These additional regulations are set in place to ensure protection of the research participants participating in research studies involving the use of a non-FDA approved drug. "Individual investigators who initiate and conduct a clinical study, as well as being directly accountable for the administration or dispensing of the investigational drug, are designated as Sponsor-Investigator." (Holbein, 2009, p.691)

A sponsor is defined as a person who takes responsibility for and initiates a clinical investigation. The sponsor may be an individual or pharmaceutical company, governmental agency, academic institution, private organization, or other organization. The sponsor does not actually conduct the investigation unless the sponsor is a sponsor-investigator. A person other than an individual that uses one or more of its own employees to conduct an investigation that it has initiated is a sponsor (see Table 2).

Table 3. Responsibilities of a sponsor under an IND (21 CFR 312) Regulations
(http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.50)

Selecting qualified investigators, training
Providing them with the information they need to conduct an investigation properly
Ensuring proper monitoring of the investigation(s)
Ensuring that the investigation(s) is conducted in accordance with the general investigational plan and protocols contained in the IND
Maintaining an effective IND with respect to the investigations, and ensuring that FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the drug
Supplying, handling and disposition of investigational products
Record keeping and record retention
Management of investigator non-compliance
Assurance of IRB review
Medical expertise, trial oversight

Overview of a department within an AHC

The department (which has been named Department A to protect its identity) had several Sponsor-Investigators prior to the year 2007. Several Investigators within the department had an interest in studying the safety and effectiveness of Radio-pharmaceuticals. A Radio-pharmaceutical is defined as a drug (compound or material)

that may be labeled or tagged with a radioisotope. These Investigators (prior to 2007) developed clinical research protocols, and submitted INDs to the FDA.

Research being conducted at an AHC entered the spotlight on September 17, 1999 due to the death of a research participant. Research restrictions and higher level oversight were implemented as a result of the event. The AHC created a centralized office – the office of Human Research (OHR) – to provide support to Investigators throughout the AHC. In addition, the AHC in collaboration with OHR reviewed all of the research being conducted and determined studies that were considered of greater than minimal risk, and needed additional oversight. Department A was considered one of the key departments with multiple high risk protocols. In order to ensure compliance, OHR developed a monitoring program, implemented in the fall of 2005, for protocols with greater than minimal risk.

OHR monitored protocols under an IND throughout the spring of 2006. The monitoring reports documented non-compliance. The Administrative leadership of OHR and SOM met with the leadership within Department A to discuss the findings and an action plan. Leadership of Department A was charged with designing a plan to dissolve non-compliance among Sponsor-Investigators. The departmental leadership took the findings very seriously and decided the department would be named as Sponsor.

Simultaneously while these discussions were occurring, leadership was in search of a new chief for a division within the department. The selected candidate brought with him previous experience of working within a centralized IND core model. He offered his expertise of Sponsor requirements and to serve as the Sponsor's authorized-representative if hired into the chief position. Soon thereafter, this gentleman was chosen as the

Sponsor's authorized-representative on behalf of the Sponsor.

My involvement

I began working in the department in the fall of 2002 as a Clinical Research Coordinator (CRC) for Dr. X on a multi-modality project that lasted until June 2007. During the five-year period, I gained extensive knowledge of clinical research conduct and advanced into a project manager position. Shortly after the completion of the project, Dr. X promoted me to a senior level project manager and requested I work with him to develop a centralized Clinical Research Coordinator core (known as RADCORE). I created training manuals, protocol file templates, regulatory organization tools, standard operating procedures, and hired several new CRCs into the group. I was proud of my accomplishments and found the core was operating smoothly. I was eager to take on more responsibilities within the department.

My involvement in the IND core began two years ago; I was a young, enthusiastic worker willing to take on extra responsibilities and sought out challenges. My role evolved early in 2010; I was promoted to Clinical Research Operations Manager. My responsibilities included developing operational processes, managing projects, and leading research staff throughout multiple cores of the research unit of the department.

Late January 2010, I received an email from my boss, Dr. X, requesting I help organize and improve the document management quality of the IND core. I had little knowledge of the current organizational structure within the IND core and was not aware of the history of the OHR audits so, I was a bit nervous about this new responsibility.

When I spoke with Dr. X he explained he needed my help organizing the

regulatory files of the IND core, creating a more effective and efficient organization system, and hiring an individual to serve as the IND Manager. He briefly explained the IND core had been centralized for three years (implemented in 2007) and was still not operating effectively. The centralized model was set in place because individual investigators did not have the resources to maintain compliance with the regulations. To solve this problem, the department was named Sponsor and an individual was appointed as Sponsor's authorized-representative. In addition, an IND core manager was hired to manage the administrative activities and monitor research protocols under INDs.

Since the IND core was a newly adapted model and not one that other department were utilizing, the AHC leadership were watching carefully. OHR has been conducting audits of the IND core throughout the 2009 academic year, and the audit findings included: lack of communication with Investigators, missing documentation, lack of training, and lack of documented communication among all working parts of the core. OHR provided recommendations for re-organizing and resolving the major audit findings. Unfortunately, the findings were not resolved and the core was at risk of being closed down. Dr. X explained a change in administrative staff was warranted, and a new individual would be hired under my supervision. Before I could go through the recruitment and hiring process, my first priority was resolving the auditing findings.

I spent the next several months going through regulatory files, creating tracking systems, and resolving most of the findings from the 2009 OHR audits. I remember feeling fairly confident in the systems I had created and felt strongly it was time to focus on recruiting and hiring an IND core manager. I met with Dr. X and Dr. Y (Sponsor-Representative at the time) to determine the responsibilities that would be associated with

the position. After a few discussions with both leaders and researching IND Manager Job descriptions, I drafted the position summary and submitted it to Human Resources for approval and posting.

I interviewed several candidates who demonstrated knowledge of clinical research, FDA regulations, Good Clinical Practices, communication, organization, and initiative competencies. With buy-in from Dr. X, and Dr. Y, I made a decision on the best suited candidate for the IND Manager position. I offered the position to an internal candidate in the department, who demonstrated all of the above mentioned qualities. She accepted the offer and started her new position in June 2010.

My goals (agreed upon by IND Manager) for the IND core included: developing a monitoring plan, Sponsor Standard Operating Procedures (SOPs), training manual for Investigators, a website, standard filing naming conversions, electronic file management, and standard file organization. In addition to all of this, I knew the daily operations had to continue. The IND Manager took the lead on filing annual reports (for each IND) protocol amendments and new protocols to the FDA. She continued maintaining the site files of protocols under each IND and defining regulatory submission processes for Investigators, a monitoring plan, and wrote out the mission of the IND core. These three tasks were quite a challenge because we did not know if our perception of the core matched the unspoken mission Dr. X and Dr. Y had intended.

Problem statement

The centralized IND core was developed and implemented to resolve non-compliance issues among Sponsor-Investigators; however, non-compliance issues were still noted on audit reports after the implementation of the centralized IND core. The

centralized model was not fully implemented, nor fully staffed to operate in the way it was structured.

There are several assumptions I have which led me to conduct this diagnosis. These assumptions include: There was a lack of planning about the infrastructure for the centralized IND core, roles were not identified and the purpose of the core was not clearly defined.

Over the past two years I have been concerned with the lack of Sponsor responsibilities remaining unmet by the centralized core. The three responsibilities not being fulfilled by the centralized core include: monitoring, drug accountability, and training. In addition to my observations, the lack of fulfillment has been documented on routine audits by OHR. I feel these issues are present because leadership did not clearly define the core's infrastructure prior to implementation.

The second assumption I have is,   operating effectively because roles were not clearly identified at the time of implementation. When I was first asked to assist with the core, I was introduced to two people: the core manager and the sponsor-representative. The other indirect members (regulatory and cyclotron) were not discussed. At the time, I assumed the only two individuals that mattered to the operation of the core were the manager and the sponsor-representative. Presently, the core manager and I meet monthly with the -representative to discuss the operations of the core. Recently, I have noticed the other indirect members are important to the operations. I'm concerned that the absence of these members from monthly meetings is hindering the effectiveness of the core. Each of these individuals has important skills that could contribute to the effectiveness of the core. The regulatory manager is knowledgeable of FDA regulations and could assist in

the development of effective processes and the cyclotron manager has the most knowledge of drug production. At this point, it is not clear how involved these individuals should be in the core.

The goals of the core have not been made clear. Initially, I had a very limited understanding of the IND core and the purpose it served within the department. I also had a very limited understanding of the role of sponsors. I read section 312 of the CFR to better acquaint myself with the regulations centered around INDs. Sponsors have specific responsibilities and per FDA regulations must be met. I do not believe leadership clearly identified if the centralized core was going to handle the full responsibilities of a Sponsor.

My goals with this capstone are to learn more about the rationale of developing a centralized core, and understand the reason the IND core is not fully functioning as a full service centralized IND core. In order to fully understand the problem, I will conduct a diagnosis of the organization described above.

In Chapter 2, I review literature pertaining to conducting an organizational diagnosis, the importance of understanding an organization's history, and the historical events leading to clinical research regulations. In Chapter 3, I outline the methods I used to explore my hypotheses. I will explain why I selected structured interview questions, as well as how I plan to carry out the diagnosis. In Chapter 4, I present the data and my interpretation of the data. I will then provide a detailed summary of feedback for the client system. I conclude this thesis in Chapter 5 with a summary of my findings and learning from performing the diagnosis.

CHAPTER 2

LITERATURE REVIEW

Introduction

In this literature review I will discuss three areas of research: organizational

diagnosis, organizational history, and the history of clinical research regulations. I will

begin by describing the important elements involved in conducting an organizational

diagnosis. I review this literature in order to demonstrate the ways in which an

organizational diagnosis can contribute to our understanding of why an organization is

not functioning effectively. The second area of research which I discuss is organizational

history. I reviewed literature centered on the importance of understanding an

organization's past and the impact it has on the present and future. The final section of

this chapter presents literature evaluating support programs at AHCs.

Organizational diagnosis

The focus of this capstone is the diagnosis of a centralized IND core within an

AHC. It is critical for me to explain the importance and relevance of conducting an

organizational diagnosis because the framework of my capstone is a diagnosis of my

current workplace. After searching through literature extensively, I was unable to find

literature specific to diagnoses of academic health centers. The lack of literature

highlights the importance of this capstone, as it begins to fill the gap within the literature.

I will present the importance of conducting a diagnosis within an organization.

Clayton P. Alderfer describes the methods of organizational diagnosis in his article

"The Methodology of Organizational Diagnosis" (Alderfer, 1980) as a process of

entering a human system, collecting data, and feeding that information back to the system

to increase understanding among the system's members. Based upon what is learned, a determination regarding change can be made. While this may seem like a lengthy task, the performance of an organizational diagnosis is a stepping stone to a successful and productive change management program (if applicable).

"The purpose of organizational diagnosis is to establish a widely shared understanding of a system and, based on that understanding to determine whether change is desirable" (Alderfer, 1980, p.459). Conducting an organizational diagnosis is important for several reasons. The first is a diagnosis can provide data valuable for testing a hypothesis, rather than speculating about the cause of the problem. The second reason for conducting an organizational diagnosis is to focus on determining the root cause of a problem, rather than focusing on the symptoms of the problem. The third reason for conducting a diagnosis is to identify factors that may be causing the problem, but are not visible. These three points emphasize the importance of understanding the overt and covert dynamics of an organization.

Managers are charged with getting an organization to operate effectively. This can be an overwhelming and challenging task, to say the least. "Understanding one individual's behavior is challenging in and of itself; understanding a group that's made up of different individuals and comprehending the many relationships among those individuals is even more complex" (Nadler & Tushman, 1980, p.35). There is a pressing need for a manager to manage organizational behavior. Nadler and Tushman (1980) state the manager can learn to predict and control organizational behavior with tools to fully understand the dynamics at play. One tool is a model. "A model is a theory that indicates which factors are most critical or important" (Nadler & Tushman, 1980, p. 36). There are

several different models that can be used when conducting an organizational diagnosis. Utilizing an organizational model can help diagnosticians understand the problem systemically.

Nadler and Tushman (1980) describe the diagnostic model as a model that describes the system, identifies the problem, and also analyzes the fits. This model is known as the congruence model. "The model also implies that different configurations of the key components can be used to gain outputs. Therefore, the question is not how to find the "one best way" of managing, but how to find effective combinations of components that will lead to congruent fits among them." (Nadler & Tushman, 1980, p. 46).

Marvin Weisbord (1976) developed the "six box model" as another model for diagnosing organizations. This model consists of six components: purpose, structure, relationships, rewards, leadership and helpful mechanisms. Weisbord (1976) explained the purpose of this model as a model allowing consultants to apply theories they know and to discover new connections.

Weisbord (1976) noted, "There are two main reasons why one might want to diagnose an organization: to find out systemically what its strengths and weaknesses are or to uncover reasons why either the producers or consumers of a particular output are dissatisfied" (p. 435).

Determining the underlying root cause is another reason why conducting an organizational diagnosis is important. There is often confusion between symptoms and root causes. A root cause is the underlying problem often masked by symptoms. Freeman and Zackrison (2001) describe symptoms and root causes with a medical metaphor.

Individuals will experience a high fever as a symptom to an underlying medical condition. In order to fully cure the fever, a medical professional must identify the underlying cause. However, this level of diagnosis may not always occur. As argued by Freedman and Zackrison (2001), "Many people settle for immediate, temporary relief they get by treating their symptoms; If they can endure it and it goes away, they've saved time and money" (p.27). One can argue that the temporary relief of symptoms is not diagnosing or treating the underlying problem. In turn, this could potentially cause more harm in the future.

The above metaphor illustrates the importance of finding and treating the root cause. The same can be applied to diagnosing an organization. Consultants and leaders, who choose to find and treat the underlying cause, can begin the diagnosis process with asking open-ended questions. The purpose of doing this is to gain perceptive from as many avenues as possible.

Alderfer (1980) describes three phases of a diagnosis: entry, data collection and feedback. I want to briefly describe the entry and data collection phases as they were specific to my experience with this capstone. Entry is the first phase of a diagnosis. Alderfer (1980) theorizes that internal (to the system) people cannot act as consultants to the system.

> All individuals have vested interests in their own organization. Even if individuals did not press their own interest, other members of the system would be unable to accept a consultant relationship from a peer, and the complete insider would be rendered ineffective as a result (p.461)

I did not experience a definite point of entry with this capstone. I've been a staff member of my organization for ten years and am familiar and comfortable with the operations of the organization. I found my experience to be the opposite. I observed the

participants as accepting and supportive of the diagnosis. Due to my personal experience and journey, to an extent, I disagree with Alderfer's perspective on internal consulting. Internal consulting can be essential for the growth and change of an organization. Internal consultants possess knowledge of background information, the system, and established relationships with people that are a benefit to conducting a diagnosis. Although, I must ask the question, will leadership accept my findings? Or would these be better received from an external consultant?

There are differences between external and internal consulting. For this literature review, I will focus specifically on internal consulting. Miriam Lacey (1976) describes the role of an internal consultant as being unique. These are usually individuals hired to serve as an organizational development professional for a specific organization. I also believe these professionals could be line managers/general managers interested in learning change management techniques to apply within their organization. My relationships with staff members, accessibility to schedules, and personal role within the organization contributed to the ease I experienced with understanding the background of the issues present within the organization.

Interviewing is a method of data collection. This is an opportunity to speak with staff members individually or as a group. "Individual interviews have a relationship-building quality if they are conducted competently and, as a result, are probably the most essential tool of any data collection" (Alderfer, 1980, p. 463). The data provided from individual staff interviews is rich. This point of the diagnosis provides the consultant with individual perspectives, archival documents, and a chance to observe reactions.

The diagnosis process is a way to determine the cause of the problem without

focusing on the symptoms. "The aim of an organizational diagnosis is to produce learning about the system for its members" (Alderfer, 1976, p.369). Taking time to really understand what is going on within an organization will produce a common understanding and ability to produce change if applicable.

Underbounded systems

As a consultant, it is important to understand the type of system you are entering so you can really navigate through the system and understand the contributing factors to the issues. Specifically for this literature review, I will focus on underbounded systems and how they are perceived. Alderfer (1980) theorizes two system types: overbounded and underbounded. But, the bigger question is, what is a system?

> A system is a set of units with interdependent relationships among them (p.269).

The systems are designed with boundaries, allowing exchanges to occur internally and externally. Alderfer identified three system categories: optimal, overbounded, and underbounded. The optimal system allows for just the right amount of permeability between the system and the outside. Overbounded and underbounded are the opposite extremes of optimal. Overbounded systems do not allow for much permeability, and underbounded systems allow for too much permeability (Alderfer, 1980). Is a system always bound to be one type versus the other? Based on Alderfer's definition of a system, I would argue the system type can be altered when there are changes to the units within. This could include the addition of a unit. How can one distinguish between the systems they are consulting to? Alderfer identified eleven interdependent variables that distinguish the difference between the two system types (see Table 4).

Table. 4. Alderfer's (1980) system type variables

1. Goals

2. Authority relations

3. Economic conditions

4. Role definitions

5. Communication patterns

6. Human energy

7. Affect distribution

8. Intergroup dynamics

9. Unconscious basic assumptions

10. Time-span

11. Cognitive work

The four variables that stood out most for this capstone included: goals, authority relations, role definitions and intergroup dynamics. I will focus specifically on these four variables and how these relate to the organizational diagnosis I conducted.

Goals are highlighted as things that partly define an organization (Alderfer, 1980). The lack of goals can cause confusion and uncertainty among individuals and groups in the system. The confusion can be twofold: either individuals are unclear about the goals, or unclear about which goals have priority. "Increasing the clarity of organizational goals or the degree of consensus about goal priority is associated with decreasing boundary permeability and decreasing the clarity of organizational goals or increasing the disputes about goal priority is associated with increasing boundary permeability" (Alderfer, 1980, p.270). Alderfer provides a detailed description of what to look for as consultants, but the

question remains, how can we achieve optimality?

The second variable to be aware of is authority relations. The boundary type of the system can be influential to the leadership style and vice versa (Alderfer, 1980). Within an organization the style of leadership impacts the organization as a whole as well as the individuals that are part of the organization. In an overbounded system there is usually a centralized and hierarchical approach to leadership. In this type of system, there is usually an agreement upon the goals, and purpose (Alderfer, 1980). On the contrary, the underbounded system results in unclear goals as well as a fragmented style of leadership. There will either be multiple authorities, or none (Alderfer, 1980). In my opinion, leadership is the important foundation and support to an organization. As consultants, during a diagnosis it is critical to review and understand the relationships with authority. Understanding how employees work with their leader can demonstrate the level of leadership involvement within the system and the level of comfort employees experience. These understandings will also help build the effectiveness of a feedback session.

The third variable is role definitions. "Individuals in organizations develop patterns of role behavior based on the expectations placed upon them by the organization modified by their own personal values, beliefs, abilities, and group memberships" (Alderfer, 1980, p.272). Often times, individuals will carry out responsibilities that are assigned to them as well as taking the initiative to find other responsibilities to complete. On the contrary, individuals may alter the responsibilities assigned to them by narrowing the focus of said responsibilities and altering the scope of work within their role. The style of authority may also impact the roles of group members. Leadership may not be

clear or direct about assigning tasks or defining, at the group level, the responsibilities. This can often be seen in an underbounded system if the authority is not clearly identified.

The fourth variable related to this capstone is intergroup dynamics. Intergroup dynamics is defined as relationships among various groups within the system (Alderfer, 1980). Alderfer (1980) breaks intergroup dynamics into two classes: 1. Task groups and 2. Identity groups.

> Task groups are defined by the kinds of work they perform and by the level in the hierarchy in which they are located. Identity groups refer to group affiliations that help individuals shape their personal identities (example: ethnic, gender, generation, and other groups determined by life experiences (274-275).

Alderfer theorizes underbounded systems will usually have intergroup conflicts between the identity groups whereas task group conflicts are more prevalent in overbounded systems. I would also note that tasks groups in underbounded systems may exhibit intergroup conflicts due to the lack of role clarity and leadership.

It is critical for a consultant to spend time determining the type of system they are entering in order to provide a successful diagnosis. Gaining a sense of understanding of the specific variables will give the consultant determination on if the variables can be changed to achieve an optimal system.

<u>Planning</u>

I was unable to locate literature specific to planning processes within AHCs. Again, I believe the lack of literature highlights the importance of this capstone and future research on this specific topic. Based on historical events, programs and regulations have been set in place as a reaction to a tragic event. I have not been able to determine if planning was done prior to implementation. The historical events

demonstrate the lack of proactive approaches with enhancing compliance.

        I reviewed literature that highlighted inaccurate planning in terms of projecting costs, demands and resources. This literature is relevant in highlighting how planning can be inaccurate, but it is not relevant to the purposes of this capstone.

History of organizations

        While the goal of this capstone is to determine why the IND core is not presently operating effectively, it is important to understand the historical events that shaped a centralized IND model as the history is a factor in the current state of an organization. For this capstone I am focusing on a specific unit within a large organization. Therefore, I will examine the literature on organizational history from this perspective. I will discuss the importance of gaining an understanding of the organization's history, and how history affects the current state. Following this, I will outline the history behind clinical research regulations.

        There are few practitioners that focus on the past when entering a client system. "Transformation cannot simply be mandated. To be effective, it must be undertaken in a way which builds on rather than runs over the past." (Kimberly & Bouchikhi, 1995, p.9)

        Kimberly and Bouchikhi (1995) argue that an organization is somewhat analogous to an individual. There is a culture that appears within an organization, which in turn produces an identity that is easily noticeable. (Kimberly & Bouchikhi, 1995). When attempting to understand behaviors of individuals, practitioners/clinicians ask questions about the individuals past in order to fully understand why they behave in a certain way. This same approach can be taken with organizations. Consultants can ask questions, and research the past to determine why the organization operates in a certain way.

> We would argue that without an appreciation for past experiences, present behavior and future action cannot be fully understood for people or for organizations (p.10).

This argument presents the value of an organizational biography. "Biography is a vehicle for illuminating the lives of individual people." (Kimberly & Bouchikhi, 1995, p.10)

Over the past few years, there has been an increase in awareness as to the benefits of a biographical approach; however, some still argue over the function of the biographical approach to research. "Some argue that they should provide comparable data for building generalizable theories, while others argue that they should provide a means for underlining uniqueness." (Kimberly & Bouchikhi, 1995, p.10) As I conducted my research, I found creating a biography of the IND core provided relevant knowledge that would benefit the current leadership, as well as providing external leadership and understanding of the uniqueness of our unit.

But, how can an organization's historical events be obtained? Simmons describes the data available from historical research as that of memories and paper records (Simmons, 1985).   Learning about the history of the organization can be gained through qualitative data, and a review of past records. Kimberly and Bouchikhi present a study demonstrating how history shapes an organization. In-depth interviews with the CEO and staff members were conducted over the course of five months. The purpose of conducting these interviews was to gather an understanding of the development of the company. Kimberly and Bouchikhi noted in their article, "The Dynamics of Organizational Development and Change: How the Past Shapes the Present and Constrains the Future", the limitations associated with the qualitative research approach. Individuals may not fully remember all of the details associated with the past. However, while there may be

limitations, the stories being told by each participant are the stories that shape the

organization's current state.   Simmons argues there is a need to build models to

understand distortion and fact (Simmons, 1985). She breaks her models into three

categories: distortions about involvement, distortions about time, and distortions noted in

the interviews. With the distortion of time, Simmons demonstrates the importance of self-

data (example: memories) because some things may be left out in the discussions. The

next aspect of the model indicates that individuals may alter in their mind the length of

time spent in specific relationships. The third aspect of the model demonstrates the

importance of observing body language and expressions during interviews. Simmons

was able to cross-examine her interviewees with paper documents to assist in recreating

the history (Simmons, 1985). Utilizing several methods of data collection can help

produce a more valid and reliable data set.

The authors demonstrate that learning the organization's history will assist in

understanding the current structure and aid in production of successful and effective

change within an organization. Kimberly and Bouchikhi state:

> And as biographies accumulate, the potential to do comparative work invariably
> increases, enabling one to examine the extent to which insights developed in one
> setting have wider adaptability and thus dramatically heightening the payoffs from
> this kind of work (p.17).

Over time, organizations change in terms of structure and culture. An organization

is shaped by its identity. Can-Seng Ooi (2002) described identity by noting "Albert and

Whetten defined organizational identity as the central, distinctive and enduring aspects of

the organization" (p.606), According to Can-Seng Ooi (2002) this type of theory can

marginalize the complexity of organizational change dynamics and decrease the reality

(p.606). Ultimately, this may provide individuals with a skewed opinion of an

organization based on a limited understanding.

How should history be presented to individuals? Ooi describes the following two processes for providing a packaged history to individuals. "The re-presentation of history involves interpreting the bygone for a uniformed public, and highlights the emotional dimension of communicating history, which has been taken-for-granted and under-theorized" (Ooi, 2002, p.607). I believe this statement highlights the importance of understanding history as well as learning effective ways to teach the history.

History is unique and defined as a narrative account of events. History is about facts of the past, but interestingly enough, these are facts that cannot be observed presently. Ooi (2002) stated "historical facts, meanings and significance have to be packaged for people" (p.607). The history needs to be packaged so that individuals can effectively understand what they are being taught without seeing it for themselves. A packaged past mainly consists of details of what happened, why it happened, and the significance of the events (Ooi, 2002). What is the motive for presenting a packaged history?

There are many reasons for presenting a packaged history. Ooi outlined the following reasons: traditions, reputation, claims and breaking away from the past. For this paper, I believed it was important to learn the history of the IND core in order to gain a deep perspective on the functioning of the core. In addition, I believe presenting these findings to current members and future members of the core will provide them with the facts of centralization and have an understanding of how to continue to assisting Investigators.

The dynamics of an organization are complex. "First, tapping into organizational

pasts is a complex process and we, as researchers, have to take into account and reflect upon our emotional responses to what we have accepted as history" (Ooi, 2002, p. 619). When we research history, our perception of what we read or hear may contribute to how we feel about the past. It is important that we do not allow inferences to get into the way of packaging history. "Second, we also re-present history, which our packaged pasts inevitably draw emotional responses from our audiences" (Ooi, 2002, p.619). When teaching people, we must be aware of the emotion that may be unleashed during the presentation. It is important to be prepared to manage these types of responses. These are important factors to take into consideration before researching organizational history.

Reviewing the past will guide individuals (organizations) to understand the behavior of the organization and learning about how to develop the future. Often times professionals wonder "why do we have to follow this process?" We may need to dig deep, but there is a reason the process was developed. Understanding the history of "why" will help organizations and managers build the knowledge base needed to define the reason a process is in place. I believe the history and past is really important as it paints the picture of what the organization has become today.

Clinical research regulations

As outlined in chapter one, there have been multiple events leading to the development of clinical research regulations over time. There is limited research on the effectiveness of the regulations developed as a result of tragic events. However, there have been articles published on the evaluation of IND support programs at AHCs.

"Complying with the FDA's regulations can be daunting and an overwhelming burden to faculty research who are rarely familiar with their obligations as sponsors of an

IND or IDE application" (Arbit & Paller, 2006, p.146). The University of Minnesota established an IND/IDE Assistance Program (IAP) in 2002 to assist Investigators with the IND/IDE process. The objectives of the program were two-fold: training/education for the research team about the regulatory progress and ongoing support to assure Sponsor-Investigator responsibilities are being met. Many people may wonder why such a program would be established at an AHC where research is high on the priority list.

The University of Minnesota established the program as a result of leadership concerns about the familiarly Investigators had about research regulations. "Unfamiliarity with the required regulations places the researcher and the university at risk of non-compliance. Research participants' safety is of course, the primary concern. Attempting to learn the regulations and how to apply them took valuable time away from conducting the clinical trials" (Arbit &Paller, 2006, p. 148). Arbit and Paller did not provide further explanation as to why learning research regulations stood in the way of conducting the clinical trials.   I think it would have been interesting to learn about the training physicians underwent prior to becoming Investigators. Perhaps, providing a more comprehensive training program for Investigators may have been an option.

The University of Minnesota documented the successes and failures of establishing the IAP. The program successfully established a system to guide Investigators in determining if an IND/IDE is applicable for their research. This is often a tedious task for Investigators and the additional level of support demonstrated a helpful tool for Investigators. In cases where an IND/IDE is required, Investigators often feel bogged down by the process. The establishment of the IAP proved to be a quick process for the establishment of research protocols. Arbit and Paller (2006) reported:

One researcher delayed progress on a study of a new surgical device for more than 12 months because he had no idea where to begin or where to turn. Within a week of contacting the IAP, a draft of the IDE application was completed and within a month, the IDE application was submitted (p. 152).

These two services provided investigators with support from experienced regulatory personnel, who contribute full time efforts to understanding FDA regulations. Other report successes with the establishment of the IAP include: development of case report forms, monitoring plans, and drug accountability logs, working with external drug vendors, Coordinator training, and assisting Sponsor-Investigators with reporting.

Along with the successes, there was some learning. The biggest challenge faced by the staff of the IAP was resistance from some Investigators, who managed and submitted their own INDs/IDEs successfully. "These individuals were reluctant to change and to accept regulatory assistance and guidance" (Arbit and Paller, 2006, p.152). To my knowledge (Arbit & Paller, 2006), when a new program is established without buy-in from all stakeholders, resistance is met. This was a key lesson learned from the University of Minnesota. On several occasions the FDA refused to provide information to the IAP regarding an IND because the IAP director was not the IND Sponsor. In turn, the IND Sponsor wrote a letter granting permission for the FDA to communicate to the IAP director.

Overall, the IAP program provided much needed support to the Sponsor-Investigators across the University of Michigan. The article did not specify if the successes and lessons learned were noted by the IAP staff or Investigators. The program was set-up to be a support for Sponsor-Investigators rather than take on the full responsibilities of a Sponsor. Is this the best type of office? Or would it be of more benefit to have a centralized Sponsor?

"In 2004, the National Institute of Health (NIH) launched the "NIH Roadmap for Medical Research" to address roadblocks to research and to transform the way biomedical research is conducted by overcoming specific hurdles or filling defined knowledge gaps" (Berro et al, 2011, p.2). One of the objectives of this program was to enhance translational research. The IND/IDE task force was put together to evaluate the support for Sponsor-Investigators. In 2008, the task force developed a pilot study to evaluate the current system for Sponsor-Investigator support at AHCs. The study consisted of surveying twenty-four AHCs that provide regulatory support. The survey was administered to the regulatory representative at each AHC. The questions were developed to assess the level of support offered at each AHC.

The results demonstrated a wide range of regulatory support provided at each AHC. The various models used to support AHCs include: Independent, Consultation and Full service (see Figure 2). These results evaluate three different types of support models within AHCs. As you noted in the figure below, there are positives and negatives to each model. Department A appears to be a full service model type. I wanted to highlight the research evaluating these various models to highlight the importance of being aware of the positives and negatives associated with each. " The NIH Roadmap for Medical Research and the CTSA initiative have contributed to increased recognition of the complexities introduced by innovative clinical research conducted at AHCs" (Berro et al, 2011, p. 6). Overall, the survey reinforced the need for regulatory support programs at AHCs. The programs will continue to provide a level of relief that professionals with solid regulatory experience are overseeing the conduct of clinical research.

Figure 2. Institutional support of Sponsor-Investigators

Models of Institutional Support of Sponsor–Investigators*

Model	Strengths	Weaknesses
Independent: Investigators are responsible for all IND/IDE regulations and responsibilities	• Investigator autonomy • No additional institutional requirements beyond complying with IRB and FDA regulations • Investigators may view this system as less bureaucratic	• High variabi and applicat regulations • Lack of insti of, and invo managing, institutional • "Reinventin each investi processes ar responsibilit • High potent issues to aris research
Consultation: Investigators can access regulatory expertise to help with all aspects of the IND/IDE process	• Provides a mechanism for some level of institutional involvement and management of institutional exposure • Enables institution to track IND/IDEs • Allows for the potential to define consistent institutional best practices • Provides opportunities to better support department/division defined models	• Investigator need to inte office • Potential for communicat between cer office and lc and investig
Full service: An institutional official or office ensures that individual sponsor investigators meet all IND/IDE requirements and responsibilities	• Permits the implementation of one standard approach for sponsor investigators to manage IND/IDE responsibilities across an entire institution • Allows for full tracking of IND/IDEs • Allows institution to develop required training and/or certification • Greater institutional control of sponsor regulatory risk • Significantly assists investigator in meeting sponsor responsibilities • Allows for centralized management and oversight of monitoring and/or auditing activities	• Potential for approving/in research if c adequately • Potential for investigator areas/investi more/quicke lower-volun areas/investi • Potential for and time to investigator- projects

Illustration 1: Figure 2: Berro et. al, 2011, p.6

Again, there is a gap of literature evaluating the successes and failures of implementing regulations and rules within the field of clinical research. The purpose of presenting the above literature was to validate the need for some level of regulatory support within an AHC. In addition, the gap within the literature validates the importance of this capstone.

The literature for this capstone is very sparse; however, the lack of literature

highlights the need for future research to be conducted within the field of clinical

research. The literature I did present within this chapter highlights the importance of

learning the history of an organization, understanding underbounded systems, planning

and review of clinical research support programs.

CHAPTER 3

METHODOLOGY

The centralized IND core was developed and implemented to resolve non-compliance issues among Sponsor-Investigators; however, non-compliance issues were still noted on audit reports after the implementation of the centralized IND core. There are several assumptions I have developed over the past two years leading to my interest in exploring the hypotheses outlined below.

The first assumption is, due to a lack of planning, the core is not fulfilling all Sponsor obligations. Over the past two years I have been concerned with the lack of Sponsor responsibilities remaining unmet by the centralized core. In addition to my observations, the lack of fulfillment has been documented as major findings by the research services office. The three responsibilities not being fulfilled by the centralized core include: monitoring, drug accountability, and training.

The first responsibility not being met is monitoring of research protocols. I have met with the IND core manager on several occasions to discuss monitoring. The core manager expressed her concerns with being over-worked with other obligations. She did not feel she could dedicate additional time to complete monitoring. We both brought this concern to the Sponsor-Representative, who in turn confirmed the importance of the tasks, but was comfortable with the lack of monitoring at this time due to the annual audits conducted by research services. While I accepted this answer, I am still concerned with the lack of monitoring. I began to question the clarity of our role as a centralized core. There are multiple responsibilities associated with being a Sponsor. Often times when an Investigator takes on this additional role, they are supported by multiple

administrative staff members. The centralized model took all associated responsibilities away and only hired one full time administrative staff member. These actions left me wondering what type of model the core was designed to be. Was the core designed to be a full service IND core?

The second responsibility not being fully met is documentation of drug accountability. There is a lack of documentation between all working parts of the core (drug production, handling, and administration). To my knowledge, each sub-group is managing their own documentation; however, there is a lack of collective documentation of these records. I'm concerned with the lack of collaboration among the key groups of the core. Prior to centralization, these sub-groups managed their drug accountability separately. I would have assumed a collective area for managing documentation would have been put in place with centralization. I began to wonder if the goal of centralizing was to improve document management practices or possibly some other hidden motive.

The third responsibility not being met is training. A Sponsor is responsible for training Investigators on regulations and providing oversight. During my first year of managing the core, I noticed the Sponsor was not fulfilling the responsibility of training. Training Investigators on regulatory requirements of protocols involving radio-pharmaceuticals is important. The lack of training often has me wondering if these Investigators really understand the radio-pharmaceutical they are investigating and their obligations as an Investigator. I have often witnessed an Investigator submit a protocol to the IND core, without a fully written protocol, and the essential documentation needed to conduct an IND related trial. In these special circumstances, the IND core manager has taken time to work directly with the Investigator to ensure they fully understand the

requirements of an IND application.

The second assumption is, due to role identification, the core is not operating effectively. I was asked to step in and help "clean up" the files after issues of non-compliance were still found on audits. Shortly thereafter, I was appointed an operations manager for the core. My role is to oversee, support, design processes, and supervises the core manager. My involvement with the other members of the core is in-direct. Over the past two years, I have worked closely with the core manager on brainstorming monitoring plans, drug accountability tracking, and training programs. We've developed templates, but we have not been able to implement any of them to date. Since, my involvement is limited; I haven't felt comfortable trying new plans. Furthermore, I'm not clear on the specific responsibilities of the indirect members of the core.

The core manager and I meet monthly with the Sponsor's authorized representative; however, the regulatory manager and cyclotron manager are absent from these meetings. I'm concerned that the absence of these key members is hindering the effectiveness of the core. Due to the lack of clarity with the delegation of roles and responsibilities, the core is not operating in the way it was structured to operate.

At the time the IND core was developed and implemented, the core supported four INDs and eight protocols. Over the past five years, the core has grown to manage ten INDs, and thirteen protocols. As previously mentioned, I supervise the IND core manager. I meet with this individual on a monthly basis to review tasks and to discuss issues (if any) that may have arisen within the monthly period. Our discussions are mainly centered on the document management process and development of operational processes. The core manager is expected to maintain complete files for INDs that were in

existence prior to centralization. Attempting to locate historical documentation has been challenging and time consuming. These tasks are expected to be completed as well as maintaining ongoing documentation and communication.

My third assumption is the goals of the core have not been made clear. Initially, I had a very limited understanding of the IND core and the purpose it served within the department. I also had a very limited understanding of the role of Sponsors. I educated myself by reading section 312 of the CFR (regulations specific to INDs). Sponsors have specific responsibilities and per FDA regulations must be met. I do not believe leadership clearly identified if the centralized core was going to handle the full responsibilities of a Sponsor.

My goals for this capstone are to learn more about the rationale of developing a centralized core, and understand why the IND core is not functioning as a full service centralized IND core. The hypotheses I will explore are:

Hypotheses:

- The centralized model was set in place without clear objectives.

- The IND core is not operating in the way it was structured to operate.

- The IND core is understaffed and unable to fully carry out the level of responsibility associated with being a Sponsor.

- Future expansion was not included in the planning when the centralized model was implemented.

Investigative methods

In order to fully explore these hypotheses, I will conduct two sets of interviews: background and current state. The purpose of these interviews is twofold: to determine

the key reasons for creating a centralized structure, and to determine if the IND is presently functioning effectively. In addition to conducting interviews, I will review audit reports, job descriptions, regulatory files, and email communications. I attempted to locate a documented vision, and business plan, but was unsuccessful.

Background interviews

In order to fully understand the rationale for the development and intended structure, I will conduct five in-depth interviews with key stakeholders. The participants chosen for these interviews were key departmental personnel involved in the decision to centralize the IND core and those who were hired as support personnel for the core. I selected the departmental leaders so I could understand why the centralization was implemented and understand the intended operational structure. I selected the administrative personnel so I could fully understand how the IND core is operating. Below is a description of the responsibilities associated with the participants I selected for the interview protocol.

Participant 001 was a member of the AHC for about five years prior to moving on to a new position. While he was at the AHC his responsibilities varied. He was hired to oversee the administrative aspects of research, as well as assist with laboratory duties. Soon after his hire date, his duties were extended to administrative support for the IND core.

Participant 002 has been a staff member of the department since 2000. Her role in the department is to ensure regulatory compliance, assist Investigators in preparation of audits, and serve as a liaison between the department regulatory committees, and the IRB.

Participant 003 was a part of the department for about five years before moving

on to a different AHC. Along with numerous other tasks (clinical and research), he was charged with maintaining a senior leadership role within the IND core.

Participant 004 supports the IND core by writing the Chemistry, Manufacturing, and Control (CMC) sections of the IND application, supplies drug accountability, and manufactures the IND related Radio-pharmaceuticals.

Participant 005 has been with the University for nearly twenty-five years and is responsible for overseeing research within the department. He assumed the role of Sponsor at the start of 2011.

I decided not to interview two groups of individuals from the background interview process: past Sponsor-Investigators, and personnel from OHR. The first group includes four previous Sponsor-Investigators. I decided not to interview these four individuals because I did not believe they would be able to provide me with the specific reasons for centralizing INDs nor insight into the current operational structure of the core. While their input and perspectives of the core is valuable, I did not believe it was relevant to this capstone. The data I am attempting to collect is to determine the operational effectiveness within the current centralized core.

The other group I will not interview personnel of OHR. The previous Director, who was involved with the development of the centralized office, is no longer an employee of the organization, and I did not have a way to contact this individual. The remaining individuals of OHR had limited involvement with the development and implementation of the core. In addition, one individual was not employed with the organization at the time of implementation. I made the decision to exclude these individuals based on the above noted factors.

<u>Interview protocol</u>

  I will use a seven-question structured interview process (Appendix A). There are six structured questions and one open-ended question which allow the participants to provide additional information about the history of the IND core. The purpose of the background interviews is to gain an understanding of the history behind the development and implementation of the centralization. The content of the questions focuses on the following: the structure of INDs prior to centralization, when the idea was born, what the rationale was, who led the redesign, the vision of the centralized core, and the communication mechanisms used to inform Investigators of the change.

  Question one: Can you provide information on the operational structure of the IND core prior to the implementation of the centralized model? I framed the first question to learn about the operational structure of IND related research within the department prior to centralization. I wanted to hear from the core members how they perceived the way in which decentralization was operating. My hope with these responses is to determine how the IND related protocols were managed prior to centralization.

  Question two: When did the idea of a centralized IND core come about? This question is designed to learn when the idea was first born. I want to learn of the time period for this thought process.

  Question three: What was the rationale for creating a centralized IND core? The third question is designed to learn what caused the department to change to a centralized structure.

  Question four: Who led the re-design of the IND core? The fourth question is

designed to gain insight as to whether the leader of the redesign was an individual or group.

Question five: How did you envision the operational structure of the centralized IND core? The fifth question is designed to learn the intended structure of the centralization. I would like to understand how the leader (and those selected to be members of the core) planned to manage the associated responsibilities of a centralized service.

Question six: What mechanism(s) did you use to inform Investigators throughout the University of the Re-design of the IND core? The sixth question is designed to learn what mechanism was used to inform previous (and future) Sponsor-Investigators of the planned centralized core. With these responses, I intend to gain an understanding of how individuals were informed of the new process.

Question seven: Is there additional information about the background development of the IND core that has not been discussed so far in this interview? The seventh question is designed to be open-ended and allow the participant to provide additional information about the background of the core.

I will contact each participant via email requesting their participation in the interview. After agreement to participate, I plan to schedule private individual interviews with the five participants. I will meet with three of the participants in person, and two on the telephone due to distance. At the beginning of each interview, I will remind each participant that their participation is voluntary and the interview will be stopped at any time if they feel uncomfortable.

I will take extensive hand-written notes during the interviews. These notes will

include documentation of responses, observation of tone, and body language. At the conclusion of each interview I will write some field notes which will include my thoughts and feelings about the interview.

<u>Current state interviews</u>

In order to fully evaluate the effectiveness of the centralized IND core, I will conduct in-depth interviews with three current staff members of the IND core as well as one external member. I selected the administrative manager, the sponsor's authorized-representative and the cyclotron production manager for participation in these interviews. I selected these individuals as their roles keep the core functioning.

There are three groups that will not be interviewed for this capstone: Radiologists, Investigators using the core, and administrative staff of OHR. I decided to exclude these groups for a variety of reasons, but mainly because their involvement with the core is limited. The Radiologists are called upon to provide scientific input for drugs that are new to the core. A new IND has not been written or submitted within the last two years therefore, their expertise has not been needed often. They are responsible for collaborating with non-departmental Investigators on the conduct of the radio-pharmaceutical component of the protocol, as well as for administering the radio-pharmaceutical. I selectively excluded this group; they are indirectly involved with the aspects of the core.

The second group I decided not to interview for this capstone is Investigators and research staff who utilize the IND core services. These individuals are valuable to our core as they request our services and keep the core running. To my knowledge, there has only been one complaint about the effectiveness of the centralized core. The complaint

was duplicate efforts were occurring. The Investigator held an IND for a separate drug (one not produced by this department). Since this was the only complaint I am aware of, I did not believe interviewing Investigators would provide much useful information for the purposes of my data collection. Their opinions and comments are valuable however**;** the focus of my data collection is on the internal infrastructure of the core.

Administrative personnel from OHR were not interviewed as well. I decided to exclude these individuals because their expertise is needed if the members of our core need assistance with regulatory guidelines. These individuals are not a part of the daily operations or infrastructure of the core. Due to their limited involvement I will not include this group in the interview process.

Interview protocol

There are ten questions included in this current state interview protocol (Appendix B). Of the ten, seven questions are open-ended as I want to investigate my underlying assumptions. The remaining three questions are close-ended questions. If I feel additional information is needed at the time of the interview, I will ask the participant to elaborate on their response. The content of the questions is centered on the current operational structure of the core. Because the purpose of these interviews is to hear from each key member their perspective on the current state and learn if they are aware of a future plan for growth, the questions are framed to facilitate my understanding of each participant's perception.

Question one: can you give me an example of what is working well about the IND core? This question uses an appreciative inquiry type format. I would like to hear from each key member their view about the strength of the core.

Question two: How would you describe your role within the IND core? This question is designed to ask each participant their role in the core. I want to understand how they view their role in the core, as well as their role with the other core members. The purpose of the question is to confirm or disprove my hypothesis that the core is not operating in the way it was structured to operate.

Question three: Can you provide information on the current operational structure of the IND core? This question is designed to learn from each participant the current operational structure of the core. My intention with this question is to learn more of the daily operations from the perspective of each participant.

Question four: What is the mission of the IND core? This question is designed to learn how each participant views the mission of the core. The purpose of this question is to determine if the perceived mission is viewed similarly among all participants.

Question five: Is the IND core satisfying all responsibilities associated with the role of Sponsor? This question is designed to learn if the core is satisfying all responsibilities. The intent with this question is to determine if each participant is aware of unfulfilled responsibilities.

Question six is: What are the number of INDs currently active under the core? What are the number of protocols currently active under the core? This is designed to determine if each member is aware of the number of IND's and protocols being held within the core. The purpose of this question is to determine if each participant is aware of how the core has grown over the past few years.

Questions seven: Do you have a limit on the number of INDs and/or protocols your core will support? and question eight: How do you plan to handle management of

additional INDs/protocols? These questions are designed to learn about the projected future of the core. My goal with these two questions is to determine two things: if the core has set a limit on the number of INDs and/or protocols it will manage, and if plans are being developed for the future of the core.

Question nine: What mechanism(s) are currently in place to inform potential Investigators of your core? This question is designed to learn about the communication mechanisms (or lack of) in place to notify potential Investigators of the services. I want to know if there is an effective process in place to inform Investigators of the core services. The purpose of this question is to learn more from each participant of the structure.

Question ten: Is there additional information about the IND core that has not been discussed so far in this interview that you would like to add? The purpose of question ten is to allow the participant to provide additional information that was not covered in the above structured interview questions.

I will contact each participant via email informing them of the purpose of this capstone and requesting their participation in the interview process. I plan to conduct in-person interviews in a private office within the department. All participants are employees of the organization and should be available to meet in person.

At the beginning of the interview, I will remind each participant of their right as a participant and the plan for maintaining confidentiality. I plan to record each interview with a tape recorder and document the responses to each question on paper, and include observations of tone, and body language. At the conclusion of each interview, I will document my thoughts and feelings from the interview.

Confidentiality

In order to maintain privacy of the participants involved in the interviews, all identifiable information (organization name and location, participant names, and titles) has been removed from this capstone. The organization has been assigned a fictional name, and each participant has been assigned a unique participant ID number.

The documented notes and tape records will be stored in a secure cabinet outside of the office. The purpose for securing these documents is to maximize the participant's privacy. At the completion of this capstone (November 2012), the notes and tape recordings will be destroyed.

Other information

In addition to conducting interviews, I examined multiple documents relevant to the IND core (Appendix D). I reviewed and compared audit reports pre and post centralization. In addition, job descriptions of the IND core manager, and correspondences with the FDA of the change in Sponsorship were reviewed.

My role

My role within this capstone is two-fold: participant and observer. I have been a member of the organization for ten years and spent the past two years as an active participant in the IND core. My role within the core is to oversee and assist with building the operational structure and supervise one of the staff members. My direct supervisor is one of the interviewees and the others are colleagues that I have worked with for the past ten years.

Due to my leadership role within the core, I am involved in the daily operations and responsible for promoting the mission of the core, as well as finding ways to remove barriers for my staff and other members of the core.

Throughout my two years leading this core, I have often observed ways in which the structure of the core is flawed. I stepped into the position without fully understanding the level of complexity involved with the role of a Sponsor and did not have a clear understanding of each individual's role within the core. Soon after my involvement began, I hired the IND manager with a narrow understanding of the number of tasks associated with the role of core manager.

Over the past two years, I have listened to and dealt with numerous complaints and concerns from the staff about the operations within the IND core. These complaints included: not fully understanding their role, feelings of being overwhelmed by the number of tasks associated with job functions, and feeling unsupported by senior leadership.

In addition, I have observed a lack of monitoring protocols. Monitoring is one responsibility associated with being a Sponsor. . As described in Chapter 2, the Sponsor is responsible for monitoring research protocols conducted under an IND. The lack of monitoring has often been discussed among all staff members over the past two years.

These frustrations and concerns of the staff members have left me feeling helpless. As the Operations manager, I do not believe I am giving them the support and direction they need to feel successful in their roles. About a year ago, I made the decision to perform an organizational diagnosis of the core and determine the root cause of the problem.

Controlling for bias

"Reducing diagnostic bias should begin with an understanding of its cause" (Armenakis, Mossholder, and Harris, 1990, p.563). As an insider of the core, I need to be

aware of things that can cause me to have a narrow perception of the ineffectiveness of the core. There are a few factors that may cause bias in this capstone. The first is, I have been an employee with the department for ten years and indirectly heard stories about the implementation of the core. The second way bias may be present in this capstone is my selection of participants and the third is my relationship with each participant. .

I always assumed the core was set-up as a result of hiring a new division chief. I based this assumption on previous off-line conversations I have had with members of the department. In realizing this may not be the full story, I decided to incorporate background interviews into this capstone. Understanding the history of creating and implementing the core from several key stakeholders within the department is important because it will provide me with knowledge of operations I was not aware of previously. In addition, I will cross reference these interviews with documentation describing the reason for implementation. Cross referencing will help eliminate bias as I will be checking against another source.

The second factor of bias is the selection of participants. I selected these participants based on my knowledge of their involvement with the core. The information I gather will be limited to the view of insiders. I wanted to gain a more global perspective of centralization by including members from the research support office, whom were involved in the development, but I was unable to do. The member who was involved in the centralization is no longer with the University and I was unable to get in contact with this individual. I tried to control bias by evaluating the role of each participant and reviewed previous documents outlining personnel within the core.

The third factor of bias is my relationship with each participant I will interview for the current state of the core. Over the past two years, I have had many discussions with each of these participants; I may have a predetermined mindset of how they will answer each question asked. In order to minimize this, I will tape record each interview conducted. This will allow me the opportunity to spend time listening to the interviews prior to my data analysis and notice if there were points I missed.

My goal with the information I gather from this capstone is to determine the best way to improve the effectiveness of the core. In order to fully do this, I believe it is important to highlight all of the issues I may uncover**.** I do not want participants in these interviews to feel they could be the problem, based on their performance. These participants may feel defensive and worry about the security of their job if these feelings arise. This concern may cause me to cover over some performance issues as I analyze my data. As you read this paper, I ask you to consider the following:

- Did I miss specific history because non-departmental stakeholders were not interviewed?

- Should I have interviewed a sampling (random) of Investigators who utilize the core?

- Did I ignore performance issues of certain staff members?

In summary there are two sets of data collection for this diagnosis: background and current state. Both sets of interviews and review of relevant documentation will occur over the course of three months. After all data is collected, I will review and analyze the results. I will specifically look for themes throughout the data and confirm or disprove

the hypotheses outlined above. The results are presented in the next chapter.

CHAPTER 4

RESULTS

Data summary

In order to obtain the information to confirm or disprove my hypotheses, I conducted two sets of interviews: background and current state, and reviewed audit reports, job descriptions, regulatory files, and email communications. The data collection process was conducted over a total of eight weeks. I will begin this section with the results of the background interviews and identify the themes which emerged during data collection. Then, I will summarize the current state interviews and the themes which emerged. I will conclude this section with a summary of the data in relationship to my hypotheses.

Summary of background interviews

I began the data collection process by conducting background interviews with several key stakeholders within the organization. The background interviews were conducted over a course of four weeks. The purpose of these interviews was to learn the rationale of creating a centralized IND core and to determine if clear objectives were developed for the operational structure of the core. As described in the methodology section of the paper, I selected individuals with active roles within the core to participate in the interview process. My goals for selecting these individuals were to understand the decision process for centralization and learn about the perception of those who were charged with outlining the infrastructure of the core, as well as those who were managing the core in its infancy. I contacted each individual via email requesting their participation in the interview. Details of the purpose of the interview and capstone topic were included

in the body of the email and I asked if they were willing to participate. Confidentiality

and privacy were assured. As a result, participant's names and titles have been removed

and the interviewees have been randomly assigned numbers ranging from 001-006.

Potential participants were requested to respond directly to me via email with their

decision. All five participants responded quickly with their willingness and desire to

participate in the background interview process

The data collected from conducting the background interviews included the

opinions of staff members about the history influencing the development and

implementation of a centralized IND core. Five individuals were interviewed on the basis

of their role within the core at the time of implementation. Three of these interviews

were conducted in person while two were conducted via telephone. The results of the

interviews are presented below in relationship to each question asked.

Question number one: Can you provide me with information on the operational

structure of the IND core prior to implementation of the centralized model? The

responses given by all participants were very similar. "There was no structure prior to the

centralization" was the statement made by four of five participants. INDs could be held

by Investigators, allowing them to take on the added responsibility of a Sponsor

(Sponsor-Investigator). One participant even went as far as to describe the structure as a

"free for all." Another participant named two individuals in the department that often

filled the role of Sponsor-Investigator.

Question number two: When did the idea of a centralized core come about? One

participant was able to provide me with the specific time frame that the idea of

centralizing was discussed—September 2006. The other participants were not clear on the specific time frame, but seemed to have an idea it was around 2006/2007. Two participants explained the idea came about as a response to non-compliance. This date correlated with the time frame provided by the participants and documents within the core. I cross-checked the dates with reports of the audit findings.

Question number three: What was the rationale for creating a centralized core? Through the responses to this question I learned about a significant tragic event within the AHC, which led to the redesign of the IND model within Department A. All interviewees identified non-compliance as the major reason. One participant explained "the rationale for creating the core was for efficiency, to minimize errors, and quality control. In addition, the core was developed to prioritize the importance of specific INDs." Another participant specifically stated "the idea came about after OHR audited IND related protocols. Leadership of the AHC decided to implement a centralized office and asked Department A to be the pilot." A third participant stated "senior leadership at the AHC approached senior leadership within Department A with the problem of non-compliance and asked them to determine the best solution. With that, Department A decided it was best to implement a centralized office."

Two participants provided a more thorough background as the reason the core was developed and implemented. Jessie Gelsinger's case - - death of a research participant in a gene therapy trial-- was the primary factor in the structure change of managing INDs. This incident occurred in September 1999. The death of this research participant put the University in the spotlight throughout the research community.

The death of this research participant sparked changes throughout the AHC. While many individuals may not see this at a national level, the changes are noticeable at the AHC. Shortly after the tragic incident, the AHC developed OHR, a centralized office to oversee the conduct of human research. One of the goals of this office was to audit all research protocols considered high risk. "The AHC addressed the problem head-on and took aggressive steps to create and implement the Office of Human Research." (Zhou, J, 2003) The members of OHR took their roles very seriously and began developing a process for auditing high risk protocols.

Department A was one of a few departments throughout the University with high risk protocols--protocols using non-FDA approved agents-- and a production facility. Compliance issues were noted on eight protocols. OHR personnel shared their findings with departmental senior leadership and requested they implement a corrective action plan. Senior leadership agreed upon a centralized model to control compliance. "One participant noted the additional reasons behind centralization were to improve efficiency, and quality control."

Question number four: Who led the redesign of the core? The responses from the participants varied. Two of five participants identified two groups involved in the development of the centralized core: senior leadership from OHR and senior leadership from Department A. One participant indicated the Compliance Director within the department was also included. Another participant also indicated the newly appointed authorizing representative was involved in the redesign as well. One participant was not sure who was involved in the redesign of the core.

Question number five: How did you envision the structure of the IND core? This question was designed to learn how each member imagined the core would operate. The responses had a mix of similarities and differences. One participant responded with "I can tell you my ideal vision, but I will tell you my vision based on the resources provided by the AHC. My vision was to build an organized regulatory submission process between Investigators, the core, and the FDA. This was the only thing the centralized core could handle with the limited resources." Another participant explained "I hoped the core would limit the number of active INDs and protocols. I imagined there would be more resources." A third participant stated "Not much changed from my perspective." The remaining two participants had similar responses. They both indicated they imagined the core as being one single point person to manage all regulatory responsibilities and monitoring.

Question number six: What mechanism did you use to inform Investigators of the redesign of the core? All five participants were uncertain of the exact method of notification. Two stated they were unsure, two thought the Investigators were notified via email, and another participant thought the notification was announced at a departmental research meeting and then disseminated to collaborators.

Question number seven: Do you have any other additional information you would like to share? Four out of five participants responded with "no. I do not have any additional information." One participant added their opinion on the positives and negatives to centralization. The participant stated "The disadvantage to a centralized model is the lack of expertise per radio-pharmaceutical. In a decentralized system, the Sponsor-Investigator has all of the knowledge needed to run the protocol."

<u>Follow up questions</u>

I did not ask follow up questions during the background interview portion of this diagnosis.

<u>Current state interviews</u>

The second set of interviews I conducted was with four of the staff members of the IND core. These interviews were conducted over the course of two weeks. My goal with selecting these participants was to gain insight about their perception of the operational structure of the core. I emailed each staff member informing them of the purpose of this thesis and requested their participation in the interview process. I contacted each individual via email requesting their participation in the interview. Details of the purpose of the interview and capstone topic were included in the body of the email and I asked if they were willing to participate. Confidentiality and privacy were assured. Each participant responded within twenty-four hours to my request and agreed to participate. The purpose of these interviews was to gather data relevant to the current operational state of the core. I asked participants 004, 005, and 006 the specific questions outlined in appendix B. Questions one through seven were focused on the current function of the core; while, question eight was structured to collect data on the plan for the future. I modified the questions for the interview with participant 002 (see Appendix C). I made the decision to do this based on my understanding of their indirect role with the core at this time.

I began the interviews with an appreciative inquiry question. I did this so I could learn from these participants what they find is working well and to hear positive

feedback. Question number one: Can you give me an example of what is working well about the IND core? All four participants provided positive feedback to this question. Three participants described the communication with Investigators to be working well, as well as document management. One participant included the coordination between the Investigator and FDA is also working well. Some of the examples given by the participants include: "documentation of drug accountability seems to be running smoothly." Another participant stated "It seems as if our documentation is well organized, our communication with the FDA is going well, and we are reaching out to Investigators to assist them." A third participant stated "The electronic files have been setup; communication with study teams is going well. We are starting to get protocols before they are submitted to the IRB for review."The fourth participant explained "We now have a point person for maintaining INDs, tracking information necessary for annual review of the INDs, compiling information and training."

Question number two: How would you describe your role within the IND core? Each participant responded with how they view their role within the IND core. Participant 005 chuckled and responded "Right now to try and stay out of people's way. My role is a high level voice to ensure the key vision of the office is being executed. The details of how that happens, I rely on the people on the ground to do." Participant 006 responded "I am the core. I do everything. I handle the submissions, communication between the study teams, the cyclotron, and the Nuclear Medicine Physicians. I maintain the files. I do everything. The only thing I do not do is scientifically review the protocols, but nobody does that." Participant 004 responded "My responsibilities are clearly having to do with preparation of the CMC section for submission and scheduling the tracer for

research participants." Participant 002 chuckled when I asked what her role within the core was. She responded "Supporting performer. At this point, I am trying to pull together a lot of the missing information for the INDs that were open prior to centralization."

Question number three: Can you provide information on the current operational structure of the IND core? Three of four participants were asked this question. All three responded with their view of the core operations. Participant 004 described the core as being lopsided. He stated "Some things run smoothly. There needs to be higher level oversight." Participant 005 described the core structure as being pretty simple. "There is a single person who runs the core with oversight from operations, collaborative support from compliance; the compliance manager is important to provide regulatory expertise. The core manager also has scientific support from physicians in the department. Part of the core manager's job is to understand what is needed and to effectively reach out to these various people." Participant 006 responded with a detailed overview of the process from protocol initiation through start up. "An investigator usually contacts a Nuclear Medicine physician and then the protocol goes to Radiation Safety and PET Ops for review. The Nuclear Medicine physician is supposed to review the protocol and represent the study team. I personally do not believe some of them review the full protocol. Somewhere along the line I get involved, usually after all that has happened. Which shouldn't be --I should be involved from the beginning. I review the protocol and send emails to the study team about the process of electronic file setup, protocol setup (if applicable). If they do not have a proper protocol, I do work with them to develop it. Then everything gets submitted to the IRB. Once it is approved by the IRB, I submit the protocol to the FDA. After that I work with the coordinators – if they have one-- on

conducting a protocol under the IND office.

Participant 006 also added "About fifty percent of the time these Investigators do not have Coordinators. Or if they do, they are overworked or have never done this type of research before."

Question number four: What is the mission of the IND core? A mixture of responses was given to this question by three of four participants. One participant was not asked this question. One participant described the mission as being a support for Investigators. Participant 004 explained "the overall vision was to have one place where all radio-pharmaceuticals were managed. This made sense for the cyclotron facility. However, there was and still is insufficient regulatory oversight when the centralized core was implemented. We need some type of regulatory office or auditor that is very hands on and present to work with each group of the core." A third participant explained "I kind of feel like the idea is very good. It is good to have a centralized office that provides all of the services needed for these Investigators to do their research. It is also good for outside groups. The thing that went wrong with the mission is it wasn't properly thought out. There is no business plan and it's impossible to do all of the things that need to be done properly."

Question number five: Is the IND core satisfying all responsibilities associated with the role of Sponsor? All four participants responded "no" to this question. I then followed-up by asking all four participants which responsibilities are not being fulfilled and why. Three of four participants described monitoring as the one responsibility not being fulfilled and believed the reason was due to the lack of resources. One participant explained training is also a responsibility not being satisfied by the core. Another

participant answered this question by stating there is a lack of high level oversight of the core. A variety of responses were received when participants described the reason why the core is not satisfying all responsibilities. Two participants explained there is a lack of resources to support the responsibilities and one participant stated there needs to be regulatory support for the core. Participant 002 stated "We are trying, but not full there yet. We need to be able to provide all of the services associated with being a Sponsor. We need monitoring, collection of data on a regular basis. Collecting the data regularly may make the annual report submissions easier." Participant 006 responded "you need more than superficial oversight. You need a separate monitor that goes out on a regular basis, who has a good rapport with the group. This person would also train the site staff." Participant 005 stated "we need a strategy for monitoring. Right now, we have a semi-strategy: auditing by OHR and monitoring by the PET center and the IRB. We need to come up with an explicit vision and plan for how the core will monitor. Maybe the plan is to allow those groups to do the monitoring and find a way to coordinate our actives with those groups and obtain the appropriate documentation."

Question number six: What is the number of INDs currently active under the core? What are the numbers of protocols currently active under the core? Three participants were asked this question. One participant was not able to answer and two participants, who are involved in the daily operations, were able to answer with explaining there are ten active INDs, and thirteen protocols under the IND core.

Question number seven: Do you have a limit on the number of INDs and/or protocols your core will support? This question was asked to three of four participants. Three different responses were received. Participant 005 explained "It depends on the

research. Everything should be driven by the research. If INDs are active and being used and people are doing research, I would continue to keep them open. That is the purpose of the office." Participant 006 stated in a tone of laughter "apparently not. There should not be a limit, but there should be more staff to provide the service. We are not providing the service. We are basically treading water and trying to keep our heads above it. "

Question number eight: How do you plan to handle management of additional INDs/protocols? This question was not clearly answered. Participant two answered "I think this is an executive type decision. From my perspective the cyclotron is underutilized. We can support more." Participant 005 explained "The office should grow with the interest of the community. And evolve its thinking with work flow and processes to support. I do not have a preset on the number of INDs we will support. "Participant 006 answered "I have no idea. If it keeps growing the way it is, I cannot manage it.

Question number nine: What mechanism(s) are currently in place to inform potential Investigators of your core? This question was asked of three of four participants. Similar responses were received. Three participants answered "word of mouth is the communication mechanism." Two participants responded "the addition of a website will be used as a communication tool." Participant 002 explained "this is a big gap for me. I do not have much communication with Investigators. These discussions usually occur between the Investigator and Nuclear Medicine Radiologist. I hope I become more involved in preliminary discussions with Investigators." Participant 005 stated "there is information on the web page we are developing. It will be mentioned at our annual research retreat. A lot of it comes from people who want to do this work and they start to ask questions and we direct them to the core. Participant 006 explained

"basically right now it is just word of mouth. I plan to do a website, but my biggest fear is making a website and getting more work."

Question number ten: Is there additional information about the IND core that has not been discussed so far in this interview that you would like to add? All four participants were asked this question. One participant answered with "no. I do not have additional information to add." Three participants answered with some feedback. Participant 002 said "we still need to establish a point where we will close out an IND. We should be encouraging Investigators to close out older protocols and move forward. When it comes to an FDA inspection, we want to make sure we can provide good records." Participant 004 explained "It would really help the core if there was more regulatory oversight." Participant 006 responded "I think the idea of a core is a really great idea. I enjoy the work. There just isn't enough time to provide everyone with the service. Not having the time I need makes me feel I am not doing my job well enough. I know that I am doing a good job with what I have to work with but, it's still that added stress of at the end of the week not getting to everything that needs to be done. "

Additional questions for participant 002

Additional question one: How often are you contacted by the IND core staff for your services/expertise? "Yes, it depends on what is going on. At some points the IND core manager and I may talk two or three times a day if there is a particular issue. But at other times we may speak once a month. "

Additional question number two: Do you meet often with the IND core? If yes, how often? "Yes. I was attending meetings with the IND core manager and OHR, but I have not been included in recent meetings with them."

Additional question number three: Do you believe the centralization has helped with compliance issues within the department? "Yes. At least it has standardized what is required of Investigators. It has brought everyone to the same level whether they are an external Investigator or an internal Investigator. We can now lay down the law and inform Investigators what needs to be done. But, we still need more staff to provide better service to help them. It all comes down to needing more resources."

Follow-up questions

I asked some follow-up questions during interviewers with participants 004 and 006.

Participant 004 was asked two follow-up questions in response to their response to questions number two and ten.

Follow-up question: Who currently completes the IND package? "I am not sure. In the past, the Sponsor and Core manager completed those sections of the IND. We haven't submitted a new IND in several years. We are in the process of working on three new INDs, but I'm not clear on who is responsible for coordinating the activities."

Follow-up question: Do you think your role within the core will change in the future? "I hope it will. I hope the cyclotron will be included more in discussion, especially beginning decisions. Investigators need to understand the cyclotron will fail sometimes. The chemistry can be very complicated. There is a false sense of security. The nature of this area is trace chemistry. There are tiny amounts of things interacting. Sometimes things do not work right."

Participant 006 was asked several follow-up questions in response to the answers they provided to questions two, three, five, eight and nine. I asked these additional

questions to learn more about their perspective on their responsibilities within the core and to determine if they feel they are being supported by others.

Follow-up question: So, nobody reviews the protocol? Participant 006 responded "PET Ops looks for operational stuff. The IRB looks for safety. Nobody reviews to determine if it is a good protocol."

Follow-up question: If an IND is already established, is the work load less? Participant 006 responded "yes. If we have an IND, an Investigator will contact us and say they would like to have a protocol under an IND. If it is a new IND there is a lot more involved. An investigator plan needs to be completed. A lot more research is involved in doing this. This could take months to a year."

Follow-up question: Are you involved with this? Participant 006 explained "Somewhat. Mostly the scientists are involved in this part. My main job is to put the package together and make sure it gets to the FDA."

Follow-up question: Why do you not feel you are close to having a monitoring program? The participant responded "because we need more staff. For the amount of INDs we support, we should have one administrative person who provides oversight and management, two monitors, and have a system to support database setup. That's another thing; we have Investigators that do not have databases."

Follow-up questions: Is there anyone else involved in the core? The participant responded "there is no one else involved in the core except for my immediate supervisor." I then asked if the cyclotron manager or sponsor representative is involved and she responded "they are not really part of the core, they manage a portion of the work that needs to be done to develop the IND, but they are not a part of the daily activities of

the core. They are not a part of the day-to-day tasks of the core."

Follow-up question: Do you think it will help if they or the sponsor-representative were more involved in the daily activities? She responded "it would help with some aspects, especially the scientific/medical because I am not a Physician. I don't really know the drug information as well as whether or not these protocols are scientifically justified. So, for that piece yes, it would help if those people were more involved."

Follow-up question: In addition, as the core grows what would really help you to continue to build the success of the core? "Honestly, I do not think the core is going to grow unless we have more staff." I probed more by saying "I mean in terms of you receiving more protocols. Things will still be coming in..." She responded to this by saying "Right. We'll get the protocol sent to the FDA, but we will not be providing the service to these Investigators that we should be. I can compare this to a pharmaceutical company. There is a monitor and project manager on each protocol and available at all times. In the current state of our IND core, we cannot provide that level of service because the manager does not feel she has the time to dedicate to knowing the protocol in depth. That is not growing; it's just piling more work onto the core."

Follow-up question: Do you feel you need more leadership from the core? Participant 006 said "yes, I would like to send the protocol to the leader, and know that it has been reviewed for all perspectives. Leadership can be a committee; it doesn't have to be one person."

Follow-up question: What specific tasks would you like to continue doing? Participant 006 stated "my first choice would be to work more closely with the CRCs and Investigators on developing the protocols. It would be ideal if I could have someone else

handle the submission. I would also like to get into more of the monitoring stuff. My title is IND manager, and I feel those activities are a manager's role. The day-to-day collecting of logs and checking in with groups should be delegated. But, there is no one to delegate these tasks to."

Other information

In addition to conducting interviews, I examined multiple documents relevant to the IND core. I reviewed and compared audit reports pre and post centralization. The audits revealed a lack of proper document management, drug accountability and monitoring. The reports did not indicate a lack of FDA communication. Annual reports and communications seemed to be up to par I draw this conclusion based on the audit reports. On the other hand, this left me wondering if there was some type of undocumented level of non-compliance. Unfortunately, I was not able to confirm or disprove that speculation. Reviewing these documents provided me with information on the progress of the centralized IND core. It took some time, but the core has established successful document management systems and communication. These documents support the theme of successful establishment of document management systems.

I reviewed the job descriptions of the IND core manager. This description was actually something I created in 2010 when looking to hire someone to fill the position. In hindsight, I realized the description is very general and does not provide enough detail on each task. The description reads "The primary function of this position is to manage the IND Office located within the Radiology Department. The manager will be responsible for serving as a liaison between Investigators and the FDA, monitoring high risk protocols and communicating with studies requiring an IND." As I mentioned

previously, I did not know the specific functions of the core at the time I hired an individual to fill the position. This document does not support a specific theme, but was able to highlight the importance of clear job descriptions.

The third set of documents I examined were correspondences with the FDA about the change in Sponsorship. The letter was detailed and explained Department A has been identified as the sponsor and an individual within the department was assigned the role of authorized-representative.

Participant 002 provided a copy of a process document during the current state interview. The document included a description of communication with Investigators, deadlines for annual report submissions and a time line for developing the infrastructure of the core.

In summary, this chapter presented the data I collected throughout this diagnosis. As outlined in chapter three, all identified participants took place in this diagnosis. In the next chapter, I will analyze and discuss the results in depth.

CHAPTER 5

DATA ANALYSIS

<u>Problem statement</u>

The centralized IND core was developed and implemented to resolve non-compliance issues among Sponsor-Investigators; however, non-compliance issues were still noted on audit reports after the implementation of the centralized IND core. The centralized model was not fully implemented, nor fully staffed to operate in the way it was structured.

This chapter will present an overall analysis of the data I collected by conducting this diagnosis.

<u>History</u>

"So it would be helpful to know certain things about an organization's past to understand its current behavior and to speculate about how it might behave in the future" (Kimberly & Bouchikhi, 1995, p.10). I have been involved in the centralized IND core for about two and a half years with limited understanding of the history behind the core. I entered this position with the plan and goal to create an efficient and effective office. About a year ago, I realized I would not be able to attain my goal without a full understanding of the reason behind centralization. The IND core was established as a result of a tragic death of a research participant. The tragic death of the research participant at this specific AHC resulted in changes to the structure within a single department. This change is similar to reactions research authorities had in the past when tragic events occurred. As outlined in chapter one, several historical events led to implementation of regulations. It seems a tragic event must occur before regulations are

implemented to protect human subjects. I began this capstone with the mindset that a clear plan was not developed before the implementation of centralization. One participant was able to provide me email communications and documents outlining the new protocol/IND process during the interview. When she provided me with these documents, I asked if she had a business plan or some type of similar document. She explained a business plan was supposed to be developed by the Director of OHR because the centralized model was supposed to be implemented throughout the AHC. Unfortunately, to her knowledge the plan was never developed and the centralized model was not executed throughout the AHC.

Emerging themes

Throughout the data collection process, several themes emerged. These themes included:

- Lack of clear goals defining the type of IND model

- Lack of group development

- Successful establishment of document management system and communication mechanisms with FDA and Investigators

- Lack of regulatory support from leadership

The themes were highlighted throughout the interview process with the core staff members. Some of these themes coincide with the literature review presented in chapter two of this paper. I will discuss each theme in detail in the upcoming paragraphs.

The first theme, lack of clear goals, was represented by responses given about the mission of the IND core. The responses provided by the participants were varied and skewed. Two participants did not directly answer the question, but rather provided their

opinion on what is and is not working. Since this important point was not mentioned, it is possible that the staff on the ground is not aware of the goals set forth by the leader of the core. The leader of the core was interviewed for this project. The response from this individual provides a clearer, broader response then the other participants.

The second theme, lack of group development, emerged with the responses provided by each individual on the current operational structure of the core and their individual roles. The participants provided in-depth explanation of the current operational structure of the core; however, the responses were compartmentalized to each participant's specific role within the core. Each participant provided a very descriptive explanation of how they view their role within the IND core. I validated these descriptions by checking the job descriptions of the staff members.

These responses led me to believe the core is functioning as specific task groups working somewhat independently of each other.

The third theme, successes of the core was established with the responses to the question, "what is working well with the core?" t. Overall, the participants described the data management and communication with the FDA and Investigators as being successes of the core.

The fourth and unexpected theme, lack of regulatory leadership, was described by two of the participants during the current state interviews. Comments were made during the interview process that highlighted the frustrations and concerns felt by the administrative staff members. One participant even went on to say they do not know where to turn when they have questions or concerns. These comments, concerns and frustrations were noted and indicate there is a need for a clearer support system.

Individuals need to feel support from leadership to feel their job is valuable and the operations are running smoothly.

In chapter two, I presented a review of the literature related to underbounded systems. The lack of leadership was highlighted by staff members and appears to be a result of an underbounded system. Two individuals were highlighted as serving leadership roles within the core. "Authority relations in underbounded systems are typically fragmented and unclear. Instead of a single authority source to whom all must ultimately answer, there are multiple and/or none to whom some intermittently report" (Alderfer, 1980, p.271). This statement fits the data I have collected. Staff members of the IND core are unsure who is their ultimate leader and do not feel they are supported. In this case, I view the core as having several authorities: the Sponsor-representative, compliance manager and operations manager. Who is the ultimate decision maker? Is it the authorizing-representative? These questions still remain. As a staff member of the IND core, I have experienced my own uncertainly with the level of leadership and how I fit into the equation.

In addition, I believe communication problems are highlighted. Alderfer (1980) theorizes communication problems in underbounded systems occur in situations when people do not create links among each group/individual nor are the appropriate people identified (p.273). I believe the communication pattern and leadership are somewhat tied together. Leadership needs to identify the appropriate people of the core and establish appropriate lines of communication.

Hypotheses

Hypothesis 1: The centralized model was set in place without clear objectives.

During the current state interviews I asked three of the four participants to define the mission of the core. The responses received were varied, yet all reflected a centralized location for INDs and support for Investigators. The participants did not elaborate on the level of support they do or should be providing to the Investigators. One participant described the core as being a centralized area for all radio-pharmaceuticals to be managed. Again, the level of management was not defined. I am still left wondering what the exact objectives of the core are at this point. Is the core supposed to be a complete Sponsor or is the core supposed to be more of a support service to Investigators? Alderfer (1980) indicates to some extent organizational goals provide some source of reasonableness for organizations. Clarity of goals cannot be found in underbounded systems as easily as optimal systems (p.270).

During the background interviews I asked the participants to provide their perception of how they envisioned the operational structure of the core. The mixture of responses leads me to believe the staff was not clear about the goals of the core. Each person had their ideal vision for the core. While this is valid and acceptable, the staff and leader should have had the same opinion on the objectives of the core.

"Participants may experience their system as floundering without a sense of direction" (Alderfer, 1980, p.270). During the current state interviews one participant said "Not having the time I need to do my job makes me feel I am not doing my job well enough. I know that I am doing a good job with what I have to work with but, it's still that added stress at the end of week of not getting to everything that needs to be done." This statement, as well as the look of uncertainly on the participant's face, lends credence to this hypothesis. This individual seems to be overworked and bearing the weight of the

core on her shoulders and feeling as if she isn't sure how to move forward. The objectives of the core need to be clearly defined. I believe once the objectives are clearly defined, staff members will feel a more defined role within the core.

Hypothesis 2: The IND core is not operating in the way it was structured to operate. The IND core was established to be a central Sponsor of radio-pharmaceutical related research protocols. I formulated this hypothesis based on my initial contact with the core. Initially, due to my limited knowledge of IND work, I assumed the core was only supposed to serve as the portal between the Investigator and the FDA. I then learned one individual within the department was the Sponsor's authorized-representative for all IND related work; the department as a whole was defined as the Sponsor. Soon after my role within the core was established, I realized several responsibilities were not being fulfilled and were the responsibility of a Sponsor. I began to wonder why that was happening. I did not believe individuals were purposely neglecting their responsibilities.

To evaluate this hypothesis, I asked participants during the background interviews to describe how they envisioned the operational structure of the core. All four participants provided overviews of how they saw the core operating. One participant even commented that his vision was altered due to the resources provided by the AHC. Two participants envisioned the core being a single individual to manage regulations and monitoring. One participant explained the vision of the core was to manage the submission process between Investigators and the FDA. Only a few responsibilities of a Sponsor are highlighted in these responses. Perhaps my question was not clear to the participants. I wanted to learn about all aspects of the core including: regulatory, monitoring, medical oversight, drug accountability, etc...The question still remains, how was the core

supposed to operate?

I asked the same question during the current state interviews. Two of the participants were also interviewed during the background interviews, one participant was not. The responses were more detailed than those received during the background interviews. Two participants described the structure as being a single individual managing the core. One participant stated the structure of the core is simple, as there is one person managing it. He continued to explain the core manager is responsible for collaborating with the various people around to support the core (examples: compliance, operations, and science). A second participant provided a very detailed explanation of the IND process. Within this description, she highlighted key individuals and groups as support to the core. Some of these groups were regulatory oversight groups that I did not include in the participation of this diagnosis. It would be helpful to include these groups when discussing the future infrastructure of the core.

Hypothesis 3: The IND core is understaffed and unable to fully carry out the level of responsibility associated with being a Sponsor. The IND core manager was labeled as the central person within the core, as well as the primary person for completing the majority of responsibilities associated with being a Sponsor. Four participants were asked if the IND core is satisfying all responsibilities associated with being a Sponsor and the response by all was "no." Two of these participants stated the reason all responsibilities are not being met is due to the limited resources and personnel within the core. Another participant stated a strategy needed to be developed for completing the monitoring task. He explained personnel outside of the core may be able to assist with this. The fourth participant again noted there needs to be a higher level of oversight.

The time commitment for each administrative task seems to be greater than the amount of time that can be given by one full time employee. Monitoring and training are two tasks being neglected due to limited resources. The question remains, does the core need to hire more personnel or can the current personnel be utilized more? During the current state interview process I asked each participant to describe their role within the core. Two participants defined their role and spoke about the same task. These dissuasions led me to believe if the roles and tasks were clearly defined within the group, there would be a more cohesive structure. Alderfer (1980) stated there tends to be unclear and conflicting role expectations in underbounded systems (p.272). There is some overlapping of roles within the core at this time. I gathered this based on the discussion with two of the participants. Two individuals stated they are responsible for obtaining documents prior to centralization. Who is ultimately the one responsible for this task?

There are several responsibilities associated with being a Sponsor. These responsibilities can be divided up. One participant described the core as being one single contact to manage regulatory submissions. During the interview he stated this individual must know how to reach out for support from operations, compliance and the physicians. I found this statement to be clear, but I am left wondering if the IND core manager is aware of this operational piece. In addition, he did not mention the cyclotron manager, the one responsible for producing the drugs. Why? I view this individual as having a specific role within the core.

I believe in order to maximize the group, the positions of the individuals listed in the above paragraph need to be clearly identified to all.

Hypothesis 4: Future expansion was not included in the planning when the centralized model was implemented. The core was established to support four INDs, and eight protocols. I was unable to locate a document describing a plan for the future of the core. During the current state interview process, I asked each participant if there is a plan to manage the future growth of the IND office. I received a variety of answers. I do not believe the future of the core has been discussed among the individuals within the core. Participant 005 provided a high level response. He explained the core should continue to grow and evolve with the expansion of clinical research. He did not provide details, such as hiring more support personnel. I am able to validate this hypothesis with the absence of a future plan, and the unclear participant responses. The lack of plan and responses is enough to validate there has been little discussion in regards to the growth of the core.

I was unable to locate literature specific to the lack of planning within AHCs and specifically to the field of clinical research. The lack of literature highlights the need to evaluate the programs established as a result of non-compliance. Evaluating existing programs will help understand if these programs are improving compliance within the clinical research field. In addition, I believe it would be beneficial to evaluate current systems within AHCs and determine methods to enhance compliance.

Earlier within this paper, I mentioned I was not comfortable trying new plans within the IND core due to my limited involvement. I felt this way and continue to feel this way because I am not confident of my role and the amount of power I have to make necessary changes. I did not explore much of my role during this diagnosis. My role is something I need to clarify with my boss in order to fully support changes within the core. On the contrary, I do feel more confident in the changes I can propose to leadership.

Completing this capstone and research has given me more knowledge and understanding of the system. I would like to further expand upon this self-exploration with learning from leadership their vision for my role.

In summary, the data I collected with this research validated the core was established without clear objectives and goals. This capstone demonstrates the importance of the need for clear objectives, goals and defined roles within the infrastructure. Establishing these aspects at the beginning will help lead to success and eliminate confusion.

One thing I did not do within this diagnosis is fully explore the different model types of an IND core. I think it would have been valuable to ask more questions regarding the type of service the core leadership would hope to perform. I did ask questions that provided some data, but not enough to really know what model is best suited for this department. This is an area worth exploring in the future. Overall, the data collected is valuable and will provide the leadership with a view of the current system.

CHAPTER 6

CONCLUSION

<u>Recommendations/Feedback</u>

This feedback is designed for the IND Sponsor-Representative. If he is interested in moving forward with a change management plan, I propose presenting this feedback to the IND core manager, cyclotron manager, regulatory manager and other indirect staff members of the core.

The centralized IND core was developed and implemented to resolve non-compliance issues among Sponsor-Investigators; however, non-compliance issues were still noted on audit reports after the implementation of the centralized IND core. The centralized model was not fully implemented, nor fully staffed to operate in the way it was structured.   Over the course of eight weeks, I collected and analyzed data to determine what is and is not working well with the centralized IND core. I conducted interviews with six staff members and reviewed archival data. I conducted two types of interviews: background and current state. The background interviews included five staff members, and the purpose was to obtain the history and rationale for creating a centralized IND core. The current state interviews were designed to obtain information on the current structure and operations of the core. I interviewed four staff members. Prior to 2007, Investigators wishing to conduct research protocols using a radio-pharmaceutical took on the role of Sponsor-Investigator. A death of a research participant led to an investigation of the conduct of research protocols throughout the AHC. The findings demonstrated non-compliance issues leading to the development of this centralized core.

At the time of implementation the core supported four INDs, and eight protocols.

<u>Why the problem exists</u>

The centralized IND core is effectively serving as the communication portal between Investigators and the FDA, as well as maintaining organized regulatory files. These two areas have improved the level of compliance among Investigators conducting research with radio-pharmaceuticals. Since its implementation, the core has grown to support ten INDs, and thirteen protocols, and has not grown in staff size.

At the time of implementation, the definition of roles and task assignments were not clearly defined other then the role of the IND core manager. The IND core manager job descriptions designated this individual as being responsible for managing the communication between Investigators and the FDA, document management, and monitoring. The IND core manager states she has been unable to attend to the monitoring task due to lack of time. However, she has recently been able to become engaged with this task and started monitoring protocols.

The IND core manager is responsible for about seventy-five percent of the Sponsor responsibilities. The remaining amount is completed by the cyclotron manager. Two responsibilities are not being fulfilled by the centralized core: monitoring and Investigator/study team training. These responsibilities have not been assigned by the Sponsor-Representative. Furthermore, the lack of fulfilling these responsibilities still categorizes the centralized core as being non-compliant.

There is a lack of role clarity of the operations manager, and compliance manager. There is little to no clear plan of how these individuals should be assisting with the daily tasks of the core. Several participants described the other participants as oversight

personnel; however, the amount of involvement they have is unclear at this time. The

members of the group meet one-on-one, yet there is a lack of standing group meetings

where all members are present.

The core has doubled the amount of INDs since 2007. The core members have not

addressed the growth nor discussed a plan for managing continued growth.

Table 4. Feedback

Category	Responses
1 **Items working well**	
Document management	4/4
Communication with FDA	4/4
Communication with Investigators and study teams	4/4
Drug accountability	1/4
2 **Items to improve**	
Monitoring	4/4
Training	1/ 4
Regulatory support	1/ 4
Additional resources	3/ 4
Discussion of future has not occurred	4/4

End result if problems are not addressed

If clarification of roles is not provided, the tasks not assigned will continue to go

left unassigned and the core will continue to be non-compliant. The lack of role definition

will also continue to isolate and fragment individuals within the group.

The inter-group dynamics should be addressed as well. The IND core is made up

of several working groups which, at some level need to work with each other to manage

successful operations of the core as a whole system. If the issue of inter-group dynamics

is not addressed, the groups will continue working independently, and without a clear

purpose/mission. This in turn will not provide a full service support to Investigators

wishing to conduct research with radio-pharmaceuticals.

If the group does not discuss the plan for managing future growth of the core, IND applications will become backlogged, and the support to ensure compliance will decrease. Unfortunately, this could result in a tragic event and result in the shutdown of the department's research facility.

Recommended solutions

- Review the complete list of Sponsor responsibilities and group them into several categories

    - Administrative

        - IND application submissions

        - Annual reporting

        - Record management/retention

        - Ongoing monitoring

    - Drug manufacturing/shipping

    - Drug receipt/logging/dispensing

    - Regulatory training

    - Medical oversight

        - Sponsor's authorized-representative

        - medical expertise

        - assistance with trail design and oversight

- Review the level of time commitment needed per task

- Schedule a meeting to review data with the IND core staff members

- Have an open discussion with the staff members to determine the best process for

managing the current workload

Expected benefit

The expected benefit is to gain a sense of collaboration among the key members of the IND core and continue building the core to support IND related research.

Other

I highlighted three questions of importance to me as I wrote the methodology chapter. These were questions I felt were worth answering at the conclusion of this diagnosis.

- Did I miss specific history because non-departmental stakeholders were not interviewed? As I conclude this diagnosis, I believe it would have been valuable to interview the individuals from ancillary departments for this paper. I believe these individuals could have offered more history into this paper.

- Should I have interviewed a sampling (random) of Investigators who utilize the core? I believe interviewing Investigators utilizing the core would have been valuable. However, for the purpose of this paper, the results would not have supported my hypotheses.

- Did I ignore performance issues of certain staff members? This is a somewhat difficult question to answer with the data I collected. It may have been worthwhile to evaluate the job descriptions of each participant I interviewed and add questions specific to each participant's role. At this point, I do not feel that would have been beneficial for this diagnosis. If measuring job performance is important to leadership, the roles need to be clearly defined first. Then, leadership can begin

to evaluate and measure job performance. At this time, I do not believe this point

is relevant to the diagnosis.

Future research

The biggest struggle with this capstone was searching for literature relevant to

assessing clinical research programs within AHCs. Unfortunately, there is limited

information publicly on the assessment of current structures and programs established as

a reaction to tragic events over time. I believe it would be beneficial to the research

community for further assessment of regulations and programs to be conducted. I believe

assessing the current infrastructure could prevent tragedy from happening in the future.

Why wait until there is another tragedy?

AHCs fit into the definition of underbounded systems. The system is

decentralized, roles are not defined and the goals are not always clear. I am not

suggesting this system be changed, but rather we take the time to learn how to work

within this system to produce solid research and minimize risk to study participants.

Overall, the core was established to minimize non-compliance and offer support to

Investigators. I think this concept is valuable and now we should take the opportunity to

enhance it.

Learnings

This capstone was a learning experience that provided me with knowledge I never

expected. I wanted to use the skills and knowledge learned from this program to

enhanced my professional skills in my current organization, as well as expand the

infrastructure within my current organization. I decided to conduct an organizational

diagnosis so I could learn what is and is not successful with the current setup of the IND

core and provide feedback to my supervisor.   I wanted to demonstrate the importance of understanding the dynamics at play.

When I first started working on the idea of conducting a diagnosis, I realized there were things from the past that shaped the centralization and I needed to learn about them before I could understand the current operational structure. I conducted a series of five interviews with staff members (past and present) to gain knowledge of the history through memories. In hindsight, it would have been valuable to include Investigators that were affected by the centralization. I would have been given a different perspective on the history.

During this process, I was provided with a document outlining the implementation plan. This document was created by a previous staff member, who did not provide this information at the time of interviewing nor during the transfer of responsibilities to the new IND core manager. Why was this document not offered before? The individual originally hired to serve as the IND core manager was asked to relinquish these responsibilities at the beginning of 2010. To my knowledge, the reason this individual was replaced within the core was because the Sponsor files were not being managed appropriately. In order to improve compliance, the vice chair of research asked me to step in and improve the document management system. I believe this transition may have caused anxiety and uncertainty with the previous staff member and left the core in a vulnerable place. This is one area that I did not explore within this capstone.

In addition, the leadership of the core changed in January 2011. The Sponsor-Representative resigned and the responsibilities were reassigned to a senior level physician. The current Sponsor-Representative juggles several leadership positions within

the department. Leadership within the core is another theme that was highlighted throughout this process. Again, this was not an area I explored during this diagnosis. If time allowed, this would be an area worth exploring as I believe the change in personnel may have impacted the goals and group structure.

I was not able to explore the leadership of the core; however, this diagnosis showed the importance of understanding an organization's history, role definition, and inter-group dynamics. Regulations related to clinical research have been developed in response to tragic events. Understanding these events in-depth can mold the future of an organization. The IND core was centralized due to a tragic event within the AHC. Did centralizing enhance compliance amongst Investigators? The answer is, somewhat. There is still so much that needs to be improved. For example, building a core that can fully support all responsibilities associated with an IND Sponsor.

Roles need to be defined clearly with the development of infrastructure. This core can grow successfully if leadership is willing to redefine the roles and responsibilities of the core. This clarity will also enhance the dynamics and enable the group to function more as a whole group rather than subgroups. This diagnosis has taught me a lot about the above, but also about myself. It has taught me that I should feel comfortable inquiring about the process, potential staff members and take the lead on defining a clear process. I believe if time is taken in the beginning to organize and establish a program, it will be successful.

During this process, I realized my role was much more than described. I am not only there to supervise the IND core manager, but there to lend a hand or provide creative ideas. I've tried my best to be a support to the IND core manager, but I haven't been

involved enough in the daily tasks to be a benefit.

This experience has been worthwhile and I would not change one piece of it. I learned how to conduct an organizational diagnosis from start to finish. An additional challenge was conducting this within the organization I am a part of currently. It took courage and strength to identify the problem and ask my colleagues for their participation. This experience has allowed me to grow professionally. I've had the opportunity to dedicate additional time to reviewing literature relevant to research regulations and other academic centers. An opportunity I did not pursue in the past. Furthermore, I had the opportunity to use my learnings from the Organizational Dynamics program and apply them to a real life situation. I was able to utilize my understanding of organizational diagnosis and apply it. In addition, this capstone allowed me to learn more about underbounded systems, the impact history has on organizations, and the purpose of planning. I have learned a great deal and am thankful for such an opportunity.

REFERENCES

Alderfer, Clayton, P. (1980). Consulting to Underbounded Systems, A*dvances in Experimental Social Processes,* 2, 267-294

Alderfer, Clayton, P. (1980). The Methodology of Organizational Diagnosis, *Professional Psychology*, 11(3), 459-468.

Alderfer, Clayton, P. (1976). The Methodology of Diagnosing Group and Intergroup relations in Organizations, 355-371.

Armenakis, AA, Mossholder, KW, and Harris, SG (1990). Diagnostic Bias in Organizational Consultation, *Omega Int. Journal of Management Science,* 18 (60, 563-572.

Arbit, Harvey. M. and Paller, Mark. S. (2006). A Program to Provide Regulatory Support for Investigator-Initiated Clinical Research. *Academic Medicine,* 81 *(6)*, 146-153.

Berro, Marlene, Burnett, Bruce, Fromell, Gregg, Hartman, Karen, Rubinstein, Eric, Schuff, Kathryn, and Speicher, L. (2011). Support for Investigator-Initiated Clinical Research Involving Investigational Drugs or Devices: The Clinical and Translational Science Award Experience. *Academic Medicine, 86 (2)*, 1-7.

Code of Federal Regulations, Title 21
(http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?cfrpart=312)

Finn, Robert. (2000). Reports bring several changes to IRBs. *Journal of the National Cancer Institute, 92*(16). Retrieved from
http://jnci.oxfordjournals.org/content/92/16/1287.full

Freeman, Arthur. M. & Zackrison, Richard. E. (2001). *Finding Your Way in the Consulting Jungle*. San Francisco, CA: Jossey-Bass/Pfieffer.

Gordon, Bruce and Prentice, Ernest. (2000). "Protection of Human Subjects in the United States: A Short History." *J Public Health Management Practice*, 6 (6), 1-8.

Holbein, Blair M E. (2009). "Understanding FDA Regulatory Requirements for Investigational New Drug Applications for Sponsor-Investigators." *Journal of Investigative Medicine*, 57 (6), 1-8.

Kimberly, John R. and Bouchikhi, Hamid. (1995). "The Dynamics of Organizational Development and Change: How the Past Shapes the Present and Constrains the Future." *Organizational Science*, 6 (1), 9-18.

Lacey, Mirium Y. (1995). Internal consulting perspectives on the process of planned change, *Journal of Organizational Change Management,* 8(3) p. 75-84.

Nadler, David A. and Tushman, Michael L. (1980). "A Model for Diagnosing Organizational Behavior" *Organizational Dynamics,* p. 35-51.

Ooi, Can-Seng. (2002). Persuasive histories: Decentering, recentering and the emotional crafting of the past. *Journal of Organizational Change Management,* 15 (6), 606-621.

Ryan. Gery. W., Bernard. Russell. H. (2003). Techniques to Identify Themes. F*ield Methods*, 15(1). 85-109.

Simmons, Valerie. (1985). Reconstructing an organization's history: systemic distortion in retrospective data. In David N. Berg & Kenwyn K. Smith(Eds.), *Exploring clinical methods for social research* (287-304). Beverly Hills, CA: Sage.

Weisbord, Marvin. R. (1976). Organizational Diagnosis: Six Places To Look for Trouble with or Without a Theory. *Group & Organizational Studies*, 19(4), 430-447.

White-Junod, Suzanne. (2012). About FDA. *Food and Drug Administration.* [July 14, 2012] Date, [from] http://www.fda.gov/AboutFDA/WhatWeDo/History/Overviews/ucm304485.htm

Zhou, Julia. (2003). Four years later, Gelsiner case still has implications. *The Daily Pennsylvania,* Retrieved from http://www.thedp.com/index.php/article/2003/11/four_years_later_gelsinger_case_still_has_lasting_implications

Nuremberg Codes. (2005). Retrieved July 1, 2012, from
http://www.hhs.gov/ohrp/archive/nurcode.html

Tuskegee Study (2009, December 4). Retrieved from Center for disease Control and
Prevention website:
http://www.cdc.gov/tuskegee/timeline.htm

APPENDIX A

BACKGROUND INTERVIEW QUESTIONS

Introduction
Thank you for agreeing to speak with me about the IND core.
You are being invited to participate in this interview because you were a key stakeholder in the development of the centralized IND core. Your participation is voluntary which means you can choose whether or not you want to participate. Before I begin I would like to tell you a little bit about the purpose of this interview. As part of my completion requirements for the Master's of Science in Organizational Dynamics, I am required to complete a capstone. The focus of my capstone is to perform an organizational diagnosis of the IND core. The purpose of this interview is to collect information regarding the background history and development of the centralized IND core.
The interview will take about 60 minutes. You do not have to answer any questions you do not wish to answer and you may stop at any time. I will maintain confidentiality throughout this interview and the writing process. Neither your name nor role will be identified. The information you provide in this interview will be identified by a participant ID. Would you like to continue with this interview?

Background interview questionnaire

- Can you provide information on the operational structure of the IND unit prior to

    the implementation of the centralized model?

- What was the rationale for creating a centralized IND unit?

- When did the idea of a centralized IND unit come about?

- Who led the redesign of the IND unit?

- How did you envision the operational structure of the centralized IND unit?

- What mechanism(s) did you use to inform Investigators throughout the University

    of the Re-design of the IND unit?

APPENDIX B

CURRENT STATE INTERVIEWS

Introduction

Thank you for agreeing to speak with me about the IND core.
You are being invited to participate in this interview because you are a key stakeholder in the IND core. Your participation is voluntary which means you can choose whether or not you want to participate. Before I begin I would like to tell you a little bit about the purpose of this interview. As part of my completion requirements for the Master's of Science in Organizational Dynamics, I am required to write a capstone. The focus of my capstone is to perform an organizational diagnosis of the IND core. The purpose of this interview is to collect information regarding the current structure of the centralized IND core and to determine its effectiveness.
The interview will take about 60 minutes. I will keep what you tell me during the interview confidential. Neither your name nor role will be identified in the capstone. The information you provide in this interview will be identified by a participant ID. Do you have any questions? Would you like to continue with this interview?

Interview questionnaire

- Can you give me an example of what is working well about the IND core?

- How would you describe your role within the IND core?

- Can you provide information on the current operational structure of the IND core?

- What is the mission of the IND core?

- Is the IND core satisfying all responsibilities associated with the role of Sponsor?

  - If no, which responsibilities are not being fulfilled? And why do you

    believe they are not being fulfilled?

- What is the number of INDs currently active under the core? What is the number

  of protocols currently active under the core?

- Do you have a limit on the number of INDs and/or protocols your core will

  support?

- How do you plan to handle management of additional INDs/protocols?

- What mechanism(s) are currently in place to inform potential Investigators of your core?

- Is there additional information about the IND core that has not been discussed so far in this interview that you would like to add?

APPENDIX C

CURRENT STATE INTERVIEW-PERIPHERAL MEMBER

Introduction

Thank you for agreeing to speak with me about the IND core.
You are being invited to participate in this interview because you are a key stakeholder in the IND core. Your participation is voluntary which means you can choose whether or not you want to participate. Before I begin I would like to tell you a little bit about the purpose of this interview. As part of my completion requirements for the Master's of Science in Organizational Dynamics, I am required to write a capstone. The focus of my capstone is to perform an organizational diagnosis of the IND core. The purpose of this interview is to collect information regarding the current structure of the centralized IND core and to determine its effectiveness.
The interview will take about 60 minutes. Neither your name nor role will be identified in the capstone. The information you provide in this interview will be identified by a participant ID. Do you have any questions? Would you like to continue with this interview?

Interview questionnaire

- Can you give me an example of what is working well about the IND core?

- How would you describe your role within the IND core?

- How often are you contacted by the IND core staff for your services/expertise?

- Do you meet often with the staff?

  - If yes, how often?

  - If not, why not?

APPENDIX D

DOCUMENTS REVIEWED

- Audit reports: pre and post centralization

- Job description of current IND core manager

- FDA correspondences

  Process document provided by participant 002