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# Total Quality System Breakdowns in Outsourced Clinical Trials

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This is to certify that the doctoral study by

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2016

Abstract

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Doctoral Study Submitted in Partial Fulfillment

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## Abstract

Numerous deaths, tragedies, and underreported drug side effects occur in outsourced clinical trials. Total quality system breakdowns occur even though quality agreement contracts and quality management systems are used by pharmaceutical organizations. The purpose of this single case study was to explore strategies clinical quality assurance managers use to avoid breakdowns in quality with outsourced clinical trials in Asia-Pacific countries. The study included a purposeful sample of 15 clinical quality assurance managers from 1 pharmaceutical organization located in the Northeast region of the United States. The conceptual framework was von Bertalanffy's general systems theory. Face-to-face semistructured interviews or e-mail questionnaires containing open-ended questions were used to gather data from clinical quality assurance managers who had a minimum of 5 years of experience with outsourced clinical trials. Coded data and themes were identified through the modified van Kaam method. The three emergent themes were the following: vendor quality management, building quality in outsourced clinical trials, and quality management systems. Results of the study may contribute to social change by helping pharmaceutical organizations' leaders develop strategies and tools to improve the quality of outsourced clinical trials.

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# Dedication

I would like to dedicate this doctoral study to my family. To my husband, who is my rock, thank you for your continuous support, encouragement, understanding, and guiding me through to complete this journey. I cannot thank you enough for believing in me and helping me complete my educational journey. Thank you to my children, Jaiden and Melania, for being my inspiration, determination, and enlightenment. I love you with all of my heart. Finally, I dedicate this study to my parents, who taught me anything in life is possible as long as you work hard and are dedicated.

To the memory of my father, Krishnakant Patel, a very special gratitude. You taught me that as long as you set your mind to something you could attain it despite life's challenges. Losing you was the lowest point in my life; however, your life teachings were the driving force for me to complete this journey. You will forever be my angel and guiding light. I love you always.

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I would like to take this opportunity to thank my committee members for helping me to meet Walden University's highest quality standards with this study. I would specifically like to thank Dr. Lynn Szostek, my chair, who always encouraged me and provided inspiration. Your positive energy and thoughts helped me reach my goal through one of the toughest times of my life, and I am grateful for having you as my chair. Thank you to Dr. Kim Critchlow for challenging me and pushing me to think outside of the box so I could reach my highest potential. I would also like to thank Dr. Kenneth Gossett for your contribution and support for the success of this study. It has been the greatest honor and privilege to work with all of you through the years in completing this journey.

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Section 1: Foundation of the Study

## Background of the Problem

Global pharmaceutical companies have been confronted with various challenges that affect their long-term viability. Challenges such as increased drug prices (Pronker, Geerts, Cohen, & Pieterse, 2011) and tighter regulatory drug approval policies to ensure data integrity and to prevent fraud must be addressed by pharmaceutical managers. Additional challenges are new clinical regulatory requirements making it difficult for pharmaceutical research and development (R&D) operations to perform clinical trials and approve a new drug (Pronker et al., 2011). The high cost of conducting clinical trials forces the pharmaceutical leaders to outsource clinical trials to developing countries. Pharmaceutical organizations address these challenges by creating an outsourcing clinical trial model for R&D sectors in Asia-Pacific developing countries. The outsourced clinical trial model saves money and time, and provides faster drug approval (Mendivil, 2012). Globalization of clinical trials increases complexity and makes it difficult to achieve global quality and patient safety (Paul, Mytelka, & Dunwiddie, 2011). According to Bate, Mooney, and Hess (2011), 1,589 out of 1,940 drugs were identified as registered in developing countries; 351 drugs were not registered, and there was limited information on their clinical trials and known side effects. Because of the complexity of clinical trials and faster completion timelines, drugs' side effects are underreported, and unregistered drugs are causing thousands of deaths and hospitalizations. In addition, there are over 3,000 deaths and 300,000 tragedies occurring in outsourced clinical trials conducted in developing countries (Soni & Singh, 2013).

## Problem Statement

The high cost of conducting clinical trials is forcing pharmaceutical leaders in the United States to outsource clinical trials to Asia-Pacific countries (Mendivil, 2012). Outsourced clinical trials, which represent 60% of clinical trials worldwide, are causing a disproportionate number of deaths, tragedies, and underreported drug side effects (Soni & Singh, 2013). The general business problem is a disproportionate number of deaths, tragedies, and underreported drugs' side effects continue to occur despite contracted quality standards and the inclusion of quality management systems. The specific business problem is some clinical quality assurance managers lack strategies to avoid a breakdown in quality with outsourced clinical trials in Asia-Pacific countries.

## Purpose Statement

The purpose of this qualitative case study was to explore strategies clinical quality assurance managers use to avoid a breakdown in quality with outsourced clinical trials in Asia-Pacific countries. The targeted population consisted of clinical quality assurance managers from one pharmaceutical organization located in the Northeast region of the United States. The information provided by the clinical quality assurance managers may contribute to social change through the identification of strategies to avoid quality breakdowns with outsourced clinical trials.

## Nature of the Study

The qualitative research method was used to explore the research participants' experiences (Corbin & Strauss, 2014). Qualitative research was the appropriate method

because it is used to provide an in-depth description of the phenomenon from direct fieldwork observations, documents, and open-ended interviews (Patton, 2005). Qualitative research methods offered flexibility, which helped me gain a better understanding of the quality management system breakdowns that occur during the outsourcing of clinical trials (Denzin & Lincoln, 2011; Corbin & Strauss, 2014). A quantitative approach was not appropriate because the purpose of the study was not to test a hypothesis, make predictions, or evaluate cause and effect of outsourced clinical trials (Bernard, 2013). A mixed-methods approach was also inappropriate because the research question did not require both qualitative and quantitative data (Brannen & Moss, 2012; Onwuegbuzie, Frels, Collins, & Leech, 2013).

The design for the doctoral study was a case study. Yin (2014) noted that if the aim of research is to provide a rich description of a phenomenon, a descriptive case study is needed. The narrative study design is used to explore the life of an individual and to report the individual's experiences. My research study's aim was not to explore an individual's experiences regarding outsourced clinical trials. Grounded theory was also inappropriate because the focus of the study was not on developing a theory grounded in the data from the field or studying a process or action involving many individuals. An ethnographic design is used to describe and interpret a culture-sharing group (Wolcott, 2008). My research study did not focus on describing or interpreting the pharmaceutical culture. Finally, I excluded a phenomenological design because I did not intend to explore lived experiences in this study (Barss, 2012).

## Research Question

The central research question proposed for the study was the following: What strategies do clinical quality assurance managers use to avoid quality breakdowns with the outsourced clinical trials in Asia-Pacific countries?

## Interview Questions

To answer the overarching research question, the following open-ended semistructured interview questions were used:

1. How do clinical quality assurance managers regulate the clinical quality management systems and adapt to changes when trials are outsourced to Asia Pacific?
2. How do clinical quality assurance managers ensure that clinical trial vendors adapt to the changes in the environment and process negative feedback?
3. What actions are taken by clinical quality assurance managers to ensure outsourced clinical trial vendors are following the agreed contracts?
4. What strategies do clinical quality assurance managers employ to ensure compliance from an outsourced clinical trial vendor after an agreed quality contract?
5. What are some risks and benefits associated with clinical trials when outsourced to Asia Pacific?

6. How do clinical quality assurance managers build successful relationships with clinical trial vendors and sustain those relationships with an ever-changing outsourcing business model?
7. How do clinical quality assurance managers ensure standard methods of communication of newly released standard operating processes, regulations, systems, and tools to outsourced clinical trial vendors?
8. In a 1-year time frame, how often do clinical quality assurance managers and outsourcing vendors reassess quality agreements, contracts, processes, and potential gaps?
9. What strategies have/have not worked with outsourcing clinical trials to ensure the highest quality of the clinical trial?
10. Is there any additional information you would like add that I may not have addressed by the interview questions?

## Conceptual Framework

The conceptual framework for the qualitative case study was based on general systems theory (Stacey, 2011). The general systems theory is a methodology used to employ a system approach to understanding complex problems and phenomena. The focus of the general systems theory is on the system structure instead of the system function. The core concepts of the general systems theory are (a) the whole system is more than the sum of the parts; (b) the system can be open, closed, or semipermeable to the environment; (c) feedback is the mediator between system behavior and goal; (d) the central variable is time; (e) change is seen as a transformation of the system; and (f)

defining the system environment boundaries will identify and establish what is inside the system and what is outside in the environment and its subparts from the system as a whole (Laszlo & Krippner, 1998).

The clinical quality assurance pharmaceutical leaders are seeking an understanding of how to deal with information and use it for sustainable innovation (Senge, Smith, & Kruschwitz, 2011). The quality of clinical trials determines the sustainability and longevity of a pharmaceutical organization. Outsourcing clinical trials to developing countries such as Asia-Pacific countries adds complexity and increases quality risks. To address these quality risks, clinical quality assurance managers need to employ strategies to avoid quality breakdowns with outsourced clinical trials. The general systems theory served as a conceptual framework for understanding the relationships in the outsourced clinical trial system (Stacey, 2011). The general systems theory is used to understand who the individuals are, what is changing, and what the individuals are faced with (Stacey, 2011). Essentially the purpose of system thinking is to identify interrelationships rather than things. Advantages of the system thinking approach include helping one manage and grasp complex situations and uncertainty where there is no simple situation (Cezarino, Junior, & Correa, 2012).

## Operational Definitions

*Effectiveness*: The extent to which improvement efforts resulted in actual quantifiable improvements (Golušin, Ivanović, Domazet, & Dodić, 2011).

*Offshoring*: Another form of outsourcing, specifically outsourcing that happens aboard (Nieto & Rodríguez, 2011).

*Outsourcing*: The process of contracting out noncore activities or transferring activities to a third party (Crisan, Butilca, Salanta, & Ilies, 2011).

*Pharmacovigilance*: A scientific activity related to the prevention, assessment, understanding, and detection of any drug-related issue or problem (Arici, Gelal, Demiral, & Tuncok, 2015).

*Standard operating procedure*: The crucial part of a quality system. The global corporate standard operating procedures provides a standard framework of quality standards for clinical development. Standard operating procedures are needed to take into account national regulations and to describe the process at the pharmaceutical organization to implement at the operational level (Chaikin et al., 2000).

*System*: A set of two or more interrelated elements with the following properties: Each element has an effect on the functioning of the whole and is affected by one of the other elements within the system. In addition, all possible subgroups of the elements have both properties mentioned above (Ackoff, 1981, pp. 15-16.)

*Total quality management*: A management method used to enhance the quality of a business organization (Mazumder, Bhattacharya, & Yadav, 2011).

*Vendor risk*: An uncertainty of choosing an appropriate vendor which ultimately affects the performance of a project (Mathew & Das Aundhe, 2011).

## Assumptions, Limitations, and Delimitations

### Assumptions

Assumptions of a study are unverified claims that the researcher assumed to be true (Bernard, 2013). One assumption I made for this qualitative research study was that a

top-ranked pharmaceutical organization's clinical quality assurance managers could provide an in-depth description of the quality management system's utility in monitoring breakdowns of outsourced clinical trials. The second assumption was the data from pharmaceutical organization's audit and inspections reports, outsourced clinical contracts, federal agencies reports, and clinical trial processes could be used to determine the gaps within the total quality management system. The third assumption was the 15 clinical quality assurance managers provided unbiased and truthful answers during their interviews. A final assumption was the outsourcing companies such as Business Process Organization (BPO) and Contract Research Organization (CRO) located in Asia Pacific were outsourcing clinical trials and had potential breaks within their quality management systems.

**Limitations**

Limitations in a research study are weaknesses within the study (Bernard, 2013). The potential weakness of the research study was exploring only one multinational pharmaceutical organization and not exploring medium and small pharmaceutical organizations. The second limitation of this qualitative study was the location of the outsourcing clinical trials organizations. The specific outsourced clinical trials region targeted for this qualitative study was Asia-Pacific countries. The outsourced clinical trial regions did not include Europe, South America, Central America, North America, and Africa. The third limitation was the study participants were from one pharmaceutical organization located in the Northeast United States. The fourth limitation was the exclusion of outsourced contract research organization's participants. The final limitation

was the inclusion of clinical quality assurance participants and exclusion of all other quality assurance and clinical trial participants.

### Delimitations

The researcher's selection of the scope or boundaries of the study define the delimitations (Bernard, 2013). The scope of the study was to explore the quality management system from one pharmaceutical organization, which was responsible for performing a particular research development function of the clinical trials. The study did not include any clinical quality assurance participants outside the Northeast United States. Clinical quality assurance managers with less than 5 years of experience were not in the study. The purpose of this qualitative study was to explore the strategies clinical quality assurance managers needed to avoid a breakdown in quality with outsourced clinical trials in Asia-Pacific countries. Therefore, the scope of the study included only clinical quality assurance managers, and all other clinical line functions were excluded. To understand why breakdowns occurred in outsourced clinical trials, only clinical trial processes, clinical regulations, and clinical quality management systems were in scope. All other nonclinical processes and systems were out of scope.

## Significance of the Study

### Contribution to Business Practice

The research study showed the benefits, risks, and quality issues associated with outsourcing clinical trials to Asia-Pacific countries. The data collected from this research study may help pharmaceutical organizational leaders contribute to the effective practice of business by assessing their outsourcing business model and quality management

systems. In addition, the data can also enhance quality agreements between pharmaceutical organizations and outsourcing clinical trial companies to reduce audit inspection findings and increase approval time on new drugs.

## Implications for Social Change

The information provided by clinical quality assurance managers contributed to social change through the creation of strategies to improve quality with outsourced clinical trials. The results may also be used to develop outsourced clinical trial best practices and standard operating procedures. The quality improvements with outsourced clinical trials may produce more effective, safer medicinal products. The quality improvements made within the clinical trial processes may provide knowledge of the quality of the drug and the adverse events associated with the medicinal product, which may ultimately help the public understand the risks related to the medicinal product.

## A Review of the Professional and Academic Literature

The purpose of this section is to provide a review of the literature to describe various pharmaceutical challenges that are forcing pharmaceutical leaders to outsource clinical trials to Asia Pacific, and to explain why quality breaks occur after signed quality contracts. To understand this phenomenon, I conducted a literature review for clarity and insight (Marshall, 2010). I provided critical analysis and synthesis of various sources of literature such a government agencies' reports, clinical regulations requirements, peer-reviewed journals, books, and dissertations. Scholars addressed the pharmaceutical outsourced clinical trial model and the various quality risks and concerns in the following areas: (a) pharmaceutical challenges, (b) outsourcing, (c) top destination for outsourcing

clinical trials, (d) outsourcing clinical business process, (e) outsourcing key risk factors, (f) total quality management with pharmaceutical organizations, (g) quality of clinical trials, and (h) clinical trials process improvements. For the professional and academic literature in the doctoral study, the focus is to review peer-reviewed books, journal articles, doctoral dissertations, and government websites. I used the Walden University library databases to search for peer-reviewed journal articles, books, and dissertations. Databases included ABI/INFORM Global, ProQuest, and SAGE Publications. I also used Google Scholar to search for relevant literature. I employed the following search terms to locate information: *outsourcing in Asia*, *outsourcing clinical trials*, *outsourcing risks*, *pharmaceutical challenges*, *quality systems*, *offshoring*, *general system theory*, *clinical trial regulations*, *total quality management*, and *continuous process improvement*. This strategy assisted in identifying leading scholars and their studies. Integration of this knowledge supported this study (Marshall, 2010). The literature review consisted of 95 peer-reviewed journal articles, government reports, dissertations, and books; 82 (86%) were published within 5 years of the study.

The purpose of this qualitative case study was to explore strategies clinical quality assurance managers use to avoid a breakdown in quality with outsourced clinical trials in Asia-Pacific countries. The literature review supported the research study's conceptual framework and provided information regarding its application (Brown-Jeffy & Cooper, 2011). I used Ludwig von Bertalanffy's (1968) general systems theory to understand the complex problems of quality breakdowns with outsourced clinical trials.

**General Systems Theory**

The conceptual framework for the qualitative case study basis was the general systems theory. The general systems theory is a methodology employed to understanding complex problems and phenomena. The concept of system science emerged due to the response of individuals wanting to understand and deal with complexity. The system theory started to emerge in the 1960s as a uniformed approach to understanding environmental factors as well as humans and how they interplay with human development and functioning (Germain, 1994). According to Laszlo and Kippner (1998), the concept of the system theory is that the system is characterized by the interaction of its components and knowing one part of the system allows information to another part of the system. The approach drew upon the application of the human activity system as well as the general system theory. Hall and Fagen (1956) defined the term *environment* in the system theory any change to the subject or environment can attribute to systems changes and the behavior. Germain (1994) described two system theories: the social system theory and the general system theory. According to Germain, both system theories had a common interest in the living system and could be used to view an individual as a system. The difference between both system theories was the general systems theory was from physical science, biologics, and cybernetics, and the social system theory derived from social psychology, sociology, and symbolic interactionism (Germain, 1994). Ackoff (1981) argued that the social system environment contained three purpose levels: the parts of the system, use of the system, and the supra system.

The general systems theory was founded in 1928 by von Bertalanffy; however, it was not until 1968 that a true scientific breakthrough occurred with the publication of the general system theory (Norlin & Chess, 1997). Von Bertalanffy grew quite dissatisfied with the cause-and-effect theories to explain the change observed in living organisms and decided to discover a definitive cause of a system relationship. Von Bertalanffy (1968) searched to understand the order among the parts in the system, and not to focus on them. Until this discovery by von Bertalanffy, a scientist focused on the reductionist process based on linear causation to understand the whole system by examining the individual parts, not how the parts related to each other (Norlin & Chess, 1997).

Von Bertalanffy argued that societies, organisms, and human organisms are open systems. Also, von Bertalanffy explained that there are systems that have a number of subsystem components that are interrelated and interdependent (Stacey, 2011). In an organization, subsystem components related to the control and management information systems and the cultures that kept harmonious teams working together. The general systems theory recognizes that a whole system needs to maintain a form of control or the subsystems will become out of balance over time. Inevitably, the system will be out of balance with the environment as well as each other (Stacey, 2011; von Bertalanffy, 1968). However, adaptive mechanisms exist within an organization that promotes changes and keeps it in equilibrium with the environment. Ultimately, there is an inevitable conflict between the two subsystems; however, according to the general systems theory, a successful organization will sustain equilibrium (Stacey, 2011).

According to Stacey (2011), the general systems theory includes the following organizational dynamics:

- It is up to leadership to manage boundaries and to regulate the system, so it adapts to changes.
- Successful management will ensure the system adapts to the changes in its environment and process negative feedback producing stable equilibrium.
- An organization is an open system, a set of interconnected parts that interact with other individuals and organizations outside of it.
- A system imports information and energy from outside itself, and transforms both the energy and information in some way to export the transformed results to a system outside itself.
- Organizations should import systems by: (1) import across a boundary separating it from other systems, (2) transform the imports within its boundary, and (3) export back across the boundary separating the system from the environments.
- Success is state of harmony, stability, and consistency.
- The relationship across the boundary is ever changing, the environment will always change, and the boundary needs a regulatory function.
- Adaption to the environment determines the stable equilibrium between integration and differentiation, between the control system and maintenance change required for success.

As globalization developed, Godfrey (2010) asserted that interdependence becomes more relevant and the complexity of the problems the organization needs to resolve increases. Consequently, the organizational need for a sustainable environment is urgent (Godfrey, 2010). Organizations use a system thinking approach for these complexities. Pharmaceutical managers use system thinking as a way to resolve complex problems and designs. Essentially the framework for system thinking is to seek interrelationship rather than things. Advantages for the organization using the system thinking approach include leaders managing and grasping complex situations and uncertainty where there is no simple situation. Godfrey (2010) summarized this approach as the practical holism when the organization learns of an effective action by looking at connections rather than parts separately (Godfrey, 2010). The three key framework ideas for the system are processes; layers, parts, and wholes; and connections (Godfrey, 2010).

**Quality Management Systems**

In a clinical setting, it is difficult to measure quality. Quality systems require implementation and development of standards within each step. Even though this requirement is not new to clinical research, a systematic approach will produce more reliable, high-quality data and a more useful product without compromising patients' rights (Human Information Technology, 2014). There are several general requirements that can improve quality systems such as training, personal roles and responsibility, policies and procedures, quality assurance and auditing, document management, record retention, reporting, and corrective and preventative action (Kleppinger & Ball, 2010). Personal roles and responsibilities need to be communicated and documented for the

clinical trial research team. It is essential for a clinical research team to create a delegation log to create accountability for each member in the clinical trial. The responsibility of training falls under the sponsor. It is up to the sponsor to ensure the research investigator and clinical research staff are appropriately trained and qualified to conduct a clinical trial (Collaborative Institutional Training Initiative (CITI), 2014). The clinical research team needs mandatory training in good clinical practices and human subject protection. It is essential that sponsors have policies and procedures in place to approve a robust Good Clinical Practice (GCP) training to the research staff as well as periodic refresher training. Food and Drug Administration (FDA) Regulations (2015) is also in agreement with the training requirement within the quality system by stating in the regulations when there is an investigational product within the clinical trial all key clinical research personnel should be knowledgeable of all applicable regulations, including those that pertain to human subject protections. Furthermore, it is also a training requirement for the clinical research team to train on the clinical protocol and document the training of the protocol. Finally, to ensure the adequacy of the training, a knowledge test is highly recommended (FDA Regulations, 2015).

Before the investigator or sponsor writes any protocol, it is essential for the investigator or sponsor to be well aware of his or her institution's procedures and policies. This can include, but may not be limited to, the handling of biological samples, protocol review procedures, confidentiality agreements, human subject protections, data management, and procedures for handling possible scientific misconduct (Code of Federal Regulations (CFR) 21a, 2015). An essential policy for the institution to have is

the record retention policy, which would specify a longer retention time frame than the one required by the federal agency (CFR 21b, 2015). It is critical for institutions to have written standard operating procedures (SOPs) in place for each clinical site. Standardization with clinical research SOP templates is essential to provide quality documentation standards within all clinical line functions (Clinical Trial Network Business Practice (CTNBP), 2014). It is imperative that SOPs be reviewed periodically to adhere to new regulatory requirements and updated processes and for all staff to adequately document SOP training (CTNBP, 2014). Another critical component in the quality system is to include quality assurance and auditing. Clinical trial teams are familiar with a sponsor audit or a regulatory agency audit. Clinical trial teams are well aware of the scrutiny of an audit when it comes to clinical database systems and quality assurance procedures (Kleppinger & Ball, 2010). If there is no implementation of quality assurance programs within the investigators' sites, there is no quality oversight (Kleppinger & Ball, 2010).

Other essential components of the quality system are document management, record retention, and reporting. All staff should understand documentation of archival procedures, and staff should demonstrate an understanding of these systems. Handling of documentation such as tracking, filing, conventional naming, document version control, and systematic backup of real-time data collection should follow standardized procedures. All clinical documentation should be in a locked area with restricted access. All computers should be qualified or validated, and password protected (Kleppinger & Ball, 2010).

The final component of a quality system is corrective and preventive action. Clinical trial teams should document clinical trial quality breaks and corrective preventative actions within the quality system to avoid any potential agency findings. Potential problems will always arise in an outsourced clinical trial; however the discovery of the potential issue should have an effective corrective and preventative action assigned. After an allotted amount of time passes, clinical trial teams should perform an effectiveness check to ensure the problem would not recur. According to Grignolo (2011), the Clinical Trial Transformation Initiative, there are four key components consisting of management responsibility, resource management, process management, and improvement. Garza-Reyes, Rocha-Lona, and Kumar (2014) presented similar views to Kleppinger and Ball (2010) that many organizations should turn to a quality management system to provide high-quality products and customer satisfaction. Rocha-Lona, Garza-Reyes, and Kumar (2013) argued that to obtain high-quality standards, organizations need to integrate the quality management system and deploy quality management tools and methods across the whole organization. Garza-Reyes et al. (2014) had slightly different elements of their quality management system (QMS) and categorized them by processes, human capital, business strategy, information technology, and management models-methods-tools. To have an effective quality management model, tools, and methods; organizations refer to the ISO guidelines, six sigma, lean and business techniques, total quality management (TQM), process re-engineering and business excellence models (BEMs) (Asif, Searcy, Garvare, & Ahmad, 2011; Garza-Reyes et al, 2014). When organizations develop a well-structured integrated QMS, it

provides a competitive advantage for customer satisfaction and higher quality products (Asif et al., 2011; Garza-Reyes et al., 2014; Jones, Parast, & Adams, 2010; Kanji, 1996).

Some of the gaps that existed in the quality management literature were that the authors did not discuss the effectiveness or non-effectiveness of the quality management system through quality metrics. If the authors discussed, quality metrics within the literature for quality management system, they would provide the audience knowledge on organization performance. In addition, there was no discussion on what the common reasons were that breaks occurred in QMS, even though the organizations had the appropriate total quality management model.

**Quality Management System Within a Pharmaceutical Organization**

Quality is an essential component of the pharmaceutical industry. Johnson and Gupta (2013) defined quality as providing practical solutions to the queries about the profits and dangers of a drug process while guaranteeing safety for human subjects. To fulfill the regulatory requirements, the sponsors need to enhance quality by improving systems and processes (Cerullo et al., 2014; Hanfield & Gosh, 2004; Johnson & Gupta, 2013) with definite standards for every clinical test procedure. It is mandatory for the sponsors of clinical trials, business process organizations, and contract research organizations to establish, maintain, control, and monitor both the quality assurance and quality control systems. In addition, for organizations that follow the systems' standard operating procedures and other clinical quality documents provide the highest quality product and services to meet customers' needs and expectations (Johnson & Gupta, 2013). For a clinical study to have quality, it must include an experimental design that is

scientifically and ethically sound; protection of the subjects' rights, safety, and welfare; competent personnel; adequate surveillance; and current, complete, and exact data. In recent years, regulatory agencies have become stricter on clinical trials specifically regarding patient security and data credibility (Johnson & Gupta, 2013). According to Johnson and Gupta (2013), the main purpose of the regulatory agencies is to execute the principles of quality management in health research to impede downfall, maximize the use of valid resources, and guarantee consistency and dependability of outcomes.

**Quality management system success factors** Pharmaceutical organizations utilized quality management systems to improve the quality of product and process to achieve continuous customer satisfaction (Khanna, Sharma, & Laroiya, 2011). Implementation of quality remains an important issue for global organizations, which are continuously trying to improve their competitiveness (Khanna et al., 2011; Johnson & Gupta, 2013). The R&D organizations are facing an evolving environment, which is rapidly changing due to globalization. Indian R&D organizations specifically are in dire need for new approaches, strategies, and techniques to have a competitive advantage (Khanna et al., 2011). One question asked by many organizations (Khanna et al., 2011; Johnson & Gupta, 2013) is why with the implementation and benefits of quality management systems do many Indian R&D organizations face numerous implementation problems? Quality management remains a challenge because the decision makers within the organization are not prioritizing critical success factors. For an organization to adopt new quality management systems, produces high risk due to the high cost associated with adoption. One of the standard practices in India is to select training and then adapt to

process carefully using various methods to reach the final decision. In order to achieve a competitive edge, organizations have shifted priorities from a low-cost production to quality, dependable delivery, flexibility, and short lead-time. They also implemented new philosophies and information technology such as quality management systems, Six Sigma, lean, business process re-engineering and business excellence models, which claims to support an organization's improvement efforts (Thawesaengskulthai and Tannock, 2011; Khanna et al., 2011). Indian organizations realized that they would not gain competitive advantage without being quality conscious (Khanna et al., 2011). The quality management system implementation depended on several factors such as communication, management commitment, and employee involvement (Kanji, 1996).

**Quality management system critical success factor** For QMS implementation to be effective within the organization, it involved the defining and deploying critical success factors (CSF). These factors included the hard factors such as systems, tools, and techniques, as well as, soft factors such as employee commitment and leadership (Khanna et al., 2011). The CSFs are the factors that can significantly affect the organization and required particular attention in the quality management systems. The CSF provided signal detections of early warning risks within management systems and avoids any surprises. In order for the successful QMS implementation, the organizations should have a thorough understanding CSFs and adoption of the QMS implementation (Salahedin, 2011; Khanna et al., 2011). One of the key points in the literature reviews (Khanna et al., 2011, Salahedin, 2011) is the ranking of the CSFs in the quality management implementation to reduce costs, increase success rate, and prevent failure.

Top management leadership is a vital factor because it is important for management to provide enough resources to ensure quality achievement, as well as, understand the concept of quality and importance of it. Management needed to understand and identify quality management goals and demonstrate understanding those objectives. One of the gaps in management leaders is their lack of intention of the quality management system. As well as, how it is implemented in various line functions within the organizations (Khanna et al., 2011). The second CSF is supplier quality management. Supplier's management focused in on the effectiveness of the quality management system within the organization. The relationship between supplier and organization is an important relationship to maintain (Khanna et al., 2011; Salaheidin, 2011). In order to have an active relationship, the organization had few supplier rather than many suppliers. There should be a clear understanding of each other expectations and each other's processes to ensure quality products. The organizations' expected proper quality management systems in place to measure/monitor delivery performed and quality of the product and has knowledge information exchanges with the supplier on the regular basis (Khanna et al., 2011). The third factor is process management. Process management should meet the criteria of the international organization for standardization (ISO) 9000 standards (Khanna et al., 2011; Candido & Santos, 2011). Frequent reviews of all aspects of clinical and manufacturing operations should be down and any corrective and preventative actions implemented. The identification of key processes and improved continuously to achieve higher quality with the product (Khanna et al., 2011). The fourth CSF is human resource management. Human resource management focus is to empower

employee management within the organization. Human resource management encouraged employees to innovate and contribute quality continuous improvement processes (Khanna et al., 2011). Quality management within pharmaceutical organization focused on an open quality culture, teamwork, and having sustainable continuous improvement. Quality management required human resources management systems to be in place to support this focus. The systems allowed information exchange between human resource and employee to ensure that employees are aware of the role and responsibilities, goals and objectives, and job training. The fifth CSF is customer satisfaction. Customer satisfaction in quality management focuses on the quality measure. The more satisfied the customer, the greater the quality measure. Organization should have systems in place to receive complainants and feedback. The sixth factor is the role of the quality department within the organization. The quality assurance department should have clear objectives, vision, missions, systems, quality policies and tools in place to implement a viable total quality culture (Khanna et al., 2011). The seventh factor is training. Training places a crucial role in the implementation of the quality management system. Khanna et al. noted quality management system key focus is adequate training and education of employees to improve their knowledge and skills. It includes general training as well as specific training and retraining of the employees. It provides a base for communication of new organizational strategies to the employees. The eighth factor is quality citizenship. Quality citizenship is when the organization adopts an ethical standard that allows the accountability and transparency of key stakeholders for their organizational performance. They promote both social and corporate responsibility and

environmental sustainability both in the present and the future. The ninth CSF is a quality system and information technology. To collect information on data such as cost of quality data, scrap data, and rework data; an effective and efficient system should be in place. The information system should enable data be transparent, collected in a timely manner, and provides feedback to the employees. The outputs of these systems allowed to measures quality performances (Kanji, 1996). The use of IT has a profound effect on quality managements by contributing to the enhancement of quality awareness, reduction of quality costs, improvement of product and processes. Finally, there is the product design. Product design is an important factor in the quality of the product. Product design must meet with quality standards, ethical standards and meet with regulatory requirements (Johnson & Gupta, 2013). Product design ultimately effects if the product to the customer is right or wrong and if it will meet the customer satisfaction. Johnson and Gupta, Khanna et al., and Saleheldin  discussed quality management systems, implementation, and the success factor, which will assist organizations to succeed in implementation. However, one gap that exists, there is no detailed discussion of unsuccessful factors that causes the quality breakdown with quality management systems. By addressing both successful, and unsuccessful factors provides the reader a comparative to understand why the factors were categorized success and unsuccessful.

**Quality management system implementation barriers** One common failure factors of quality management system within an organization is improper implementation (Cândido & Santos, 2011; Dahlgaard-Park, 2011; Hoonakker, Carayon, & Loushine, 2011; & Kanji, 1996). Many organizations' find it difficult to effectively implement

quality management systems, which in turn have lost the momentum to adopt an efficient model and instead have only set quality management system initiatives (Cândido & Santos, 2011; Manjunath, & Kumar, 2013). Due to the difficulty of implementing quality management system, there is a decline rate within many organizations in adopting quality management systems (Cândido & Santos, 2011; Dahlgaard-Park, 2011) and instead are turning to other management strategies such as ISO 9000 management strategies (Cândido & Santos, 2011). There is a common theme among the literature review by authors Cândido and Santos, Dahlgaard-Park, Hoonakker et al., Kanji, Manjunath and Kumar, and Moballeghi (2014) agreed the reason for failure of many organizations quality management system models is that it requires total quality cultural change for everyone within the organization. In addition, there is also agreement that top managers and executive leaders need to take an active leadership role have the commitment from everyone within the organization committed to the quality goals.

Sebastianelli and Tamimi (2011) acknowledged additional factor analysis of QMS barriers, which reveals five common obstacles such as lack of customer focus, inadequate resources of QMS, inadequate human resources development and management, lack of quality planning, lack of leadership for quality. As well as, provided framework for evaluating the significance of top management related obstacles for QMS success, as well as, provided additional guidance in developing strategies for a complete and effective QMS transformation (Sebastianelli & Tamimi, 2011). Yusof and Aspinwall (2011) introduced other QMS barriers, which are not mentioned by other authors such as training and development of staff at ad hoc can hinder improvement effort. In addition, the lack of

financial resources, this can affect organizational processes as well as management not delegating a task, which can stifle teamwork. All of the elements above can hinder QMS implementation, and there is a vast literature on how QMS can help to improve the quality and how difficult it is to implement. However, there is scarce current works of literature that provided a framework for organizational leaders to develop strategies to have an effective QMS in their outsourcing the models in developing countries (Moballeghi, 2014). A gap in the literature it does not discuss the difficulties that developing countries have in identifying QMS barriers and critical success factors of QMS implementation (Moballeghi, 2014). As the trend to outsource to developing countries is becoming part of many global organizations, the focus for future studies on how to implement a successful QMS implementation. Furthermore, the study's aim of proper guidance to benefit manager within these developing countries where there is a lack of information on how to overcome these implementation barriers and can promote new systematic way of thinking in various cultural context (Moballeghi, 2014). One of the gaps in literature is there is no analysis of what an organization does after identifying QMS barriers. There is no clear guidance for an organization to remove a QMS barrier. The final gap in the literature is QMS success factors are implemented within the organization; however, sustainability is not discussed (Asif, Searcy, Garvare, & Ahmad, 2011). I think if future studies address these gaps in the literature more global organizations will have the tool and skill set to implement and sustain an effective QMS model.

**Pharmaceutical Organizations Challenges**

Pharmaceutical organizations are faced with various challenges that relate to regulations, advance in technology, globalization, product competition, innovation of new knowledge, and outsourcing (Duppada & Aryasri, 2011). Outsourcing clinical trials is the biggest trend of pharmaceutical business approach to gain the competitive advantage, to gain quicker regulatory approval, and to produce efficient and effective clinical trials by outsourcing organizations (Kara, 2011; Sharma, 2010). Pronker et al. (2011) agreed with Kara that due to the drug price increase the supply chain is under scrutiny. The drug pipeline is decreasing, and the cost of drug development is increasing. Consequently, this is leading to more out of pocket expenses for patients for drugs. The increase of drug development costs and having a competitive advantage is leading clinical trials and research development functionality to outsource to India.

There are vast amount of peer-reviewed literature, which analyzed the challenges that pharmaceutical organizations face. Hafner and Popp (2011) and Lamittina (2012) discussed some these challenges, such as tremendous amount of the financial loss to other generic organizations when patent expires. For example, the top ranked pharmaceutical companies such as Bayer lost its patent rights to Nexavar, Roche lost patent for Tarceva, and Pfizer denied the patent rights to Stuten and lost billions of dollars. The effect of the tremendous amount of financial loss causes the pharmaceutical company to consider outsourcing.

Pammolli, Magazzini, and Riccaboni (2011) agreed that the pharmaceutical organization specifically in research and development are facing tremendous challenges.

One of the challenges the R&D organization face is complexity in the productivity of the pipeline. Pharmaceutical R&D productivity from the mid-1990 has experienced a downturn. From 1998 to 2008, the number of new molecular entity approved per year as declined. According to recent estimates, the average time to pass approval through US clinical trials ranges from six years to eight years (Pammolli et al., 2011). Innovation in pharmaceuticals is a cumulative process, and, unfortunately, the markets where effective compounds are available there is high POS. In the established markets, the patent innovates drugs are at the same level as the older drugs. Consequently, R&D investments tend to focus on new therapeutic targets, which are characterized by high uncertainty and difficulty, but lower expected post-launch competition (Pammolli et al., 2011).

Adobor (2012) also agreed on the increasing challenges such as increasing speed in drug development, domestic cost increase, various challenges of competition, emerging markets, global clinical sponsors, outsourcing critical parts of the value chain activities specifically drug testing and contract clinical organization is causing ethical and moral issues. There are advantages for pharmaceutical giants to outsource medical research for lower cost to Asia Pacific. However, the contract medical research that is being outsourced is in jeopardy until the ethical issues and concerns associated with outsourcing business models are not being addressed or recognized. One gap in the literature is there is discussion on challenges that pharmaceutical organizations face, however, there is no discussion in the literature on how the challenges affect the pharmaceutical organization such as employee morale, loss of jobs, adapting to new culture and technology.

**Drug development costs** According to Rosier, Martens, and Thomas (2014), the estimated cost of the drug development can range from 800 million US dollars to 1 billion. Investments for pharmaceutical companies in the development of new drugs is a considerable risk, due to the fact it is unknown if the new drug is safe in patients until the end of drug development (Rosier et al., 2014). American's spend $2.6 trillion dollars on healthcare last year (Hassanzadeh, Modarres, Nemati, & Amoako-Gyampah,2014) and the healthcare expenditure shows over 12.9% of total expenditures is with the pharmaceutical and it is the fastest growing portion of healthcare spending (Hassanzedeh et al., 2014). There is an agreement between the authors this is at the increasingly high prices of prescription drugs, especially with specialty drugs and brand names, and rising associated costs with research and development of new drugs. Pharmaceutical organizations argue the rise of cost is due to the fact the process of drug development in R&D is extremely expensive and requires substantial capital expenditure (Hazzanzedeh et al., 2014; Drain, Robine, Holmes, & Bassett, 2014). For a pharmaceutical organization to make a cancer drug, it cost them around $1.75 billion for R&D and almost ten years to grow through the various test and market. American pharmaceutical organizations alone spend over $45 billion on developing new drugs or modifying current drugs.

## Outsourcing

For the pharmaceutical organization to meet the challenges of increasing cost of drug development and stricter regulation, they are turning to outsourcing clinical trials. Outsourcing consists of operation functions or transferring of internal functional services to a third party service provider and controlling the sourcing through the partnership or

contract management (Mariani, Falotico, Zavanella, & Mussini, 2014). A vast amount of literature provided the benefits and motivations for pharmaceutical organizations to outsource. The three major reasons for motivation for outsourcing are target health policies, public health development strategies, and public spending cuts (Mariani et al., 2014). Outsourcing does provide potential benefits, however there are also several disadvantages ( Mariani et al., 2014; Roberts, 2001; & Sharma, 2010 ) cost savings is lower than expected and not available over the long term; liability for vendor action, being over-dependent on vendors and losing control over the standard of service delivering (Mariani et al., 2014).

The outsourcing of various functional departments within R&D, to CRO or BPO, is a frequent practice (Huysmans et al., 2014) among pharmaceutical organizations to lower costs and achieve faster approval timelines. However, the majorities of the outsourcing projects are prone to failure (Huysmans et al., 2014) and increase costs for pharmaceutical organizations to repair the damage. Due to the high risk of failure, many scholars suggest a variety of outsourcing risk factors that leads to unsuccessful project outcomes, as well as possible remedies to mitigate them. There are many empirical studies, which continue to report frequent failures in outsourcing projects. Huysmans, De Bruyn, Beazeer et al. (2014) used the concept of modularity for an alternative perspective to analyze risks related to outsourcing projects. The approach assisted in supplementing existing outsourcing risk analyzes with new, additional, or more profound insights into outsourcing risks. In addition, it served as an additional basis to list a more exhaustive enumeration of required mitigating actions, which leads to successful outsourcing

projects (Huysmans et al., 2014). In the BSkyB, the case showed the alternative perspective that illustrates a reanalysis of a failed outsourcing case documented in the literature and available court proceedings. According to Huysmans et al. the BSkyB case shows the specific way how the poorly designed modular structures at the project communication, technical, and project management level could identify ex-ante. The identification explained the manifestation of ex-post outsourcing risk factors such as managing user expectation, lack of required skills, managing user expectation, communication problems, project management, and significant integration requirements.

**Top destinations for outsourcing clinical trials** The author Langer (2011) provided an in-depth analysis of benefits and risk to outsourcing to India and China from the intellectual property. The comparison of the large pharmaceutical companies of the research and development spend provided excellent data on how much each company is spending on R&D costs. The author slightly touched on the quality aspects, however not much detail or analysis on the breakdown of the quality and the recovery from it. Surve and Tembhurne (2013) drew the same conclusion as Langer that India and China are the top destinations for outsourcing. Surve and Tembhurne discussed how the trend for pharma and life sciences industry is favoring of outsourcing both research and manufacturing to India. India became the most sought out destination for outsourcing due to low cost (Drain et al., 2014). Frost and Sullivan (2011) study results showed India's contract research and manufacturing estimated at $895.44 million in 2006 and increased 43 percent over the previous year. Clinical research currently is 16% of their revenue.

The leading driver to outsource clinical trials to India costs and compliance issues are becoming prohibitive for them in the West.

Novak, Beloserkovsky, and Payeur (2014) acknowledged there are changes in the geographical regions in the global clinical trial landscape. The reasons for increase global clinical trials: (a) increased prevalence of chronic diseases, (b) aging population, (c) the embrace by physicians and payers of evidence-based medicine, (d) and patient's common belief that they will benefit from treatment and medical technology, and (e) access to medical treatment through participation in clinical trials (Novak et al., 2014). The newly growing regions for clinical trials have moved to East Asia, and South Asia is the fastest growing regions. A great hike has registered with China by +30% and South Korea by +29%. Both countries represent almost +7%. India has the most significant growth at 40% due to the considerable advantages such as the acceptable quality of services and good patient recruitment (Novak et al., 2014).

A recent research study conducted by Yathindranath, Kureishi, Singh, et al. (2014) in the evolution of clinical trial landscape of Asia Pacific explores the increase in global trials in the region. The method used for the study was an extraction of clinical trial data from 15 commercially available online databases for global clinical sites and trials including Asia registries. The clinical trial registries such as: Australian New Zealand Clinical Trials Registry, ClinicalTrials.gov; the International Standard Randomized Controlled Trials Number; Clinical Trials Registry, India; Clinical Research Information Service, Republic of South Korea; Japan Primary Registries Network; the Sri Lanka Clinical Trials Registry assisted with gaining access to the data (Yathindranath et

al., 2014). In order to analyze the latest trends in Asia Pacific, two-time periods (2009-2010 and 2011-2012) were collected. The results from the study showed that in comparison of the two-time periods Asia Pacific is stable with the volume of clinical trial site numbers and clinical trial numbers. The primary destinations for agencies inspections there are the change in geography, therapeutic areas of clinical trials observed and conducted. The study concluded the top ten destinations in Asia Pacific for major clinical trials destinations are Taiwan, Japan, South Korea, India, and People's Republic of China (Yathindranath et al., 2014). The rising standard of medical care and the standard of living in developing countries such as Vietnam, Philippines, and Indonesia is causing an increase in local clinical trials.

The major component of the increase in global drug development is the emergence of Asia. Asia is still in the infancy phase when it comes to the perceived potential in the pharmaceutical industry; however, growth is steadily increasing. The reason for growth is due to the financial consideration of the clinical trials such as reduced per patient costs and shorter recruitment timelines, which are primary drivers of the growth (Horsburgh et al., 2014). One of the active contributors to the growth of clinical trials in Asia Pacific is oncology. The rapid growth in Asia Pacific is due to the total investigator site pool, as well as, the number of experienced and inexperienced or naïve sites, which are being, activated (Horsburgh et al., 2014). In April 2013, more than 9,000 ongoing clinical trials in Asian Pacific countries were listed in the ClinicalTrials.gov database, 20% of the global clinical trial landscape (Horsburgh et al., 2014). Twenty-seven percent consisted of Asian-Pacific studies were Phase I, Phase II or

Phase III oncology trials. Additionally, less than 10% of all patients enrolled during the observed period were involved in oncology studies.

**Outsourcing clinical business processes.** Pharmaceutical organizations increased sourcing their clinical business processes through third party service providers, a standard practice known as BPO. Globally, the BPO market earns $279 billion dollars in their clinical trial services, and it will continue to grow at 25% annually (Lacity, Solomon, Yan & Willcocks, 2011). In the last 15 years, many academic researchers studied this market and produced findings relevant to practice. In previous research, many outsourcing vendors have been reviewed; however, the entire body of BPO research has never been considered. Lacity et al. conducted a study to fill this gap. The research consists of total studies and reviews 87 empirically robust BPO articles published between 1996 and 2011 in 67 journals to answer three research questions: What has the empirical academic literature found about BPO decisions and outcomes? How do BPO findings compare with Information Technology Outsourcing (ITO) empirical research? What are the gaps in knowledge to consider in future BPO research? The study provides researchers of a broad overall broad understanding of BPO. However, the BPO practice continues to evolve as more pharmaceutical clients and suppliers on every continent are actively participating in the global sourcing community. One gap that remains is a quality of the BPOs' clinical trial processes provides for their pharmaceutical client.

Lahiri, Kedia, and Mukherjee (2011) agreed with Lacity et al. (2011) there are significant gaps in the understanding the context of the offshoring service providers.

However, even though there are gaps in the research on understanding BPO as a whole, many organizations still outsource their business processes. Essentially, organizations disaggregated their value chain and transition over their parts to the providers for a successful delivery and execution of the processes. The primary inspiration for an organization to move to BPO is cost savings, adding flexibility of business operations, greater risk spreading, increased focus on core business activities, and reduced to market (Lahiri et al., 2011). For BPO to partake in the rapidly growing market, they offer a wide variety of value-added services to their expertise. BPO are no longer providing information technology services, banking, and capital market, mortgage services, however now extended to include clinical trial services. Pharmaceutical organizations tend to contract with BPOs for their clinical trial services. The BPO contracts are long-term in nature than in traditional offshore outsourcing contracts requiring business partners to remain focused on building and sustaining value-creating relationships (Lahiri & Kedia, 2009). One gap with BPO that remains is the lack of understanding their quality as an ongoing business partnership.

Scholars suggested that the quality of ongoing business partnerships needs to be high to enable collaborating organizations to realize valuable outcomes (Lee, 2001). The partnership quality is how well the partnership delivery outcomes match the participants' expectations. According to Lee, the current context of partnership quality refers to the perception of the extent of fulfillment of expected outcomes arising out of the inter-organizational relationship between provider and client. Prior research (Lee, 2001) shows that partnership quality as a valuable relational resource allows providers to perceive

nature of their cooperative relationships with clients, as well as, encourage them to consider ways to enhance or strengthen the same in order to perform better. Lee suggested the knowledge might enable providers to gauge their ongoing partnerships on various parameters such as compatibility with policies and culture, sharing benefits and risks, business understanding, and dependability. In addition, if there is such an understanding, providers are in a position to enhance performance by escalating commitment, coordination, and trust, increasing flexibility in accommodating changes, and considering clients as business partners and not just customers of services (Lee, 2001).

One of the top destinations for BPOs is India. Dzever and Gupta (2012) agreed the BPO is extensively growing and one of the sought out BPO destination is India due to the observation of clients that the BPO industry in India people work 'when the rest of the country sleeps'. There is the majority of BPO in India accommodates and work the European and USA time frames. Therefore, meaning most BPO employees in India work the night shift or the graveyard shifts.

**Outsourcing key risk factors** As the outsourcing trend continues to rise, it is important for the organization to consider potential risk factors that occur when outsourcing and the importance of having a risk framework before signing any contracts with outsourcing vendors or BPOs. Critical risk factors to a client are associated with financial, complexity, contract, execution, legal, planning and control, the organizational environment, scope and requirements, the user and team (Alaghehband, Rivard, Wu, & Goyette, 2011). One of the important risk-based decision-making factors would be the

regional location of the outsourcing organization. The more information the organization has on the outsourcing region's geopolitical instability and economic volatility the lower the risk (Holbrook, 2011).

Gholami (2011) conducted a qualitative study to determine the critical risk factors when outsourcing IT projects. The results showed the five key risk factors are financial risks, technical risks (such as database, communication infrastructure, software risk, security, and licensing), managerial risk, behavioral risks, and legal and political risks (Gholami, 2011). One of the common mistakes that senior management make in the outsourcing business model is not having the understanding or having the knowledge of the risks, the right tools to handle the risks and developing an effective mitigation for the risks (Ghandi, 2011 & Gholami, 2011).

One of the main reason organizations benefit from outsourcing is a reduction in cost, however when outsourcing processes to offshore location increases strategically risks as a result of vendor to clients deliberate actives (Gholami, 2011; Liu & Nagurney, 2011). Organizations need to conduct a quality assessment as part of the determining factor in choosing the most appropriate vendor that the organization determines has the quality and the right equipment (Yu & Thomas, 2011). Ghandhi (2011); Gholami, (2011); He, Weeks, Buyske, et al.(2011); and Yu and Thomas, (2012) agreed when choosing a vendor for long-term business process a vendor assessments are key. Pharmaceutical organizations' need a complete understanding of the vendor organizational structure, trading relationship, operational manager, general management practices, quality culture and understanding their financial for successful projects. The

most common vendor risks during a quality assessment are knowledge transfer, lack of active vendor management, incomplete contracting trust (Hamlen & Thuraisingham, 2012).

Organizational management's awareness of offshoring BPO's cultural risk factors that often occur with client/organization and vendor relationships (Holbrook, 2011; Mosher & Mainquist, 2011) can alleviate future problems. Culture plays a significant role when dealing with offshoring vendors. Communications, management style, understanding each other culture, gender issues, quality management, and team harmony are at risk if client and vendor have serious communication break (Holbrook, 2011).

**Quality of Clinical Trials**

With the developments of global markets quality has become the central focus. Previously, many companies have forgotten to include quality as part of their strategic objectives (Devpura, Garza–Reyes, Kumar, Rocha–Lona, & Soriano–Meier , 2014). However, now quality measurements and quality performance are the key focus of numerous companies in the global markets. A single case study conducted on a multinational Fortune 500 pharmaceutical company who has built a conceptional quality model in their strategic objectives to explore how quality model affects their processes (Devpura et al., 2014). The results showed a company who had a total quality management built into its model earlier showed greater global competition, advanced programs, and effective quality processes. In addition, European companies include the ISO 9000 criteria for a quality model and emphasis on the quality culture were the highest marked for their quality products (Devpura et al., 2014). When research

organization conduct clinical trials, it is important for them to adhere to good clinical practices. Adhering to these practices will help to avoid an audit finding from sponsor and health authority agencies (Karbwang, 2013).

One major need for consumers is for a drug developed by the pharmaceutical organization to provide safe and effective therapeutic drugs to promote, cure, and treat diseases, as well as, health and prevention (Sasaki, McGibbon, Lee, Murray, & Pharr, 2014). The pharmaceutical organization's ability to consistently deliver these products declined in the last few years due to job losses, site closures, an increase of R&D costs, and productivity lags (Sasaki et al., 2014). Due to the decline, pharmaceutical organizations are finding alternate methods to produce consistently and deliver products with the decrease in cost. Pharmaceutical organizations are turning to CRO and BPO in Asia Pacific to reduce drug cost and approval. However, one question arises, what quality measures or steps are taken to provide a safe and effective drug? In recent years, both the FDA and European Medicines Agency (EMA), identifies the significant limitation of clinical trial oversight conducted by pharmaceutical organizations. An example of lack of clinical trial monitoring were illustrated when Johnson & Johnson, Pfizer, and ICON, received FDA 483 warning letter for significant lapses clinical trial oversight (Cerullo et al., 2014).

India is similar to many other countries in the division of their medical regulatory structure between national and state authorities (Sackman & Kuchenreuther, 2014). The national authority for pharmaceutical regulations in India is known as The Drug Controller General of India (DCGI). The responsibility of the DCGI is to approve new

drugs, import drugs, and biological in selected category, approval of clinical trials and quality standards in the country. Sackman and Kuchenreuher agreed with FDA on the DCGI quality standards especially due to the citing quality-control problems ranging from data manipulation to sanitation. Due to concerns of the quality issues associated with the clinical trials the FDA and other regulatory bodies have increased inspections of Indian plants in response to the high amount of outsourced clinical trials being conducted. Pharmaceutical organizations are reassessing their Indian outsourced contracts with these plants and giving careful consideration to moving forward with developing new strategic partnerships (Sackman & Kuchenreuther, 2014). There are high concerns with data quality and data integrity, which impacts manufacturers' perception of India's clinical trials system. India became the most sought destination for the pharmaceutical organization for clinical trials due to the large and diverse patient pool, as well as, low drug trial costs makes the country an attractive. However, India has recently seen increased number of clinical trials fall dramatically due to allegations of noncompliance to protocols and organizations taking advantage of disadvantaged patients (Sackman & Kuchenreuther, 2014). Hanfield and Gosh (2004) and Sackman and Kuchenreuther agreed that due to noncompliance response manufacturers are forcing to either to move their trials to another country or encounter significant delays in clinical trial approval, which is ultimately holding their organizations back.

For clinical trials to have the highest quality, it must adhere to good clinical practice (Cerullo et al., 2014; Handfield & Ghosh, 1994; Johnson & Gupta, 2014; Sackman & Kuchenreuther, 2014). GCP is defined as an international scientific and

ethical quality standard for conducting, designing, recording and reporting trials that involve the participation of human subjects (ICH, 2015). According to ICH, clinical trials must be compliant with GCP guidelines to ensure the protection of the rights, safety, and well-being of the research trial subjects, as well as, ensuring data integrity. The principal objective of the GCP guideline is to provide a unified standard for current good clinical practices amongst the European Union (EU), United States, and Japan to have quality standards and mutual acceptance of clinical data by the regulatory federal agencies within their jurisdictions (ICH, 2015).

Adherence to GCP is the essential quality criterion for conducting clinical trials. The GCP standard practice applies to all parts of the clinical trial process. Pharmaceutical or any research and development organizations that do clinical research needs to build GCP requirements into their clinical trial processes to ensure quality in a clinical trial (ICH, 2015; Johnson & Gupta, 2013). Under the GCP guidelines, the quality of the clinical trial is a continuous sequence, which commences with designing, conducting, recording, and reporting of the clinical trials (Johnson & Gupta, 2013). Compliant with the GCP quality standard throughout the clinical trial conduct guarantees that the data reporting analysis results are credible and reliable, as well as, ensures the rights, safety, and well-being of the human subjects.

Consequently, even though there is no change to ICH GCP (2015) guidelines over the years, adherence to these principles have become more difficult to attain, due to the changing scenery of conducting the clinical trials (Johnson & Gupta, 2013). Lad and Dahl (2013) shared a similar concern for the role quality plays in clinical trials and

processes. Despite the acknowledgment of importance that is placed on quality assurance in the clinical research process and clinical trials, there is still a high-level concern for quality assurance program implementation in foreign academic teaching hospitals or a similar institution. Even though, the fact that quality assurance is expected in such programs that certify and accredit Institutional Review Boards (IRBs), very little is known about the role of the IRB in programs of clinical research quality assurance. In the IRB programs, clinical quality assurance needs to be defined, and processes placed in achieving quality assurance (Lad & Dahl, 2013). According to Lad and Dahl, essential elements of the quality assurance program are continuous education and training at site level, as well as, auditing and monitoring program, which reinforces the understanding and knowledge of quality assurance.

In order to measure the quality of a clinical trial, an audit needs to be conducted to ensure adherence to the clinical protocol, sponsors' clinical trial process, and clinical regulations. One of the quality breakdowns in a clinical trial process is the auditing of the informed consent (Lad & Dahl, 2014a). An informed consent is one of the essential clinical documents for clinical trials and can be defined as documentation, which informs the clinical trial participant about the clinical trial and the risks and benefits associated with the clinical trial, as well as any unforeseen risks associated with the clinical trial. Informed consent emphasizes the clinical trial participants' rights and volunteer participation in the clinical trial (Lad & Dahl, 2014b). An audit of the informed consent should be conducted to ensure adherence to the federal regulations requirement. The informed consent is a signed documentation from the voluntary participants to participate

in the clinical trial process and documents the conversation between the sponsor and voluntary participant in the clinical trial. Sponsor's conducting audit of the informed consent will help to ensure better alignment to the clinical protocol and federal regulation and will help ensure less scrutiny of regulatory agency inspections and IRB.

**Clinical Trial Process Improvement**

The data from this study might impact social change by providing awareness, knowledge, and risks associated with quality breakdowns when the pharmaceutical industry is outsourcing R&D. Outsourcing R&D caused negative relationships with pharmaceutical companies employees with the outsourcing employees (Mendivil, 2012). Due to outsourcing, internal resources are being laid off; morale is decreasing, and strained resources. The research data may provide insight to the leaders the effects it has on their internal employees and how to improve and build a better relationship with internal resources and outsourcing associates (Mendivil, 2012). Furthermore, it may also provide ways to enhance business practices and the conduct of an outsourced clinical trial quality to bring the safest most effective medicinal product to patients faster.

According to Paul (in press), there is an extremely competitive race for a pharmaceutical organization to bring the first new drug therapy to the market. The pharmaceutical organizations' face increasing challenges such as drug cost pressures, difficulties in obtaining patient recruitment, and drug target population. Even when the pharmaceutical industry meets its challenges, there is always an unexpected regulatory finding of the testing procedures and quality of the trial, which can derail an entire clinical program. The last decade global regulatory agencies have been placing increased

scrutiny on clinical data quality. Due to the increased regulatory scrutiny, there is a stimulus for the development of more effective and consistent quality management systems (Paul, in press).

Jones, Parast, and Adams (2010) have a similar view to Mendivil (2012) and Paul (in press) however, a different approach to how to improve process improvements while organizations are facing challenges. Jones, Parast, and Adams argued that process improvement initiatives do not always provide the best results; however, organizations need to frame it within the systematic process improvement structure. Emphasis on elements such framed within a systematic process improvement structure. Elements vision, skills, resources, action plans, and incentives are necessities to have an effective six-sigma implementation (Jones, Parast, & Adams, 2010). A deficiency in any of the above stages of process improvement will have an adverse effect on the desired outcome of any project. Similarly, Wong, Tseng, and Tan (2014) agreed to boost organizations' performance they need to configure business process model in order for the team performance to improve continuously.

## Transition

The purpose of this study was to explore one pharmaceutical organization's clinical quality assurance management team's knowledge and experience of the quality management system breaks when outsourcing clinical trials to Asia Pacific. The in-depth description data lead to highly successful outsourced clinical trials. In the literature review, I discussed various components of the general systems theory, quality management system, clinical trials processes and regulations, outsourced clinical trials,

current challenges that pharmaceutical organizations are facing and discuss the decision to move to an outsourcing model, as well as, discussing the risks and benefits of outsourcing clinical trial to the top outsourcing destination Asia Pacific.

In the Section 2, I will discuss in detail the doctoral study. The rationale for why I chose the qualitative case study design and the importance of the role of the researcher, the inclusion and exclusion criteria of the participants for the study, the population and sampling, the data collection techniques and data analysis. A detailed discussion in each of the above sections will explore pharmaceutical leaders' procedural policies leading to successful outsourced clinical trials. In Section 3, I will describe the application to practice and to implement change. In addition, I will provide a detail description of (a) overview of the study, (b) presentation of the findings, (c) application to professional practice, (d) recommendations for action, (e) recommendation for the further research, (f) reflections, and (g) study conclusions.

# Section 2: The Project

Section 1 of this doctoral study presented research information on various pharmaceutical challenges such as regulatory laws, patent expiries, the high cost of developing drugs in research, and development pushing pharmaceutical leaders to outsource clinical trials to developing countries in an attempt to be more cost effective. In Section 1, I explored the current problem that exists when clinical trials are being outsourced to developing countries. In Section 2, I will provide a detailed description of the research method and design of the study. Furthermore, Section 2 contains (a) researcher role, (b) the participants for the study, (c) the research method and design, (d) population sampling, (e) ethical research, (f) data collection and organization techniques, (g) data analysis, and (h) the reliability and validity of the study.

## Purpose Statement

The purpose of this qualitative case study was to explore strategies clinical quality assurance managers use to avoid a breakdown in quality with outsourced clinical trials in Asia-Pacific countries. The data collected from clinical quality assurance managers provided information on why breaks occur or do not occur within the total quality management system after agreed quality contracts to reduce the risk in clinical trials. Participants came from the clinical research and development sector of one pharmaceutical organization located in the Northeast region of the United States. The information provided by clinical quality assurance managers may contribute to social change through the creation of strategies to avoid quality breakdowns with outsourced clinical trials.

## Role of the Researcher

My role as the researcher for this qualitative case study was to gain access to the investigational research site and gain the trust of my research participants (Hancock & Algozzine, 2011; Marshall & Rossman, 2014) to gather good data.. My role was to isolate and define the qualitative categories and phenomenon. According to Fink (2000) and Hancock and Algozzine, the researcher needs to understand the research being studied. In order for me to understand the research, I answered the question of what in the research is going to be studied, why it is going to be studied, and how it is going to be studied. The answers to these questions will drive what will become the background in the study analysis and reporting.

I have 15 years of experience as a global development quality manager both in clinical trials and manufacturing sites. The study participants were quality assurance colleagues; however, they were from different line functions within the clinical quality assurance organization. Line functions within clinical quality assurance include but are not limited to eClinical, outsourcing, audit, clinical, compliance, training, vendor, drug regulatory, and pharmacovigilance. As a global quality manager, I am trained and frequently certified on clinical trial ethics and human subjects' rights. In addition, I completed the National Institute of Health (NIH) web-based training course Protecting Human Research Participants, exhibiting my knowledge of ethical behavior and the research process (Appendix E). My role as a researcher was also to recognize my personal bias and bias to the research. My role within the organization is quality assurance manager. Because of my role, I mitigated the effects of my prejudice and bias

to ensure impartiality to the research conclusions (Hancock & Algozzine, 2011). I used methodological triangulation from different sources to increase the reliability of the data (Barratt, Choi, & Li, 2011). The use of methodological triangulation minimized bias from me as well as the participants. Furthermore, I used member checking of interview transcripts to minimize bias and help identify data analysis themes and data results (Onwuegbuzie, Leech, & Collins, 2010).

For this study, I was the data collection instrument. I used an interview protocol to manage the available time of the interview session and focus on the 10 interview questions. I took detailed notes during the individual semistructured interviews in an appropriate private interview setting (Hancock & Algozzine, 2011). I transcribed the interviews verbatim into a Word document, analyzed and coded the data, as well as, verified and reported the data (Fink, 2000; Hancock & Algozzine, 2011). To ensure the ethical and legal requirements of research were followed, I collected the participants' signed informed consent forms prior to conducting the interviews (Hancock & Algozzine, 2011).

## Participants

Suri (2011) noted the researcher choosing participants for semistructured interviews must establish a sampling strategy conceptually aligned with the research purpose, which adequately addresses the research design. The criteria of the research participants included a minimum of 5 years of experience within the clinical quality assurance organization. Only clinical quality assurance managers who had experience with Asia Pacific outsourced clinical trials were included. Participants were at least 18

years of age or up to 65 years of age to enter the study. The strategy to gain access to the purposive sample of the 15 clinical quality assurance managers was from an invitation via e-mail or through teleconference meeting invitations (Appendix A). I followed up with a phone call or e-mail to answer any questions or concerns the participants may have about the study. After participants gave confirmation to volunteer for the study, I sent an informed consent form (Appendix B). Once I received the signed informed consent, I asked participants if they would like to have a face-to-face interview, phone interview, or e-mail questionnaire. The face-to-face interview was the ideal method; however, alternate methods were used if participants were unable to make the face-to-face interviews. Building a relationship with the participants helps the researcher gain access to the data (Patton, 2005).

To establish a working relationship involving trust, open communication, and positive interaction with the clinical quality assurance participants, I drew upon my interpersonal skills. It was critical for me to build trust; be patient; be a thoughtful, sensitive, empathetic listener; and be respectful of the participants (Marshall & Rossman, 2014). The positive work relationships created a safe and comfortable atmosphere for the participants during the interview process. The data collected from clinical quality assurance managers provided information on why quality breaks occur in outsourced clinical trials in Asia Pacific after agreed quality contracts.

## Research Method and Design

In this section, I expand upon the information presented in Section 1 on the research method and design. I describe various research methods and designs while

justifying why one particular research method and design was chosen. I justify why the qualitative case study was the best-suited research method and design to answer my research question: What strategies do clinical quality assurance managers use to avoid a breakdown in quality with outsourced clinical trials in Asia-Pacific countries?

**Research Method**

There are three research methods a researcher chooses from: qualitative, quantitative, and mixed methods. In a qualitative study, the researcher's specific interest is trying to uncover the meaning of the phenomenon of those involved (Merriam, 2014). Marshall and Rossman (2014) and Merriam noted that qualitative studies are used for descriptive or exploratory research that focuses on participants' lived experiences and settings. Bartkowiak (2012), Marshall and Rossman, Merriam , Patton (2005), and Thomas and Magilvy (2011) agreed the key benefit of qualitative research is to understand how people interpret their experiences through various research designs. To understand the reasons why breaks occur or do not occur in quality management system Asia-Pacific outsourced clinical trials, in-depth description from clinical quality assurance managers was needed to understand the phenomenon. Merriam noted there are four characteristics that identify qualitative research methodology: (a) the primary instrument for data collection and data analysis is the researcher, (b) the product is descriptive, (c) the focus is on meaning, process, and understanding, and (d) the process is inductive. Maxwell (2012) emphasized that when a researcher possesses any of the following five intellectual goals for the study, the best methodology is qualitative: (a) generating new grounded theories, (b) identifying unanticipated phenomena and

influences, (c) understanding the process by which actions and events take place, (d) developing casual explanations, and (e) understanding the participant's perceptive. Similarly, Hsuan and Mahnke (2011) recommended qualitative research for process inquiries to seek understanding of how pharmaceutical managers manage the outsourcing R&D and address gaps in the process. Kurkkio, Frishammar, and Lichtenthaler (2011) noted that qualitative research is used to seek information on new process developments when little if any information is given in prior studies. Hunt (2011) noted that if a researcher uses the following five methods within his or her research, then the research is qualitative: (a) seeks answers to questions, (b) collects evidence, (c) systematically uses a predefined set of procedures to answer the question, (d) produces findings that were not determined in advance, and (e) presents findings that are applicable beyond the immediate boundaries of the study. Bernard (2013) suggested that a qualitative method was appropriate to gain insight from pharmaceutical R&D leadership on how outsourcing clinical trials to Asia Pacific was affecting the overall quality of the trials and how one could improve quality business practices. The optimal way of collecting data was through face-to-face semistructured interviews or telephone interviews that aligned with the qualitative research method of collecting data and the researcher being the instrument to collect data. The qualitative research method allowed for more flexibility, and interview questions were open ended.

For quantitative research, there are specific research questions that are answered by proposition tests or hypotheses being examined (Marshall & Rossman, 2014). Merriam (2014) emphasized the focus of quantitative research is how much or how

many. Bernard (2013), Johnson and Christensen (2008), and Oleinik (2011) noted the goals of the investigation for the quantitative methodology are confirmation, description, prediction, control, and hypothesis testing. Quantitative methodology was not appropriate for this study because there were no numeric data being collected or hypotheses being tested. To gain insight into quality trial processes from the R&D participants, open-ended questions were needed; quantitative research relies on fixed response options. Quantitative research does not provide flexibility because questions are closed and participants' responses do not influence how or which questions are asked next.

The final methodology is mixed methods, which is used when a researcher collects both quantitative and qualitative data from either a series of studies or a single study (Cameron, 2011; Mengshoel, 2012; Tashakkori & Teddlie, 2010). The mixed methods approach helps the researcher determine whether an intervention works or why it does not work, as well as how it delivers (Farquhar, Ewing, & Booth, 2011). According to Farquhar et al., mixed-methods are particularly advantageous in research when the process evaluation is challenging and most of the interventions are challenging. Cameron, Farquhar et al., Onwuegbuzie et al. (2013), and Tashakkori and Teddlie noted that mixed methods would not be appropriate for gaining insight into pharmaceutical leadership knowledge of the clinical trial process for outsourcing clinical trials.

**Research Design**

Five primary research designs exist in qualitative research: phenomenological, grounded theory, ethnographic, narrative, and case study. In order to explore the clinical quality assurance managers' knowledge of quality management system breakdowns in

the outsourced clinical trial in Asia Pacific, I used a single case study. A single case study was also preferred by previous researchers examining pharmaceutical R&D leadership's knowledge of management and barriers within the internal R&D departments to enhance applications of the knowledge management team (Lilleoere & Hansen, 2011). Similarly, Zhang, Pawar, Shah, and Mehta (2013) conducted a case study to investigate how to assess outsourced work and manage outsourcing relationships in the pharmaceutical industry. Jensen (2012) recommended case studies as the best approach for the offshore outsourcing process to provide a detailed description of influential factors of the process.

According to Yin (2014), a case study is an empirical inquiry conducted to investigate a contemporary phenomenon in depth and within a real-world context, especially when the boundaries between the phenomenon and context may not be apparent. The case study was the preferred method because the central research question was what question, the focus of the study was a contemporary phenomenon, and I had no control over behavioral events (Yin, 2014). In addition, Yin noted that multiple sources of data in the case study allow a researcher to address a broader range of historical and behavioral issues. In this single case study method, sources of data such as documentation, archival records, responses to semistructured interviews, and direct observations were used (Yin, 2014). I continued to interview the clinical quality managers until data saturation was evident. Data became saturated when I determined the reviewed data no longer had the new experience, perspective, and information. Chikweche and Fletcher (2012) noted that data is statured when there is no new coding, themes, and can replicate the results .The three classifications of case studies are

descriptive, exploratory, and explanatory (Yin, 2014). In this case study, I chose descriptive because the goal of the research was to provide a rich description of quality management system breakdowns of clinical trials in developing Asia-Pacific countries (Denzin & Lincoln, 2011; Yin, 2014).

I excluded the narrative research design because the focus of this study was not on the lived experience of one or two individuals, and data collection was not through collections of stories or experiences (Goulding, 2005). Additionally, the phenomenological design was not chosen because the goal of the research did not have an emphasis on the phenomenon explored or any individual or group who experienced the common phenomenon (Merriam, 2014; Moustakas, 1994). Hays and Wood (2011) suggested a grounded theory would not be appropriate for my study because the focus of the research was not to develop a theory, and the focus of the research was not a particular action that occurred over time. Finally, the ethnographic design was not appropriate because my research aim was not to focus on a culture-sharing group (Goulding, 2005).

## Population and Sampling

The participants for this study were 15 clinical quality assurance managers working in the R&D clinical sector in one pharmaceutical organization located in Northeast region of United States of America. The 15 participants who met all the eligibility criteria entered the study. The participant's age was a minimum of 18 years to 65 years of age, working in or previous worked in clinical quality assurance organization of the pharmaceutical organization. Participants will have at least 5 years of experience

with clinical trials and have experience working with outsourcing organizations or business process organizations.

The sampling method used for this qualitative case study is purposeful. Merriam (2014), as well as, Suri (2011) noted a purposeful sample should be at least 15 participants to gain in-depth, rich data. Additionally, Boeije (2010) recommended a sample size of at least 15 participants would be suitable or until data saturation. The sample of the research participant occurs purposely to gain the knowledge of the varied experience of the participant's knowledge of quality management system breaks for outsourcing clinical trials. The research participants were clinical quality assurance managers who are contributing to quality and vendor oversight of the clinical trials on a daily basis. Part of their job description is to adhere to regulations and standard operating processes, as well as, handling quality breakdowns in the system, process, and clinical trials. Clinical quality assurance managers mitigate risks of the clinical trials, conduct risk and gap assessments of the clinical trial processes, participate in sponsored or federal inspections, and are the point of the contact for outsourced clinical trials in Asia Pacific when there are issues, concerns, or questions. Clinical quality assurance participants have the essential information needed for this research study.

Patton (2005) noted that power and logic of purposeful the sample come from selecting information risk cases for study in-depth. The purposive sample approaches of 15 participants were face-to-face semistructured interviews with open-end research question, which allowed the participants' knowledge of outsourcing clinical trial process phenomenon (Bartkowiak, 2012; Suri, 2011). Yin (2014) noted that conducting

semistructured interviews will bring forth insight and help the focus stay targeted on the study topic. The open-ended interview questions provided a guide conversation between the participants and myself, as well as, allowed the interviewees to build on their ideas, concepts, and thoughts. Furthermore, the semistructured interviews allowed me to follow up with questions through member checking to expand on their experiences. The interviews took place in the private setting environment such as a private and isolated meeting room within the pharmaceutical organization.

## Ethical Research

Ethical research requires qualitative researchers to show they are trustworthy, reliable, and credible (Patton, 2002). I submitted the research study proposal and informed consent to the Walden University's Institutional Review Broad (IRB) for review and approval prior to collecting any data on participants. The informed consent provided information to the research participants: (a) the nature of this case study; (b) inform him or her of their rights that no harm, coercion, or deception will come to them in the study; (c) protection of their privacy and confidentiality; (d) protect the vulnerable groups; and(e) selecting participant equitably (Abramson & Abramson, 2011; Yin, 2014). Each of the research participants received an informed consent (Appendix A) and given ample time to read and determine if they may want to participate in the study. A participants' signed informed consent was collected before entering the study. A copy of the signed informed consent was given to the participant for their records. Furthermore, this initiated the enrollment of the participants in the study.

The study did not involve participants who are particularly vulnerable or unable to give informed consent. To minimize risk to the human subjects, I utilized consistent procedures, sound research design, and avoided unnecessary risks to subjects (FDA Regulations, 2015). The risks to subjects were reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that is expected to result (FDA Regulations, 2015). The research participants voluntarily participated in the study and could withdraw from the study at any time or choose not to answer an interview question if they are uncomfortable to do so. The participant could withdraw by contacting me via e-mail or telephone if they are no longer interested in participating in the research study. The participants could withdraw from the study at any time. All data collected from participants who have withdrawn are destroyed or deleted from the database, and any written documents are destroyed. To protect the identity of the study participants, I assigned a code CQA1-CQA15 to each participant. To protect the identity of the pharmaceutical organization, I assigned a code name XYZ pharmaceutical organization. In order to enter the study, the participants must be at least 18 to 65 years of age, as well as, mentally stable (FDA Regulations, 2015). During the study, there were no compensations, gifts, reimbursements, and free services for participation in this research study (FDA Regulations, 2015).

In order to protect the rights of the participant's data, it was maintained in safe, secure locked storage and archived for 5 years. Participants' personal information was stored on my personal computer files and on a memory stick. Participants' data were protected by encrypted, and password protected computer files and labeled by the

participants' coded name. After 5 years, data will be destroyed through shredding of documentation and deleting data from the computer files. I signed a confidentiality agreement (located in Apendix D) due to the highly confidential information received from the research participants..

## Data Collection Instruments

In this single case study, I am the primary data collection instrument through face-to-face, or telephone semistructured interviews or e-mail interviews. Yin (2014) noted one of the most key sources of case study evidence is the interview. Chenail (2011) and Denzin and Lincoln (2011) recommended that in conducting qualitative research the researcher is the key person who is obtaining the participant's data and, therefore, the instrument. I conducted semistructured interviews to allow both myself and the participants to have in-depth interviews through a conversation style and build a level of comfort and familiarity to allow for a sustainable, meaningful interview (Barratt, 2012). In addition, Chenail summarized that when a researcher facilitates a conversational style that a context is created where the participants feel comfort and share rich data through their lived experiences. Cook (2012) and Barratt, (2012) recommended that online interviews provide participants more flexibility and time to answers questions Online interviews also provided extra confidentiality of the sensitive topic that most participants may not feel comfortable in a face-to-face environment (Markham, 2008). Gill, Stewart, Treasure, and Chadwick (2008) were also in alignment that semistructured interviews was the best approach because it explored the individual experiences, views, and beliefs on specific matters such as the quality of the outsourcing clinical trial processes.

Interviews were the most appropriate method of collecting data in a qualitative case study because they provided a deeper understanding of the social phenomena and can be used to collect detailed insights about the quality of the outsourced clinical trial processes from the R&D participants (Barratt, 2012; Chenail, 2012; & Gill et al., 2008).

The processes, I followed for collecting data from the participants: (a) study invitation and informed consent to the research participant Appendix C and Appendix A; (b) research participant signed the informed consent to participate in the research study; (c) both the research participant and me scheduled an appropriate time and date for the interview; (d) conduct the interview in a confidential interview setting; (e) for research participants who did not want a face-to-face interview, they completed online questionnaire and returned to the researcher within a few days; and (f) follow up meetings were also scheduled on any interview transcripts that need further clarification. The semistructured interview consisted of 10 construct study specific sets of open-ended questions located in Appendix B. The data collection instrument was critical in identifying themes in data collection. Since, I am the data collection instrument all participants' data coded by experiences and perception from the interviews.

Yin (2014) recommended establishing quality tests in qualitative case study research are reliability and validity. Bernard (2013) defined validity is the trustworthiness and accuracy of the instrument. In this case study, I (a) reviewed interview questions to ensure interview questions meet the aim of the research study, (b) the questions were clear and concise for the research participant to understand, (c) prepare for the interview sessions to provide for consistency of all R&D participants, and (d) utilize the pyramid of

evidence from peer-reviewed research and expert opinion is the basis for ensuring reliability and validity of the data collection instrument. In order to enhance data through reliability, I transcribed my interview notes verbatim into a Word document. I utilized NVivo 10 software to generate themes and patterns from the interview transcripts (Gill et al., 2008). At the end of each interview session, I conducted a member check by e-mailing each research participant the interview transcript to ensure the information transcribed correctly. In addition, follow up interviews questions were asked if interview answers are unclear. Merriam (2014) and Bernard (2013) recommended researchers organize data through themes, patterns, and concepts for descriptive data analysis coding. According to Yin (2014), process check improves the instrument, questions, and measures of the instrument. I conducted a process check after interviewing two research participants to improve the interview questions or methods.

## Data Collection Technique

The data collection techniques for this single case study were a face-to-face semistructured interview, telephone interviews, or e-mail questionnaire; and documentation from literature reviews, XYZ pharmaceutical organization's quality reports, and federal government reports. The advantages with documentation are stability, unobtrusive, specific, and broad (Yin, 2014) and the advantages of interviews are it is targeted and insightful (Gill et al., 2008; Yin, 2014; Merriam 2014). Yin noted one of the most significant utilization of documentation is to corroborate and augment the evidence from multiple sources. The semistructured interviews consisted of 10 opened ended research questions to collect information from the research participants of the quality of

clinical outsourced trial processes located in Appendix C. Merriam summarized the importance for a researcher to conduct interviews is to obtain a kind of information through a conversation with purpose (Patton, 2005). In addition, Barratt (2012); Chenail; and Merriam noted that semistructured interviews provide flexibility of the research questions, specific data required from all of the participants, interview guide consist of mix of structure questions, and majority list of research questions for the interview are to be explored. Face-to-face semistructured interviews are preferred, however due to the multiple locations of the R&D clinical sites within the XYZ pharmaceutical organization alternative method of telephone and e-mail questionnaire is given to allow for the participation flexibility. Cook (2012) and Barratt (2012) recommended online interviews provided participants more flexibility and time to answers questionnaire. It also provided extra confidentiality of the sensitive topic that most participants may not feel comfortable in a face-to-face environment (Markham, 2008). Even though there are strengths in conducting interviews and collecting data from documentation there are also associated disadvantages such as retrieve ability of documentation, documentation access, response bias for interview questions, reflexivity, and participants uncomfortable to answer questions on sensitive topics (Yin, 2014).

After the completion of the first two interviews, a process review check of research questions and responses to ensure the aim of the research (Yin, 2014). After interviews were transcribed, the text is downloaded to NVivo 10 software. Once the data was transcribed verbatim, a member check occurred. The participants' reviewed transcripts for accuracy.

## Data Organization Technique

All data collected from interviews, informed consents, interview transcriptions, and documentation are stored on my locked password protected the computer. In addition, to avoid data from being lost or damaged, data was also stored on a password protected memory stick. Merriam (2014) and Maxwell (2012) recommended for large amount of data collection from field notes, documentation, and interview, the qualitative researcher needs to find a structure to organize data. While Yin (2014) noted the case study database should be orderly where the data is retrievable. Data collected from documentation and interviews labeled and filed in the main study folder quality data file and the subfolder were labeled with participant's coded name clinical quality assurance participant (CQA) 1-15 where all corresponding informed consents, transcripts, and hand written notes were stored and filed. All raw data collected from this study in a locked password protective storage container for five years. After 5 years, I will destroy data by deleting all data from memory disk and the password protective laptop.

## Data Analysis

Data analysis involves immersion of the data, organizing the data, generating themes and patterns, coding the data, integrating and summarizing the information that the researcher has read and observed, thus providing meaning to the data (Marshall & Rossman, 2014). What strategies do clinical quality assurance managers use to avoid a breakdown in quality with outsourced clinical trials  in Asia-Pacific countries?

1. How do clinical quality assurance managers regulate the clinical quality management systems and adapt to changes when trials are outsourced to Asia Pacific?
2. How do clinical quality assurance managers ensure that clinical trial vendors adapt to the changes in the environment and process negative feedback?
3. What actions are taken by clinical quality assurance managers to ensure outsourced clinical trial vendors are following the agreed contracts?
4. What strategies do clinical quality assurance managers employ to ensure compliance from an outsourced clinical trial vendor after an agreed quality contract?
5. What are some risks and benefits associated with clinical trials when outsourced to Asia Pacific?
6. How do clinical quality assurance managers build successful relationships with clinical trial vendors and sustain those relationships with an ever-changing outsourcing business model?
7. How do clinical quality assurance managers ensure standard methods of communication of newly released standard operating processes, regulations, systems, and tools to outsourced clinical trial vendors?
8. In a 1-year time frame, how often do clinical quality assurance managers and outsourcing vendors reassess quality agreements, contracts, processes, and potential gaps?

9. What strategies have/have not worked with outsourcing clinical trials to ensure the highest quality of the clinical trial?
10. Is there any additional information you would like add that I may not have addressed by the interview questions?

Denzin and Lincoln (2011) noted the use of triangulation in qualitative research secures in-depth understanding of the central research question. In addition, Marshall and Rossman (2014); Oleinik (2011) and Yin (2014) asserted that methodological triangulation strengthens the quality of the case study because multiple sources provide multiple measures of the same phenomenon. The use of methodological triangulations from various sources such as documentation from XYZ pharmaceutical organizations' quality reports and federal agencies reports and interviews allowed me to form an understanding of the quality management system breaks (Jensen, 2012). Once the data was collected from the interviews, I transcribed interview notes verbatim to a Word documents; the NVivo 10 software assisted with identifying, sorting, and coding of themes and pattern analysis. Yin supported computer-assisted tools such as NVivo software because it is a tool to help guide researchers to categorize and code large amounts of data. Denzin and Lincoln noted NVivo software assists researcher in data coding, content analysis, and helps to identify themes and patterns. Yin noted the conceptual framework assists in data analysis in a case study, which provided structure to analyze the research question. One of the strengths of using the case study is the diverse data sources through triangulation, which provided an accurate understanding of the phenomena. Hence, the use of reflexivity and triangulation improved my understanding

of the complex nature of the phenomenon, as well as, allowing me to explore the subjective experiences of the quality assurance managers.

The conceptual framework for this study developed from von Bertalanffy's (1968) general systems theory. For outsourced clinical trials to have the utmost quality, the clinical trials must adhere to standard operating processes, quality management system, and federal and local regulations. In order to maintain the highest quality standards, the pharmaceutical organization must have a robust quality management system. Laszlo and Kippner (1998) noted the concept of the general systems theory is it integrates with complex component relationships and identifies boundary maintaining processes or entities. Senge et al. (2011) noted leaders are seeking to understand how to deal with information and how to utilize it for sustainable innovation. In order for the pharmaceutical organization to enhance the outsourcing quality environment, organizations' leaders should integrate compliance or beyond compliance to their business environment.

## Reliability and Validity

### Reliability

The main concern in a qualitative research study is to produce reliable and valid results (Merriam, 2014). Yin (2014) defined reliability as demonstrating data collection procedures repeats with same results. Wahyuni (2012) compared reliability to the dependability of the qualitative research through operational processes. In order for another researcher, to produce reliable and valid results they must follow the same operational procedures to produce the same finding and conclusions. To ensure

dependability, prior to the interview I reviewed interview questions and prepared for the interview to ensure reliability. Merriam (2014) noted in a qualitative research study, a human instrument can make the study more reliable by training and practicing. Seidman (2012) noted recordings enhance reliability by preserving the participant words, and it becomes the source data, and researcher should ensure the quality checks are made to the recorded prior to interviews. A list of follow-up questions is created from interview transcripts to allow further clarity on participants' responses. To enhance the interview process, I conducted a transcript review check after the first three interviews to verify interview accuracy (Yin, 2014). Therefore, to ensure reliability for the study, I utilized member checking for (a)notes and data, (b) audit interview questions for consistency, (c) review interview transcripts for any errors, (d) practice my interview skills, and (e) document all data collection procedures. In addition, I demonstrated the credibility of this single case study design by achieving data saturation through credible processes (Houghton, Casey, Shaw, & Murphy, 2013).

**Validity**

In this qualitative single case study, I used both internal and external validity tests to establish quality in case study research (Yin, 2014). For internal validity is when the researcher interpretation is correct when there is no direct observation (Yin, 2014). In the external validity, domains are established in order for the results to generalize (Yin, 2014). Maxwell (2012) described validity as the creditability of the description, conclusion, interpretation, and explanation. Merriam (2014) noted achieving credibility in qualitative research studies can be achieved through the personal experience phenomenon

to obtain thick, rich, descriptions and in-depth participant interviews to receive rich data. To ensure internal validity/credibility, I transcribed semistructured interviews verbatim and reviewed transcripts for any errors, and used follow-up questions for clarity and member checking. In addition, all interview transcripts will be e-mailed to the research participants for review to ensure data accuracy. I used the NVivo 10 software for theme and pattern analysis. In addition, member checking ensured transcript review; peer debriefings were conducted after to discuss gathered data and used methodological triangulation by collecting data from multiple sources (Yin, 2014). Marshall and Rossman (2014) recommended addressing any concerns with the validity the researcher constructs to capture through credibility, transferability, dependability, and confirmability.

To establish external validity for this qualitative single case study, I used the methodological triangulation method (Yin, 2014). The data collected from interview transcripts and documentation such as field notes, government reports, and xyz pharmaceutical organization's quality reports will provide validity. Maxwell (2012) noted triangulation can reduce the risks of bias and strengthen the validity. Furthermore, Yin noted the researchers who utilize using multiple sources of evidence in case studies are rated highly in terms of overall quality. Marshall and Rossman (2014) also recommended triangulation and member check as the strategy for internal validity in a qualitative research study. While Trotter (2012) noted in qualitative research creditability equates to internal validity. To establish dependability, credibility, and transferability, I triangulated data from documents and interviews; use member checking as participants review their

interview transcripts and develop rich, thick descriptive themes and pattern (Harper & Cole, 2012) through NVivo 10 software. Transferability of this study is by referencing the research sources to allow future researchers, as well as, the readers to determine whether the information transfers to enhance clinical business practices (Nawakitphaitoon, 2014). Therefore, to improve the credibility or trustworthiness of the data and quality, I used semistructured interviews, member checking, and researchers' notes.

## Transition and Summary

The purpose of this qualitative case study was to explore quality breaks when clinical trials are outsourced in Asia Pacific region. In Section 2, I described the (a) researcher role, (b) the participants for the study, (c) the research method and design, (d) population sampling, (e) ethical research, (f) data collection and organization techniques, (g) data analysis, and (h) the reliability and validity of the study. In Section 3, I will describe the application to practice and implication for change. I will provide a detail description of the following (a) overview of the study, (b) presentation of the findings, (c) application to professional practice, (d) the implications for social change, (e) recommendations for action, (f) recommendation for further research, (g) reflections, and (h) study conclusions.

Section 3: Application to Professional Practice and Implications for Change

## Introduction

The purpose of this qualitative case study was to explore strategies clinical quality assurance managers use to avoid a breakdown in quality with outsourced clinical trials in Asia-Pacific countries. In this study, I conducted semistructured interviews with 15 clinical quality assurance senior managers to explore strategies on how to avoid quality system breakdowns with outsourced clinical trials. The three emergent themes that I identified from the participants' interviews were the following (a) quality vendor management of outsourced vendors, (b) building quality in outsourced clinical trials, and (c) quality management system. All of the research participants reported that to improve quality and avoid quality breaks with a clinical trial, managers should maintain a robust quality management system and closely monitor the outsourced vendor. The research participants also reported that a close relationship between vendor and client characterized by trust and communication correlated to outsourcing success. The final strategy, which the majority of the research participants reported to be the principle method for research and development to maintain and improve drugs and service quality, was implementation of a quality management system. Exploration of the clinical quality assurance outsourcing strategies may provide process improvements to the outsourcing clinical trial business model, higher quality submissions to regulatory agencies, and a decrease in quality improvement costs.

## Presentation of the Findings

The overarching research question for this study was the following: What strategies do clinical quality assurance managers use to avoid quality breakdowns with the outsourced clinical trials in Asia-Pacific countries ? To answer the overarching research question the following open-ended semistructured interview questions asked were:

1. How do clinical quality assurance managers regulate the clinical quality management systems and adapt to changes when trials are outsourced to Asia Pacific?
2. How do clinical quality assurance managers ensure that clinical trial vendors adapt to the changes in the environment and process negative feedback?
3. What actions are taken by clinical quality assurance managers to ensure outsourced clinical trial vendors are following the agreed contracts?
4. What strategies do clinical quality assurance managers employ to ensure compliance from an outsourced clinical trial vendor after an agreed quality contract?
5. What are some risks and benefits associated with clinical trials when outsourced to Asia Pacific?
6. How do clinical quality assurance managers build successful relationships with clinical trial vendors and sustain those relationships with an ever-changing outsourcing business model?

7. How do clinical quality assurance managers ensure standard methods of communication of newly released standard operating processes, regulations, systems, and tools to outsourced clinical trial vendors?
8. In a 1-year time frame, how often do clinical quality assurance managers and outsourcing vendors reassess quality agreements, contracts, processes, and potential gaps?
9. What strategies have/have not worked with outsourcing clinical trials to ensure the highest quality of the clinical trial?
10. Is there any additional information you would like add that I may not have addressed by the interview questions?

To explore clinical quality assurance managers' strategies to avoid quality breaks with outsourced clinical trials, a qualitative case study was the optimal approach. Due to the XYZ pharmaceutical organization's policy on audio recording, the face-to-face interviews were not audio recorded. However, the face-to-face interviews were transcribed from notes taken during the interview into Word documents and sent to the research participants for transcript review. I used the NVivo 10 software to assist with the coding and analysis of data collected from interviews and questionnaires to identify potential themes. I identified three emergent themes: (a) quality vendor management, (b) building quality in outsourced clinical trials, and (c) successful management and implementation of quality management systems.

**Theme 1: Quality Vendor Management**

The clinical quality assurance senior managers reported that the strategies to avoid quality breaks with outsourced clinical trials were to manage quality oversight of the outsourced vendor. To improve quality and avoid quality breaks with a clinical trial, vendor should maintain a robust quality management system and closely monitor the outsourced vendor. Kennedy, Nordrum, Edwards, Caselli, and Berry (2015) noted the following ways to improve vendor quality: (a) build quality culture, (b) provide risk management tools and detectors, (c) monitor progress through metrics, (d) communicate service standards, and (e) provide education and training. Similarly, Medina and Richmond (2015) noted that there were increased numbers of industry-wide quality breaches and consequential drug shortages, which fueled FDA interest to improve the quality of pharmaceutical organizations. One method for quality improvement involved quality metrics by FDA inspectional resources, use of the risk-based paradigms, and communication of the quality status of various companies to other stakeholders. Medina and Richmond found the most valued metrics within the pharmaceutical organization were FDA metrics, such as warning letters and observations. Medina and Richmond stated that the survey respondents were hesitant to share information on metrics for key process indicators that would signal quality problems sooner. Medina and Richmond agreed with the FDA Request for Quality Metrics (2015) that the pharmaceutical organization is the most important stakeholder for the development and rating of quality metrics. Both Medina and Richmond and the FDA Request for Quality Metrics argued

that senior level management's commitment to quality was a key factor in evaluating the overall quality culture within the pharmaceutical organization.

The results of the research study confirmed findings from similar studies (Kennedy et al., 2015; Medina & Richmond, 2015; Temkar, 2015) that quality oversight and management were critical to avoiding quality breaks with outsourced clinical trials. Examples of research participants' (coded CQA1-CQA15) responses included were the following:

- "Vendors go through a qualification process, are periodically audited, and are monitored on an ongoing basis. Have regular scheduled QA meetings with vendors to review/discuss the status of issues and projects." (CQA7)
- "Clinical quality assurance has country specific quality assurance associates as checkpoints in Asia Pacific to monitor and oversee activities in outsourced clinical trial vendors." (CQA15)
- "Per procedure, all clinical vendors require some level of oversight by the pharmaceutical organization. Larger strategic vendors have operational oversight and executive level steering committees to provide high-level oversight and feedback. At an operational level, Key Performance Indicators are used by study teams to monitor vendor performance and act as an indicator that corrective actions must be taken. Key Performance Indicators have been standardized for all high risk clinical services." (CQA8).

- “A clinical quality assurance representative is assigned to the study based on function the outsourced vendor would provide. This ensures a more focused and consistent approach to managing quality breaks.” (CQA4)
- “CQA holds quarterly contract/statement of work reviews with our vendor as well as an annual governance meeting” (CQA5).
- “A checklist based on the activities delegated to the vendor should be created and used as a tool for the continuous oversight of the vendor. This can be carried out by on site audits, review of resulting data or questionnaires to the vendor that request documented evidence of fulfilment of the contract requirements.” (CQA6).
- “Frequent audits, particularly close audits of CVs and training records are certainly important to ensure the appropriate personnel are being assigned as per the contract—which should specify clear and detailed requirements. In addition, a sound signals detection program is needed that incorporates data management oversight at the sponsor as well as automated monitoring of the data and documentation on an ongoing basis.” (CQA1)
- “The only way to actually determine if vendors are following conditions in the contracts is to audit them and hold them accountable to a Corrective Action plan.” (CQA9).
- “The strategies we use to ensure quality at outsourced clinical trials is using quality oversight such as audit activities, measuring key risk and compliance indicators.” (CQA3)

- This is a very delicate aspect, and needs to be handled as such. Stability in how the vendor relationship is managed is essential, particularly during the post-qualification trial execution phase, where robust vendor oversight and close collaboration between sponsor and CRO are the key items to look at." (CQA11)
- The qualification of clinical vendors and outsourcing of clinical trial activities is performed via an approved XYZ pharmaceuticals standard process, irrespective of the region where the services will be performed. This process has been designed to take into account the risks associated with the service being outsourced (primarily looking at risks to patient safety and data integrity so that providers of similar services are assessed via process and level of scrutiny)." (CQA8)

Research participants reported that vendor quality management of the outsourced clinical vendor was essential to avoid any quality breaks. To establish quality oversight to outsourced vendors, clear metrics should be determined and communicated to vendors to ensure continuous quality. Clinical quality assurance senior managers should work with specific clinical quality assurance groups and vendor operational excellence teams to assess vendor and quality vendor contract agreements. The majority of the research participants agreed that auditing vendors and implementing corrective and preventative action plans enhances vendor accountability. Furthermore, the majority of the research participants noted that the creation of a quality governance board was a key success factor in vendor quality management. The quality governance board assisted both the

clinical quality assurance managers and outsourced vendors to discuss quality issues, audits, corrective and preventative actions, and current challenges. The board also provided a platform to escalate potential risk and quality issues.

The FDA Warning Letters (2015) noted that the even though the clinical trials are outsourced to vendors, the ultimate responsibility and accountability for the clinical trials is with the pharmaceutical organization. The expectation of the FDA is pharmaceutical organizations perform vendor quality management (FDA Warning Letters, 2015). Recent FDA warning letters issued to the pharmaceutical organizations were due to lack of vendor oversight of the contract research organizations (FDA Warning Letters, 2015). Research participants supported implementing the vendor quality management program to avoid quality breaks with outsourced clinical trials not only in Asia Pacific but in all geographical regions of outsourced clinical trials.

**Theme 2 Building Quality in Outsourcing Clinical Trials**

**Awareness of risks and benefits**. The increased growth in outsourcing, specifically with clinical trials, was triggered by pharmaceutical organizations' effort to reduce cost and focus on strategic plans (Abdul-Halim, Ee, Ramayah, & Ahmad, 2014). The driving factor for many pharmaceutical organizations to outsource clinical trials and clinical line functions was to reduce drug development cost and patient recruitment. The outsourcing of various clinical line functions within R&D to CRO or BPO has been an increasing trend (Huysmans et al., 2014) among pharmaceutical organizations to achieve faster regulatory approval timelines. However, the majorities of the outsourcing projects have been prone to failure (Huysmans et al., 2014) and have ultimately increased costs

for pharmaceutical organizations to repair the damage. When any functionality of clinical trial is outsourced, there are risks and benefits. The ultimate key question is do the benefits outweigh the risks? If so, how can pharmaceutical organizations ensure high quality and success with the outsourcing? The majority of the research participants reported that there is far more risk than benefits when outsourcing to Asia Pacific. The following are examples of the research participants' responses:

- "In the past, we have seen that some risks include lack of clinical trial support experience at the vendor and extremely high vendor personnel turnover. This can be disruptive to the management of the trial." (CQA8)
- "One risk to outsourcing to Asia Pacific is high turnover rate with Data Management and Information Technology associates which leaves no consistency and information lost and having to retrain new associated to projects" (CQA14)
- "Language barriers, time zone differences, lack of understanding clinical protocols and clinical processes." (CQA2)
- "Risks are: cost savings are not as great as expected, underestimation of the effort needed for ongoing quality/compliance, vendors lack experience and high turnover of associates at vendors, weak with soft skills." (CQA7)
- "Risks may include a general language barrier, where the written and spoken language in Asia Pacific are dramatically different that the EU and US. In addition, local customs and regulations are solely managed by the CPO. If the CPO is not well staffed, trained, or otherwise equipped, they

may work in a vacuum and can miss important coordination with Global partners." (CQA10)

- "Such relationships are particularly vulnerable to distance, time differences and assurance of adequate training in regulations and guidance. Potential delays in communication or vendor may need immediate assistance with an emergent situation during hours when US counterparts are typically unavailable."(CQA5)

Research respondents had similar perceptive on risks, as well as, benefits. The two major benefits that majority of the research participants discussed was cost benefits and participant pool population for targeted diseases in the Asia Pacific region. Examples such as:

- "Cost savings are meant to be the primary benefit." (CQA1)
- "Benefits clearly include adequate penetration and enhanced understanding of local markets and related challenges, as well as favorable costing." (CQA11)
- "In my experience, one of the benefits of clinical trials outsourced to Asia is cost, i.e. lower cost than the rest of the world. There is a large pool of skilled resource. (CQA4)

Research participants' responses on the benefits and risks associated with outsourced clinical trials confirmed with current, as well as, past literature reviews (Abdul-Halim et al., 2014; Huysmans et al., 2014; Mariani et al., 2014) on the risks and benefits for outsourcing clinical trials. Research participants concurred having a quality risk

management system and tools in place for data signal detection helped to determine what clinical trials and clinical trial site were at higher risk.

**Stronger vendor-client relationship.** The majority of the research participants reported that building better vendor-client relationships may enhance quality services by minimizing quality risks with clinical trials. St. John, Guynes, and Vedder (2014) conducted a study on the complexity of the IT vendor-client relationship, examined social exchange factors difficult to address in vendor contract agreements, and the success factor for vendor-client relationships. Their participants stated that a close relationship between vendor and client characterized by trust and communication correlated to outsourcing success (St. John et al., 2014). Similarly, a case study conducted by Moe, Šmite, Hanssen, and Barney (2014) reported that companies had challenges with poor communication, high turnover employee rate, domain knowledge, a lack of commitment of external developers, as well as, cultural challenges. The termination of all four medium sized outsourcing companies resulted because of low quality services. Research participants' responses were consistent with literature reviews (Moe et al., 2014; Schwarz, 2014; St. John et al., 2014 & Qui & Chan, 2015), which reflected in their response to build better vendor-client relationships:

- "Good communication, clear escalation paths, and continuous involvement QA can use their broad experience to provide advice about the planned clinical trial procedures. They can give an independent viewpoint, uninfluenced by other project concerns or pressures." (CQA6)

- "Regular, transparent communication and modeling integrity in vendor relationships encourages the flexibility and rapid response necessary to meet/exceed quality standards and adjust when needed." (CQA5)
- "The clinical quality assurance also tracks trends on quality breaks and discusses with the vendors where the same type of quality break occurs more frequently than normal." (CQA4)

Similarly, St. John, Guynes, and Vedder (2014) noted lack of communication between client and vendor leads to lack trust, which leads to relationship failure. Time is a key element on why the vendor-client relationship fails. The failure of the relationship contributed to individuals who are too busy, separated by distance, time zones, and language barriers. A common recommendation to build successful vendor-client relationship is to communicate at least 10 minutes per day (St. John et al., 2014). Some research participants felt vendor-client relationship could use improvement so clinical quality assurance could be more proactive instead of reactive:

- "Setting up of regular meetings with the vendor and being pro-active. Unfortunately, I don't believe we do this very well and with all that we have in place, we are still in a reactive mode."(CQA9).
- "Unfortunately there is still lack of communication between various outsourcing vendors, IT, and the clinical line functions. It seems when quality breaks occurs that is when all parties come together to discuss in the reactive mode." (CQA13)

The majority of the research participants' responses aligned with Qi and Chau (2015) stating the keys to building a successful vendor-client relationship are communication and trust. Both literature reviews and research participants' responses concluded that having, maintaining, and building vendor-client relationships contribute to better quality services and decrease quality breaks.

**Theme 3: Successful Management and Implementation of QMS**

The majority of the research participants' felt that the principle method for research and development to maintain and improve drugs and service quality is through successful management and implementation of a quality management system. All of the research participants' felt implementing and maintaining the quality management system provided document controls, controlled systems, standard operating processes, regulatory requirements, and training provided better quality services. The following are ways that clinical quality assurance managers regulate quality management systems, so it protects and adapt to changes when clinical trials are outsourced to Asia Pacific:

- "Ensure SOPs and other documents are in place and involved personnel are appropriately trained. Ensure compliance is being monitored." (CQA12)
- "Ensure that internal guidance is aligned with local/regional health authorities and to ensure the outsourcing partners are trained and evaluated for compliance on a regular basis." (CQA5)
- "Clinical QA needs to actively monitor activities performed by the business, as well as performing their own reviews of SOPs at the vendor

and requiring corrective action for deficiencies found. SOPs in Asia Pacific need to be highly detailed, much more so that QA is accustomed to seeing and requiring." (CQA1)

- "We have quality risk management tools and systems that give provide us signal detection on the possible risks that exist at clinical sites to help determine what sites may need to be audited." (CQA15)

In addition, research participants agreed that the way to ensure the quality management system adapt to changes in its environment, process negative feedback, and produce stable equilibrium is by setting up quality management standards, such as ISO 9000. Many of the research participants agreed that the key critical success factors of implementation of QMS are communication from R&D senior management and R&D colleagues who understand the importance of it. However, one research participant responded that negative feedback process could be challenging and focus should be more process oriented than personnel.

- "Negative feedback is particularly challenging culturally. I think keeping the focus as much as possible on procedures rather than on personnel can be helpful, but it is very important to work on developing an attitude of quality vigilance and self-reporting on the part of the local personnel and management."(CQA1)

I noted the results of the study tied into existing literature, which showed that for an organization to increase performance and quality services a QMS must be successfully implemented. (Li, TU, & Lui, 2015; Kaziliūnas, 2010; Zelnik, Maletič, & Gomišček,

2012). Kaziliūnas (2010) also noted that a quality management system based on international standards, such as ISO 9000, may enhance quality performance and services. Similarly, Zelnik et al. (2012) discussed that the organization's senior leaders need to motivate and understand the ISO 9000 standards, as well as, commitment to successfully implement a QMS. One reason QMS is not implemented successfully is the lack of involvement from both senior management and all employees (Zelnik, et al., 2012). Both literature (Calabrese & Corbò, 2014; Kaziliūnas, 2010; Li et al., 2014) and research participants' responses aligned on how to successfully implement and manage a QMS to produce higher quality product and services.

The results of the research study aligned with the study's conceptual framework of the general systems theory. According to the general systems theory, environmental influences and time causes the whole system, as well as, its subsystem to be out of balance and less maintained and controlled (Calabrese & Corbo, 2014; Kaziliūnas, 2010; Stacey, 2011). Pharmaceutical managers used system thinking as a way to resolve complex problems and designs. Leaders utilizing system thinking seemed to be at an advantage for managing complex situations and uncertainty where there is no simple situation. I noted the results of the research study confirmed with the existing literature on effective business practice. Schmiedel, vom Brocke, and Recker (2015) noted that organization's culture plays a key role in the success or failure of a business practice to be effective. In many organizations to measure if a business process is effective or not, heavily relies on the organizational culture of self-reporting to report gaps or deviations within the process. Research participants' responses concurred with the literature that for

a process to be effective there needs to be self-awareness and self-reporting culture to address quality issues or gaps in the process. Many researcher participants' felt the need for clear communications of the new processes, training, audit findings and standardizations across various business line functions would improve compliance.

## Applications to Professional Practice

The purpose of this qualitative case study was to explore what strategies some clinical quality assurance managers use to avoid breakdowns in quality with outsourced clinical trials in Asia-Pacific countries. I identified three emergent themes to avoid quality system breaks in outsourced clinical trials. The results of the study revealed that strong vendor-client relationships, vendor quality management, and a successfully implemented and managed QMS were key success factors to maintain and sustain high-quality in outsourced clinical trials business practices. The majority of the research participants' felt that building strong vendor-client relationships with key business line functions, outsourcing clinical vendors and quality assurance managers were essential to building trust. The research participants' felt that attending quality review board meetings and governance steering committees to discuss ongoing challenges, metrics, risks, processes, and having an open and clear communication on a regular basis assisted in building effective quality processes. Qi and Chau (2015) study results aligned with research participants' responses that the leading success factors on the outsourcing relationship in China were the successful formation of vendor-client relationship through communication, quality, and trust. Wong, Tseng, and Tan (2014) noted to boost

organizations' performance they need to configure business processes and a quality culture model for the team performance to improve continuously.

The research participants stated senior management and employees need to commit to the QMS to produce high-quality product and services. Zelnik et al. (2012) also agreed that organization's senior management should have motivation and understanding of the ISO 9000 standards, as well as, a commitment to quality to implement a QMS. Pharmaceutical organizations utilized quality management systems to improve the quality of product and process to achieve continuous customer satisfaction (Khanna, Sharma, & Laroiya, 2011).

Implementation of quality remains an important issue for global organizations, which are continuously trying to improve their competitiveness (Khanna et al., 2011; Johnson & Gupta, 2013). To gain global competitive advantage and to avoid quality system breaks in outsourcing clinical trials, pharmaceutical business leaders can incorporate these strategies to build quality within their organization. Also, the research data provides insight to the leaders how to improve vendor-client relationships to build a better relationship with internal resources and outsourcing vendor resources (Mendivil, 2012).

## Implications for Social Change

The results of this study might bring about social change by improving strategies for various organizations' senior leaders to improve business relationships and producing high-quality products to the customer. Senior leaders may want to use this information for positive social change by creating quality culture awareness and commitment at all

levels of management from both the vendor and organization. The quality culture commitment from senior leaders may enhance the self-reporting culture; provide empowerment and accountability amongst employees.

The data from this study may also assist communities economically by creating quality assurance job opportunities globally to monitor the quality of products and services. The quality improvements with outsourced clinical trials may produce a better, more effective, safer drug to society. The quality improvements made within the clinical trial processes may provide better knowledge of the quality of the drug, as well as, drug side effects, which will enhance drug's side effects reporting to federal agencies. Furthermore, the data from the study may improve individuals' knowledge of the quality of the drug and change their behavior by self-reporting their drug side-effects back to the organization to improve drug labeling. Ultimately, enhancing drug label information may assist physicians to dose patients accordingly and to inform better the patients of known side-effects.

## Recommendations for Action

Pharmaceutical business leaders need to secure funding for quality commitments and programs for clinical quality assurance managers to ensure proper quality oversight to the outsourced clinical vendor. Such funding should cover frequent travel to build vendor relationships, conduct audits, and provide training to enhance quality with vendors. The clinical quality assurance managers, as well as R&D senior leaders, need to communicate their quality commitments throughout the organization and implement a sustainable quality plan.

Kennedy et al. (2015) noted the ways to improve vendor quality were the following: (a) build quality culture, (b) provide risk management tools and detectors, (c) monitor progress through metrics, (d) communicate service standards, and (e) provide education and training. Senior leaders should be aware and plan for offshoring BPO's cultural risk factors that often occur with client and vendor relationships (Holbrook, 2011; Mosher & Mainquist, 2011) to avoid future quality problems. Culture plays a significant role when dealing with offshoring vendors. Communications, management style, understanding each other culture, gender issues, quality management, and team harmony are at risk if client and vendor have a serious communication break (Holbrook, 2011). Both Medina and Richmond and the FDA Requst for Quality Metrics (2015) argued that senior level management's commitment to quality was a key factor in evaluating the overall quality culture within the pharmaceutical organization.

The study results would be the most beneficial for the R&D senior leaders. The strategies identified from this study could provide R&D senior leaders with approaches to avoid a breakdown in quality with outsourced clinical trials. Prior to this research, there was limited information on how to avoid quality system breaks in outsourced clinical trials. For the study results to reach a wider audience, the results should be disseminated through business journals and scholarly literature. The results of this study may assist pharmaceutical organization leaders gain insights on how to improve their outsourcing models, vendor quality management, vendor-client relationships, and quality management systems.

## Recommendations for Further Research

My recommendations for future research and improvements in business practices are to duplicate this study from different global regions and different sample populations. The clinical quality assurance managers have a robust quality background and training to analyze risk and detect quality issues within clinical trials. The reason, I would recommend another sample population, such as clinical trial managers is to gain insight on the ongoing quality breaks seen in outsourced clinical trials. A different sample population will bring further insights to pharmaceutical senior leaders to enhance quality strategies and practices. My final recommendation is to study the practices of clinical outsourced vendors from various geographic regions. The information from such studies may provide insight and strategies to enhance quality business practices.

In research studies, there are limitations or weaknesses, and this study is no exception. Two limitations of this research study were that I only explored one multinational pharmaceutical organization and did not explore medium nor small size pharmaceutical organizations. I recommend other researchers to explore numerous and various sized pharmaceutical organizations to gain further strategies to avoid quality system breaks. Duplication of this study from different global regions and from a small to medium size pharmaceutical organizations may determine if clinical quality assurance managers' strategies are different or similar to this study. Another limitation to this study was only including pharmaceutical organization and not CROs, BPOs, and biotech organizations. My final research recommendation is to explore strategies that senior leaders of outsourcing vendors utilize to avoid quality breaks. Exploring the strategies of

outsourcing vendor management's leaders may assist R&D pharmaceutical leaders to enhance quality business practices and outsourcing models.

## Reflections

This study was a success in exploring what strategies some clinical quality assurance managers use to avoid a breakdown in quality with outsourced clinical trials in Asia-Pacific countries. As a clinical quality assurance manager within the organization from one sector of the overall development quality assurance organization, it was not clear to me why quality breaks occur to outsourced Asia-Pacific clinical trials. I needed additional clarity on why some pharmaceutical organizations seem more successful than others. Over the last 10 years, an increasing trend for pharmaceutical organizations to outsource clinical trials and clinical line functions to Asia Pacific. Asia-Pacific countries are the most sought out destination for clinical trials, which raised interest in the quality of outsourced clinical trials. My curiosity grew over the years; however, there was very little research on quality aspect clinical trials and ways to improve outsourced clinical trials to avoid quality breaks. The information of this study showed me that even though various clinical quality assurance managers, from various concentrations of the clinical trials, participated in the study, they all agreed on the strategies to avoid quality breaks in outsourced clinical trials. While a few research participants were business colleagues and my career is within the clinical quality assurance arena, I utilized reflexivity to check for sources of personal bias. I used the methodological triangulation to ensure validity within the research study. The data collected from interview transcripts and documentation such

as field notes, government reports, literature reviews, and the XYZ pharmaceutical organization's quality report provided validity. I ensured study reliability by member checking to verify the accuracy of my interpretations.

## Summary and Study Conclusions

The high cost of conducting clinical trials forces the pharmaceutical leaders to outsource clinical trials to developing countries. The outsourced clinical trial model saves money, time, provides faster drug approval, and provides patient recruitment when clinical trials are outsourced (Mendivil, 2012). Consequently, globalization of the clinical trials increases complexity, as well as, making it difficult to achieve global quality and patient safety (Paul et al., 2011). In developing countries, 1,589 out of 1,940 drugs are identified as registered, and there were 351 drugs not registered with limited information on drug's clinical trials and known side effects (Bate, Mooney, & Hess, 2011). Because of the complexity of the clinical trials and faster completion timelines, drugs' side effects are underreported and causing thousands of deaths, hospitalization due to tragedies, and lack of drug registry (Soni & Singh, 2013)

The pharmaceutical senior leaders should address outsourced clinical trial risks and complexities by creating sustainable quality management plans to avoid quality system breakdowns in outsourced clinical trials. The results of this study indicated that building vendor-client relationships, having vendor quality management and successful implementation of QMS can help avoid quality system breaks. The ultimate goal for both pharmaceutical organizations and outsourced clinical vendors is bringing the safest and most effective drug for patients to have a better life.

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# Appendix A: Consent Letter for Participant over 18 Years of Age

You are invited to take part in a research study titled Total Quality Systems breakdowns of Outsourcing Clinical Trials. The research objective is to improve quality of outsourced clinical trials in Asia Pacific developing countries. The researcher is inviting Quality Assurance Managers who have experience in the clinical arena in the pharmaceutical industry and have worked with outsourced vendors to be in the study. This form is part of a process called "informed consent" to allow you to understand this study before deciding whether to take part.

This study is being conducted by a researcher named Hemali Barrios, who is a doctoral student at Walden University. You may already know the researcher as a Quality Assurance colleague, but this study is separate from that role.

**Background Information:**
The purpose of this study is to explore what strategies some clinical quality assurance managers use to avoid a breakdown in quality with outsourced clinical trials in Asia-Pacific countries. The information provided by clinical quality assurance managers may contribute to social change through the creation of strategies to avoid quality breakdowns with outsourced clinical trials.

**Procedures:**
If you agree to be in this study, you will be asked to:

- Attend thirty to forty five minute interview session either face-to-face or telephone interview. After each interview you will be asked to review interview transcripts for accuracy.
- If either interview session is not viable then e-mail questionnaire will be sent to you to return to the researcher within three business days from receipt.
- A follow up 15-30 minute session may be needed if the researcher needs to clarify your interview answers or if you would like additional sessions to further add to the interview questions

Here are some sample questions:

1. How do clinical quality assurance manage to regulate the clinical quality management systems, so it protects and adapt to changes when outsourced to Asia Pacific?
2. What are some risks and benefits associated with clinical trials when outsourced to Asia Pacific?

**Voluntary Nature of the Study:**
This study is voluntary. Everyone will respect your decision of whether or not you choose to be in the study. No one at [redacted] will treat you differently if you decide not to be in the study. If you decide to join the study now, you can still change your mind later. You may stop at any time.

**Risks and Benefits of Being in the Study:**
Being in this type of study involves some risk of the minor discomforts that can be encountered in daily life, such as, stress or being uncomfortable being interviewed. Being in this study would not pose risk to your safety or wellbeing. The benefit of being in the study is providing information that can help improving quality for outsourced clinical trials.

**Payment:**
There will be no payment or compensation for participating in this study.

**Privacy:**
Any information you provide will be kept confidential. The researcher will not use your personal information for any purposes outside of this research project. Also, the researcher will not include your name or anything else that could identify you in the study reports. Data will be kept secure by encrypted, and password protected computer files and labeled by the participant's coded name on the researcher personal computer. Data will be kept for a period of at least 5 years, as required by the university.

**Contacts and Questions:**
You may ask any questions you have now. Or if you have questions later, you may contact the researcher via [redacted]. If you want to talk privately about your rights as a participant, you can call [redacted]. She is the Walden University representative who can discuss this with you. Her phone number [redacted]. Walden University's approval number for this study is **IRB approval is 09-01-15-0155581** and it expires on **August 31 2016**

The researcher will give you a copy of this form to keep, if you choose a face-to-face interview.

Please print or save this consent form for your records if you choose to do an e-mail questionnaire or telephone interview

**Statement of Consent:**

I have read the above information and I feel I understand the study well enough to make a decision about my involvement. By signing below, or replying to this e-mail with the words, "I consent", I understand that I am agreeing to the terms described above.

Printed Name of Participant

Date of consent

Participant's Signature

Researcher's Signature

# Appendix B: Interview Questions

1. How do clinical quality assurance managers regulate the clinical quality management systems and adapt to changes when trials are outsourced to Asia Pacific?
2. How do clinical quality assurance managers ensure that clinical trial vendors adapt to the changes in the environment and process negative feedback?
3. What actions are taken by clinical quality assurance managers to ensure outsourced clinical trial vendors are following the agreed contracts?
4. What strategies do clinical quality assurance managers employ to ensure compliance from an outsourced clinical trial vendor after an agreed quality contract?
5. What are some risks and benefits associated with clinical trials when outsourced to Asia Pacific?
6. How do clinical quality assurance managers build successful relationships with clinical trial vendors and sustain those relationships with an ever-changing outsourcing business model?

7. How do clinical quality assurance managers ensure standard methods of communication of newly released standard operating processes, regulations, systems, and tools to outsourced clinical trial vendors?
8. In a 1-year time frame, how often do clinical quality assurance managers and outsourcing vendors reassess quality agreements, contracts, processes, and potential gaps?
9. What strategies have/have not worked with outsourcing clinical trials to ensure the highest quality of the clinical trial?
10. Is there any additional information you would like add that I may not have addressed by the interview questions?

Appendix C: Invitation to Participate in Research Study

Dear_____,

This is to notify you that Walden University Doctoral student Hemali Barrios is conducting a research study titled Total Quality Systems breakdowns of Outsourced Clinical Trials. The purpose of this qualitative case study is to explore pharmaceutical leaders' procedural policies to ensure that outsourcing companies use proper quality clinical trial processes. This knowledge ensures outsourcing companies use proper quality clinical trial processes in order to enhance data quality of the clinical trial.

Your participation will consist of a 30 minute interview session. This study is voluntary. Everyone will respect your decision of whether or not you choose to be in the study. No one at [redacted] organization will treat you differently if you decide not to be in the study. If you decide to join the study now, you can still change your mind later. You may withdraw any time during the research study. Any information provided during the study is confidential. Feel free to contact me to express your interest in participation.

Thank you for your consideration.

Sincerely,

Hemali Barrios

Appendix D: Confidentiality Agreement

**Name of Signer: Hemali Barrios**

During the course of my activity in collecting data for this research: "Total Quality System Breakdown in Outsource Clinical Trials" I will have access to information, which is confidential and should not be disclosed. I acknowledge that the information must remain confidential, and that improper disclosure of confidential information can be damaging to the participant.

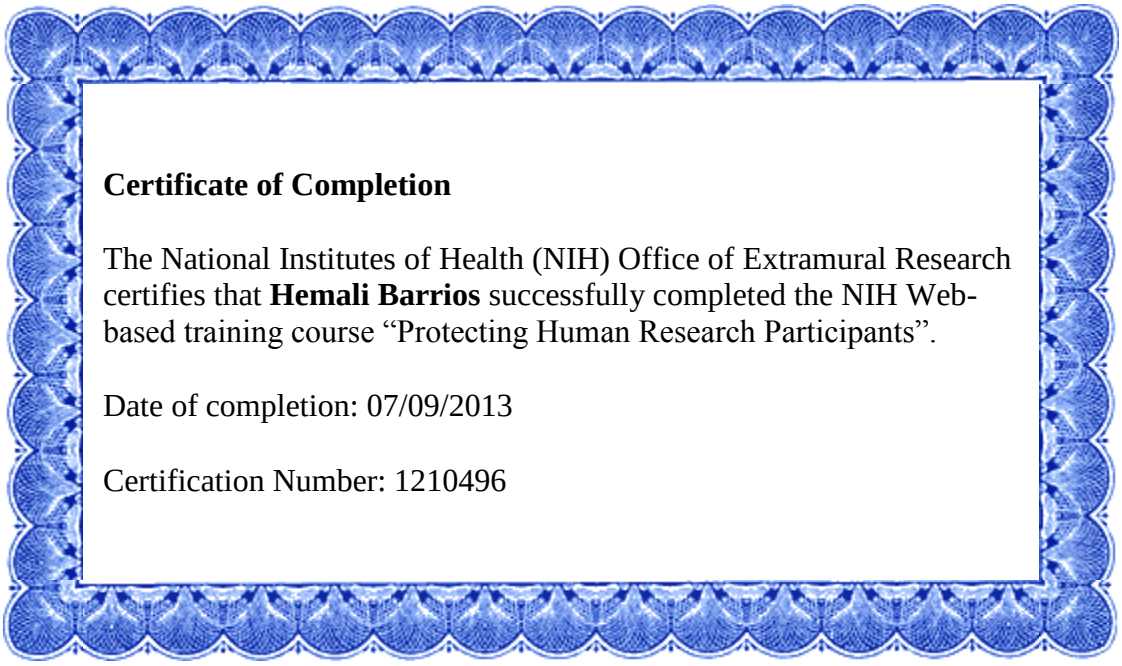
By signing this Confidentiality Agreement I acknowledge and agree that:

1. I will not disclose or discuss any confidential information with others, including friends or family.
2. I will not in any way divulge, copy, release, sell, loan, alter or destroy any confidential information except as properly authorized.
3. I will not discuss confidential information where others can overhear the conversation. I understand that it is not acceptable to discuss confidential information even if the participant's name is not used.
4. I will not make any unauthorized transmissions, inquiries, modification or purging of confidential information.
5. I agree that my obligations under this agreement will continue after termination of the job that I will perform.
6. I understand that violation of this agreement will have legal implications.
7. I will only access or use systems or devices I'm officially authorized to access and I will not demonstrate the operation or function of systems or devices to unauthorized individuals.

Signing this document, I acknowledge that I have read the agreement and I agree to comply with all the terms and conditions stated above.

**Signature:** **Date:**

Appendix E: Protecting Human Research Participants



**Certificate of Completion**

The National Institutes of Health (NIH) Office of Extramural Research certifies that **Hemali Barrios** successfully completed the NIH Web-based training course "Protecting Human Research Participants".

Date of completion: 07/09/2013

Certification Number: 1210496

Appendix F: Organizational Consent

[redacted]

July 23, 2015

Dear Hemali Barrios,

Based on my review of your research proposal, I give permission for you to conduct the study entitled Total Quality Systems breakdowns in Outsourced Clinical Trials within the [redacted]. As part of this study, I authorize you to gain access to the purposive sample of clinical quality assurance managers from an invitation via e-mail or through teleconference meeting invitations. In addition, authorization for any follow-up question with a phone call or e-mail to answer any questions or concerns the participants may have about the study via e-mail, in person, or via teleconference. A copy of the approved IRB informed consent will be sent to me prior to obtaining access to potential research participants. After participants gave confirmation to volunteer for the study, I will authorize you to send an IRB approved informed consent to the clinical quality assurance managers via e-mail or in person. According to [redacted] policy there will be no audio recorded sessions with research participants. I authorize you to collect data by conducting semistructured interviews via e-mail, in person, or teleconference. I understand the semistructured interview will consist of 10 construct study specific sets of open-ended questions and after each interview the researcher will transcribe verbatim the interview and will perform a member check with each research participant to review transcribed interview scripts to ensure accuracy of the researcher data interpretation. I understand that the research study will be published and any [redacted] identifiers will be de identified. Dissemination of the results will be given to each participants or stakeholder by debriefing sessions for overall study results. Individuals' participation will be voluntary and at their own discretion.

We understand that our organization's responsibilities include: giving access to research participants (clinical quality assurance managers), and the use of [redacted] conference rooms to conduct interviews, and allow review of [redacted] policies and quality reports. It is assumed that the supervision of the research activities is by Walden's University's remote faculty members. We reserve the right to withdraw from the study at any time if our circumstances change.

I confirm that I am authorized to approve research in this setting and that this plan complies with the organization's policies.

I understand that the data collected will remain entirely confidential and may not be provided to anyone outside of the student's supervising faculty/staff without permission from the Walden University IRB.

Sincerely,

[redacted]

[redacted]