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Evaluation of Capacity for Best Practice of Clinical Vaccine Research in Western Kenya

Sylvie Anne Kwedi
Walden University

Walden University

COLLEGE OF HEALTH SCIENCES

This is to certify that the doctoral dissertation by

Sylvie Kwedi

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Review Committee
Dr. Michael Schwab, Committee Chairperson, Public Health Faculty
Dr. Cheryl Anderson, Committee Member, Public Health Faculty
Dr. Georjean Stoodt, University Reviewer, Public Health Faculty

Chief Academic Officer

Eric Riedel, Ph.D.

Walden University
2012

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Abstract

African institutions that perform health research need to continuously evaluate their practices in order to ensure compliance with international standards of good clinical practice (GCP). This mixed-methods study, undertaken at one clinical research site in Western Kenya, was an evaluation of GCP compliance at the site, research participants' satisfaction with research procedures, and research participants' comprehension of informed consent. The qualitative portion of the study involved audit of the site's compliance with GCP standards. The quantitative portion was an assessment of participant satisfaction and informed consent comprehension, undertaken through interviews with a sample of 297 participants. Thematic analysis of the qualitative data showed that the site's performance conformed with GCP standards. Descriptive statistical analysis of the quantitative data showed that the majority of study participants were content with study procedures. A majority understood those parts of the informed consent process related to study duration and purpose but not those parts of the informed consent process related to the purpose and benefits of the study. Univariate chi square analysis showed no statistically significant differences in the level of satisfaction by age, occupation, or level of education, and there were no statistically significant differences in the level of informed consent comprehension by duration in the study or staff levels of experience. Implications for positive social change include guiding future health research capacity-building efforts in Africa toward better compliance with GCP standards and development of higher quality of informed consent procedures.

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ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 - 1346

Dedication

Thank you to my daughter, Kaéla, who is the greatest gift and the brightest light in my life. She is my main cheerleader and she never let me off the hook. A continuous thank you to the world of TB vaccine research which has expanded my knowledge, provided excellent professional support, and brought me my life partner and husband, Dr. Désiré Nolna.

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Chapter 1: Introduction to the Study

The African continent is afflicted with a number of infectious diseases, including tuberculosis (TB). Of the 22 countries with the highest burden of TB, Kenya ranks 13th on the list, according to the TB report of the World Health Organization (WHO, 2009), in which an estimated 132,000 new TB cases were reported, with an incidence of 353 cases per 100,000 population. TB continues to fuel the HIV epidemic in this region. TB cases and deaths in HIV patients also are a growing problem in Kenya. The WHO (2009) estimated that there were 15,000 TB deaths for HIV positive individuals in Kenya. The incidence of TB in these individuals is estimated at 39 per 100,000 population (WHO, 2009). These data show that TB is a disease that should be actively fought in Kenya.

The burden of TB in Kenya continues to raise concerns. Although the WHO (2009) estimates include the per capita incidence of TB to be stable or falling in five of the six WHO regions in the period between 2003 and 2006, it is not likely that the prospects epidemiological targets set for 2015, as stipulated in the Millennium Development Goals, will be met. Vaccinations against TB will combat an epidemic such as this one. A vaccine could have a significant impact on the burden of TB globally, but it would need to be combined with other with TB control efforts (Murray, 2008; WHO, 2006).

As part of TB vaccine development, clinical trial field sites in areas that have high TB incidence need to be developed. Areas that are highly burdened with TB also usually have high poverty rates and little infrastructure (Aeras, 2010). In order to show the vaccine's efficacy and effectiveness, clinical trials with large study samples need to be

conducted in places with high TB incidence but with limited infrastructure for clinical research (Aeras, 2010). Significant investment is thus required for building capacity that will enable the accomplishment of clinical trial objectives (i.e., show vaccine efficacy).

Capacity Building for the Conduct of TB Vaccine Trials

Along with partners, Aeras Global TB Vaccine Foundation—a nonprofit organization dedicated to the development of new and effective TB vaccines—invests millions of dollars to build and maintain infrastructure necessary for the conduct of larger phase clinical trials (Aeras, 2010). Since 2005, the identified sites have been developed with the following infrastructure:

- Development or expansion of their physical facilities to meet the demands of large-scale TB vaccine trials. This includes building offices, clinics, and full-service laboratory facilities and providing state-of-the-art laboratory equipment. This investment ensures adequate capacity to support Aeras-sponsored clinical trials, but also establishes microbiology laboratory facilities that meet the requirements of Good Laboratory Practice (GLP).
- Development and training of a staff corps that is knowledgeable and proficient in the execution of their responsibilities while conducting ethical and regulatory compliant clinical research. The staff members are provided with the core foundation of knowledge and skills in clinical research on topics including Good Clinical Practice, GLP, research ethics, epidemiology, biostatistics, infectious disease, and other areas related to the conduct of community-based TB vaccine research in accordance with international standards.

To date, in partnership with various institutions, Aeras Global TB Foundation has sponsored the conduct of epidemiological studies in the following areas (Aeras, 2010):

- Worcester, South Africa: Through collaboration with the South African Tuberculosis Vaccine Initiative (SATVI), two large epidemiology studies and one large BCG clinical trial sponsored by Aeras have been completed. The adolescent cohort study involving the participation of approximately 6,400 adolescents was completed but a sub group of 1,200 participants are still being followed.
- Kisumu, Kenya: Partnering with the Kenya Medical Research Institute/Centers for Disease Control and Prevention (KEMRI/CDC), a study targeting to enroll 5,000 adolescents for assessing the TB incidence in this age group was initiated in 2008. A similar study is being conducted with 2,500 infants.
- Iganga, Uganda: Partnering with the Infectious Diseases Institute at Makerere University, a study targeting to enroll 2,500 infants for assessing the TB incidence in this age group was initiated in 2008.

The scope of this dissertation was originally conceptualized as a larger quality improvement project in all three sites where Aeras Global TB Vaccine Foundation conducted epidemiology studies (South Africa, Kenya, and Uganda). The project was to include a GCP audit of the sites, process evaluation of site operations, and staff observation. A 12 months intervention was also planned to inject best practice research methods in the sites. The process evaluations would have occurred pre and postinterventions so see the effect of the quality improvement best practices introduced to the processes. Due to changes with my affiliation with the organization, the scope of the

dissertation is now restricted to a cross sectional study that includes GCP assessment, participant satisfaction, and informed consent comprehension of one site and at one point in time. Funds for the comprehensive project with all three sites are no longer available.

The research for this dissertation was only conducted at the Kisumu site in Kenya. This site is currently conducting epidemiology studies to characterize the incidence of TB in infants and adolescents. The main goals of these studies are as follows: (a) estimate the 1 year incidence of TB disease and the annual risk of infection with M. tuberculosis in the target populations, (b) estimate the prevalence of TB infection and disease in the target populations, and (c) estimate the rate of hospitalization and mortality. Hence forth, the Kisumu site will be referred to as "the site" throughout the remainder of the document.

Global Investment in Capacity Building for Health

In 2000, world leaders committed to a collective partnership to reduce (a) extreme poverty, (b) hunger, (c) illiteracy, and (d) disease universally (United Nations, 2009). They thus pledged to collaborate and infuse in resources to meet the following eight Millennium Development Goals ([MDGs] United Nations, 2009):

1. Eradicate extreme poverty and hunger
2. Achieve universal primary education
3. Promote gender equality and empower women
4. Reduce child mortality
5. Improve maternal health
6. Combat HIV/AIDS, malaria, tuberculosis and other diseases

7. Ensure environmental sustainability
8. Develop a global partnership for development

Three of those goals are directly related to improving health systems around the world. Capacity building in health research in developing countries is a key component of the MDGs (United Nations, 2009). Various researchers have shown that countries in the developing world are in need of a health research structure in order to meet the goals of improving health and achieve better health outcomes (Lansang, 2004).

In the past couple of decades, funds have been available to the global health community for building and strengthening health systems. From 1990 to 2007, development assistance increased from U.S.$ 5.59 billion to U.S.$ 27.79 (Global Forum for Health Research, 2009). These funds are originating from a variety of funders such as international development agencies, global health initiatives, development banks, foundations, nongovernmental organizations (NGOs), and other organizations.

The global health community has recognized that 10% of the world's health research funds are applied to health problems of 90% of the world population (Global Forum for Health Research, 2009). This is also known as the 10/90 gap in health research. The burden of neglected diseases such as HIV/AIDS, TB, and malaria add to impact of the 10/90 gap. In the past 10 years, world leaders have been increasingly devoting higher investment of their GDP to health research. For example, in April 2009, U.S. President Barack Obama has committed to allocating 3% of the country's GDP to Research and Development ([R&D] Global Forum for Health Research, 2009). A significant portion of these funds are allocated to researching neglected diseases such as

HIV/AIDS, TB, and malaria. In 2007, $U.S. 2.56 billion were spend on R&D for neglected diseases (Moran, 2009). According to Moran (2009), the leading funders were the US National Health Institute ($US 1.25 billion), the Bill and Melinda Gates Foundation ($US 0.45 billion), and the European Commission ($US 0.12 billion). The main recipients were the International AIDS Vaccine Initiative (IAVI), Medicines for Malaria Ventures (MMV), the European and Developing Countries Clinical Trial Partnership (EDCTP), the International Partnership for Microbicides (IPM), and Aeras Global TB Vaccine Foundation.

Capacity Building that Strengthens Health Systems in Sub-Saharan Africa

Clinical trials have been emerging throughout the African continent. Most activities are concentrated in South Africa, the location of 892 of the 1,627 clinical trials ongoing in Africa (Mboya-Okeyo, 2009). Pharmaceutical manufacturing capacity is also burgeoning in the continent. Plans are in place for boosting the drug development industry in Africa (Mboya-Okeyo, 2009). All these clinical research sites have benefited from investments in capacity building for clinical trials sites in Sub-Saharan African. Organizations such as the European and Developing Countries Clinical Trials Partnership (EDTCP) have increasingly allocated funds for enhancing the ability to conduct clinical trials in order to ultimately address the high burden of disease in the area. In 2003, the EDTCP was setup by the European Union with € 200 million for a 5 year period in an agreement found in Article 169 of the European Commission treaty (Matee, 2009). Organizations such as the EDTCP recognize that the health systems in the developing world can be strengthened by the implementation of product development programs. The

EDTCP's core mission is the advancement of needed drug and vaccine products through clinical trials into Phase II and III, which ultimately will be used by the population for enhanced health promotion (Matee, 2009).

There is evidence that capacity building for particular health programs ultimately ends up enhancing health systems in areas where they are most needed (Dongbao, 2008). In response to the HIV/AIDS pandemic, funds were dispensed by donors in the global health communities, such as the United States President Emergency Plan for AIDS Relief (PEPFAR). These programs are responsible for increased training of health care workers in the receiving countries (Dongbao, 2008). Capacity building initiatives for health research are occurring in Africa, especially in response to the HIV/AIDS pandemic. Particularly, initiatives such as the Global Fund to Fight AIDS, TB, and malaria and the World Bank Multi-country AIDS Program (MAP) have been able to affect health systems and policies in areas where change is critically needed (Biesma et al., 2009).

Noted Gaps Not Fulfilled by Past and Existing Capacity Building Efforts

In recent literature, the lack of an enabling research environment has been noted as a hindrance for the growth of health research in the developing world (Biesma et al., 2009). The other barriers cited were lack of competent institutional leaders, insufficient funds for research and salaries, poor career structure and inadequate infrastructure (Biesma et al., 2009). Biesma et al. (2009) reported that only 2% of people with doctoral degrees had had more than two grants after training, even though doctoral training had been completed as many as 15 years earlier. This lack of grants and financing for research contributes to the slow growth of health research in Africa.

There have been limited assessments of compliance with international standards of clinical research conducted in the developing world, especially in Africa. Insight can be gained into problem areas in noncompliance through looking at data from the US Food and Drug Administration (FDA) inspections worldwide (Varshavsky & Platonov, 2004). According to Varshavsky and Platonov (2004), 80%-85% of deficiencies were in the following areas:

1. Inadequate consent form
2. Inadequate drug accountability
3. Protocol violations
4. Inadequate/incorrect records and
5. Failure to report adverse drug reactions

Given the need for an effective vaccine against TB, invalid data or studies due to any of the five deficiency categories listed above cannot be afforded.

Research has been conducted to shed light on the community's and the participants' role in the clinical trials. In Sub-Saharan Africa, most of the research on vaccine trial participation has been conducted in the HIV/AIDS field (Mitchell, 2009). Some of this research included qualitative studies that provided an in-depth understanding of participants' perception of study processes related to recruitment and retention. In these studies, researchers seem to be mainly concerned with understanding the participants and their communities in order to power vaccine trials adequately and to show proper statistical significance for the study outcomes (Mitchell, 2009). These researchers were more concerned with aspects of research that address an adequate

sample size and minimizing loss to follow-up (Mitchell, 2009). A good number of qualitative research studies were geared towards investigating the potential participants' "willingness to participate" (Thapinta, 2002). Some researchers delved into the participants' experiences by asking for their perceptions to help understand the social and cultural nature of conducting trials in resource limited settings (Stadler, Delaney and Mntambo, 2008). In Stadler et al.'s (2008) study, qualitative data were obtained in order to understand the experiences of women enrolled in a microbicide feasibility study. The participants were interviewed and participated in focus groups. Stadler et al. found that the women were empowered by participating in the study even though they lived in a culture and society that fears or denies AIDS. This sense of empowerment may have come from the knowledge gained in participating in the study. They were able to engage in discussions regarding the importance of knowing one's HIV status and also became more aware of health as related to sexuality and reproduction (Stadler et al., 2008). This study is an example of asking for research participants' opinion on their experiences in a clinical research study. My research will go further by obtaining the participants' opinion with the aim of improving the quality of the conduct of clinical research.

Statement of the Problem

The main reason for conducting health research is to provide the evidence that is required for justifying the need for improving health. The global health community continuously invests into health programs due to the needs for better health outcomes throughout the world. Particularly, developing countries stand to benefit from health research as their health issues keep increasing in magnitude. Hanney and Block (2006)

affirmed that, by innovating and collaborating, building health systems helps in the conduct and use of information to inform policy, improve health, and close the gaps in health equity. In other words, health research is critical in order to keep ensuring public health and well-being.

In the past few years, there has been increase in clinical research studies of vaccine efficacy being conducted in Sub-Saharan Africa (Matee, 2009). Since this research involves human volunteers who need to be protected, it is critical to assess whether the research is being conducted according to international ethical standards for clinical research such as GCP (ICH, 2010). Still, there have been no studies of this kind. In addition, according to the Centers for Disease Control (CDC) and prevention (2010), because most of this research is conducted as part of research capacity building efforts, it is important to understand the extent to which the experience or understanding of the research participants is linked into the quality improvement process.

The clinical research site in Kisumu has had investment in terms of capacity building. Due to the amount of capacity building activities that have occurred at that is site in the past few years; the site is expected to have a decrease in the findings from various audits and assessment from 2008 to 2012. Findings are comments and observations made by auditors at the time of inspection.

Purpose and Significance of the Research

Developing capacity for quality management for vaccine clinical trials will not only help in the field of vaccine research, but it is also expected to build infrastructure for health. An assessment of the gaps between the current processes and the standards of

operation for the clinical trial sites is needed in the region. This study is a process evaluation of compliance with international GCP standards at one clinical vaccine site, including an assessment of participants' understanding of, and satisfaction with, recruitment, enrollment, informed consent, and other research activities.

Social Change

Research is key and essential to improving health. However, in Africa, health research as a discipline still lags behind although its population is affected by a significant disease burden (Matee, 2009). The continent has potential for addressing health issues; however, political, financial, and intellectual support is required in order to realize that potential. There have been several efforts in place to improve health research capacity in Africa and currently the results of such capacity are visible, although unevenly distributed through the regions (Mboya-Okeyo, Ridley, & Nwaka, 2009). The Kisumu research site is an example of some of the successful efforts for capacity building for health research in Africa. The social change effected by this evaluation study of the Kisumu site is in the success stories of high quality research capacity in Africa. With the results from this evaluation study, the site will be able to attract more research and, thereby, continue to impact public health in that area of the world.

The social change effected by this research is also related to the participants' opportunity to voice their opinions on the clinical research that has come into their community. In the field of health research, community members are asked to participate in research studies and provide data that inform science and/or health. In reviewing the available body of literature for this evaluation study, it seems that few research studies

provide participants with the opportunity to voice an opinion that can enhance the quality of the manner in which a research study is conducted. With this study, it is expected that giving participants a voice in the process of continuous improvement of the clinical research is beneficial in two ways: it should provide a valuable source of data on the relative efficacy of the research process, and it should provide an avenue of empowerment for the participants, by making them a part of the planning of research procedures. The results of this study will inform researchers and study sponsors on the role that participants can play in strategizing and planning for studies within their communities. As a result of this evaluation study, the inhabitants of the research site can know that the research staff is applying ethical standards that ensure that their rights as participants are not being abused or their rights are not disregarded. In the future, when they are approached to participate in additional research studies, they can agree to participate with confidence that the research staff places importance on quality assurance so to continuously improve on the effectiveness and efficiency of research processes and achieve better research results that will ultimately improve health systems in their area.

Conceptual Framework

The conceptual framework of this study draws on the proceed-precede model for evaluation of community-based public health programs, developed by Green and Kreuter (1999). This model includes the development of a logic model, which shows the key factors, concepts, and variables that influence the overall coherence of a program and its evaluation. Logic models have been used in the evaluation of clinical trial networks by Kagan et al. (2009) to engage stakeholders such as scientists, managers, and community

members in the articulation of their experience of the scientific research enterprise, a procedure that is being used in this study. As outlined by Kagan et al., this allows for an evaluation that is meaningful and useful to the participants, and appropriate for the context of interest. Figure 1 presents a conceptual framework for the evaluation of clinical site capacity, and the roles played in this process by (a) participants in the clinical research, (b) program sponsors and funders, (c) regulations and guidelines, (d) the success of the research studies, and (e) the ultimate impact of the research on the region's health systems.

In addition to Figure 1, which portrays a theoretical framework for the examination of participant understanding and satisfaction, I also draw on the health belief model, according to which human behavior can be better understood and even predicted when personal and social beliefs are understood (Glanz, 2002). In this case, the attitudes of participants in clinical trials – towards the research, for example, or towards health and sickness - would be expected influence their behavior as study participants. Factors likely to influence participants' attitudes towards the research include participant-study staff interaction, usability of the documentation, physical infrastructure, convenience, accessibility, financial factors, procedures and tests, and flexibility of timing of procedures.

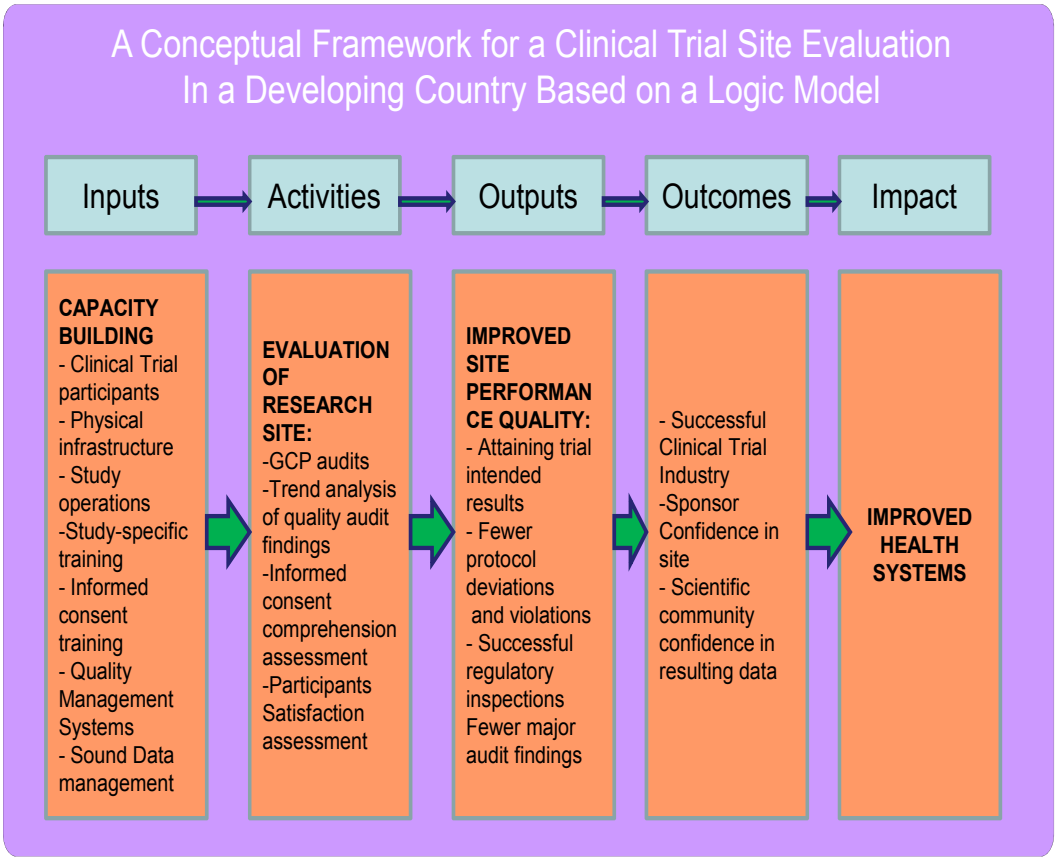

Figure 1. Conceptual framework for a clinical trial site evaluation in a developing country based on a logic model (Kagan et al., 2009)

The environment of this study is the Kisumu site of the Aeras infant TB incidence cohort study, which has a prospective and observational design (Aeras, 2008). The following are specifics on the infant cohort TB study:

- The study enrolls infants born in the Karemo division of the Nyanza district in Western Kenya. The planned study is targeting sample size of 2,900.
- Infants are enrolled during a period of 1 year and are followed for up to 2 years. Enrollment occurs in the villages and during antenatal clinical visits.

- Follow-up is conducted at home every 4 months to collect data on signs and TB symptoms or history of household contact with TB. Any identified suspected cases of TB are referred to the case verification ward where a comprehensive work up is performed (tuberculin skin test, early morning gastric washings for TB smear and culture, chest X-ray, and HIV test).
- Data collection includes perusal of source documents such as TB registers, medical charts, and in and out-patient surveillance data.
- Data are collected on personal digital assistants (PDAs) and case report forms (CRF) electronically and on paper
- The incidence rate is calculated "as the number of new cases of TB, diagnosed by a clinician and confirmed by one or more positive cultures" (Aeras, 2008, p. 33).

Research Questions

1. To what extent is the research site's performance in areas impacting data integrity and protection of participant's rights and safety in line with GCP and with international ethical and regulatory standards?
2. What is the historical trend of quality data including deviations, audit findings, and monitoring findings in the past 2 years?
3. What is the measurable level of participant satisfaction with recruitment, enrollment, and follow-up activities?
4. What is the measurable participants' level of comprehension of the informed consent form?

Assumptions and Limitations

This evaluation study was conducted within an ongoing epidemiology study which aims to determine the incidence of TB in a particular study area. Since each site is unique, it is unlikely that the study results can be generalizable to a similar population in other settings. However, the randomization aspects of the sample size calculation provide greater confidence in the generalizability of the results within the epidemiology study populations.

For assessment of informed consent comprehension, some study participants completed the questionnaire more than a year after they consented to participate in the study. It may be difficult for participants to recall some information about the informed consent process due to the long lag in time.

The nature of this study is geared towards the site's capacity to conduct clinical research according to local regulations and international standards. The informed consent comprehension was meant to be a snapshot of the staff's ability to impart information so the level of understanding by participants can be deemed satisfactory. This assessment could only include the respondents' self-reports of comprehension, as well as their perception of the understanding throughout the informed consent process. Nonetheless, this snapshot still provides an indication of the site's staff capacity to properly administer informed consent.

Summary

In order to properly proceed with clinical trials for TB vaccines in Kenya, it is critical to conduct an evaluation of clinical research capacity building effort in that part of the world. There have been a limited number of studies inquiring on the quality of clinical research conducted in Africa. In this study, a GCP audit checklist, a trending analysis of historical findings of various compliance assessments, evaluation of participants' satisfaction, and the informed consent comprehension are used to evaluate clinical research performance in a site in Kisumu, Kenya. These data are expected to provide the basis of a way forward in setting-up infrastructure for research conduct within stringent quality guidelines and international regulations. Social change will be effected by showing's the site's capacity for alignment with local and international standards while research participants are given an opportunity to contribution to the quality improvement process.

In Chapter 2, the literature review includes an illustration of a gap for researchers who have inquired into the point of view of the research studies' participants as well their comprehension of the informed consent process. In Chapter 3, details are provided on the study design, the data collection methods, and tools such as the GCP audit checklist, a Participant Satisfaction Questionnaire, and Informed Consent Comprehension Questionnaire. The details of data analysis methods, the study site, and the population and ethical considerations are also presented. Chapter 4 presents data analysis and study findings that include an analysis of the study sample demographics, an analysis of the results of the GCP checklist scores, a trending analysis comparing current and historical observations and findings on compliance, an analysis of the participations satisfaction survey data, an analysis of the informed consent comprehension data, and a summary of all results. In Chapter 5, the study outcomes are summarized and conclusions as well as recommendations are made to reinforce the impact of capacity building for clinical research in Africa.

Chapter 2: Literature Review

Capacity for clinical research needs to include the main elements of research operations such as human resources, physical infrastructure (laboratories, clinical facilities, offices, etc), data management infrastructure, ethics considerations, and quality assurance systems. In the literature review that follows, I aimed to find publications and documentations focusing on these elements for clinical research globally and then specifically to Africa. The review starts with literature on quality management for clinical research in general to highlight the critical importance that quality assurance holds in the field of clinical research. The review then branches into the area of ethics since clinical research involves human volunteers, and ethical considerations should then be at the forefront of this field. Since participant satisfaction is at the heart of this evaluation study, I found a few articles where the participants' opinions were sought. The literature review concludes with an examination of program evaluation studies such as the one proposed as well as evidence of how research can be used to build capacity for health systems.

For this literature review, the search first covered major commercial data bases: PubMed, and Walden University Library Academic Search Complete/Premier. The words searched included: *research capacity building, health research in Africa, TB vaccine research, TB vaccine development, regulatory guidelines for vaccine research, quality assurance in Africa health research, patient satisfaction, research participation satisfaction, and informed consent comprehension.* Next, searches were made on references of the articles that seemed more pertinent to the topic of the dissertation. This process was repeated a number of times. The point of saturation was considered to be

reached when new articles ceased to emerge. Many of the selected references were published between 2000 and 2010. Older references were included if they were exceptionally relevant to the review.

Quality Management for Clinical Research Studies

Quality management is an integral piece of capacity building (Sobngwi, 2001). Quality elements in research include a focus on valid protocols, meaningful informed consents, appropriate attention to patient safety, and complete and accurate recording of results (Lönnroth, 2008). Quality cannot be achieved by testing and oversight alone. Routine monitoring on site has been the standard for the sponsor or funding source for a product or intervention to assure performance, but has not been enough for large outcome trials and has failed to detect noncompliance (Lönnroth, 2008).

Various international organizations have collaborated to formulate guidelines for the ethical conduct of clinical research. Documents such as the World Medical Association Declaration of Helsinki, the International Conference on Harmonization (ICH)/GCP, the Belmont Report (Ethical Principles and Guidelines for the Protection of Human Subjects of Research), and the Nuremberg Code (Directives for Human Experimentation) were published to sum up the directives for ethical considerations for clinical research (Bohaychuck, 1991). In an effort to harmonize procedures that are used to standardize the practice of clinical research globally, the ICH (2010) devised a set of ethical and scientific quality standards for "standard for designing, conducting, recording and reporting trials that involve the participation of human subjects" (p. 12). These standards are commonly known as GCP. The European Union, the United States, and Japan are the

main countries in the ICH that devised the standards (ICH, 2010). However, the clinical research practices of Australia, the Nordic countries, and the WHO were also considered as the GCP standards were compiled. The ICH adopted an "informal consensus" process in developing the guidelines (Grimes, 2005). In other words, they gathered industry and regulatory experts and agreed on the set of guidelines through scientific consensus (Grimes, 2005). Governments around the world then adopted these standards into laws. For example, the U.S. Food and Drug Administration (FDA) has incorporated GCP into the Code of Federal Regulations. The GCP guidelines emphasize ethics, documentation, monitoring, and audits (ICH, 2010). By showing that a study has complied with these standards, researchers are able to have assurance that the study data are sound and that all rights, safety, and wellbeing of study volunteers were protected throughout the study. The intent was also to create standards for the manner in which clinical trial data were submitted to the regulatory agencies so the review and feedback can also take a form that is understood globally (ICH, 2010). Although the GCP have been criticized for not being inclusive nor evidence-based, they are used around the world to show that ethical standards are respected and that quality assurance is accounted for.

Collecting Quality Assurance Data

The quality of a clinical trial and its ensuing results is dependent on the level of adherence to ethical norms during the conduct of the study (Minnies et al. , 2008). In planning, designing, conducting, analyzing, and reporting research, scientists are obligated to show their commitment to protecting the rights, safety, and welfare of research participants (NIH, 2004). In particular, researchers working in the developing

world need to pay particular attention to the participants' interests since the imbalance of power between the funding organizations and the community may lead to the appearance of impropriety. Traditionally, quality management is targeted to "elements of structure, process and outcome" of the research in terms of "supervision, training, peer review, recording and reporting" (Tuberculosis Coalition for Technical Assistance- [TCTA], 2007, p. 19). In this study, the participants' feedback on the conduct of the study is woven into the plans for quality improvement of clinical research.

A study may be well designed to obtain the intent outcomes. However, if the systems that are in place are faulty, the data obtained could be suspect and the study will not have any value, regardless of the resources spent in its conduct. Sandman et al. (2006) focused on quality assurance with the intent of safeguarding the data obtained from clinical trials. Sandman et al. thus approached the issue of quality assurance with measurements that are intrinsic to the study and the data collected. Through collaboration with 28 clinical trials site performing studies on various TB therapies, a quality assurance (QA) program was set-up with specific performance indicators intending to inform the program on the progress of the studies against preset goals (Sandman et al., 2006).

Due to the multisite and multi continent aspect of the consortium in the Sandman et al. study, it was important to have harmonized systems and evaluation tools to ensure the standardized conduct of the studies. Sandman et al. (2006) thus implemented a QA system that was used to collect assessment information at regular intervals that was fed into an electronic system in real time. This system allowed for site to site comparison and prompt implementation of corrective action (Sandman et al., 2006). The indicators were

related to study performance, such as percent eligible participants enrolled, adherence to treatment, percent follow-up visits completed, and treatment completion rates (Sandman et al., 2006). These indicators provided information on the performance of studies and, thereby, allowed for an assessment on the quality of activities as the studies are conducted. With this approach to quality assurance, Sandman et al. were able to show the value of staying on top of performance assessment in real-time. Sandman et al. set up a framework that can be replicated in other consortia so to facilitate the coordination of large, multisite, and multi continent clinical trial programs.

Assessing participants' satisfaction also allows for an avenue for the community participatory involvement in the quality management and improvement of the research. The community needs to have a catalytic relationship with researchers to allow the community to become agents of change needed to enhance the health and development of that community (Doherty, 2000). In reality, participants may take a more active role in research than it is perceived. The participant's active involvement in the research goes beyond giving consent and being recipient of the research intervention. Phenomena such as the placebo effect and the Hawthorne effect demonstrate that trial participants are not merely passive contributors to research study (Bowera, 2004).

Collecting Data on Study Ethics

Ensuring the ethical handling of participants that take part in clinical trials in developing countries is essential when research is being designed and/or funded by sponsors in the high income countries. It is crucial to ensure that participants have a comprehension of the scope of the research study, risks, benefits, and the voluntary

aspect of their participation (ICH, 2010). In South Africa, the quality of informed consent in a vaccine trial was assessed in order to identify aspects of the study enrollment process that can be improved on its quality (Minnies et al. , 2008). In this study, Minnies et al. (2008) found that participants' levels of education were predictive of their levels of comprehension. In an international setting, especially in the developing world, research study materials such as the informed consent documents need to be culturally appropriate in order to promote better comprehension.

With the increasing level of activity for clinical research in Sub-Saharan Africa, issues related to ethics have been raised in the research community. Oduro, Aborigo, Amugsi, Anto, Anyorigiya, Atuguba, et al. (2008) conducted a study geared towards assessing the understanding and retention of information provided to participants during the informed consent process in Ghana. The study by Oduro et al was set-up in a manner similar to the present evaluation study in terms of nesting an informed consent study in the midst of an epidemiology study involving children in preparation for a vaccine trial. In the Ghana study, the site was being prepared for a malaria vaccine efficacy study (Oduro et al., 2008). It was acknowledged that special care needs to be taken when research is being conducted in resource limited settings whose culture is different from the culture of the countries to which western researchers are accustomed. Oduro et al. also noted that the research (i.e., intervention trials and social science research) had been conducted in the same study area which made many participants aware of the notion of clinical research.

Research ethics were further explored by Oduro et al. (2008) when they evaluated understanding and retention of informed consent information by administering a questionnaire to mothers whose children were previously enrolled in the malaria cohort study. Questions were focused on evaluating the understanding of the main themes of the informed consent form such as introduction to the study, study procedures, risks and benefits, confidentiality, and the voluntary nature of participation into the study (Oduro et al., 2008). Oduro et al. showed that there was an understanding of the general research concept, which was divergent from previous conclusions from similar studies. Oduro et al. attributed this appreciation of the concept of research to the level of research activity in this geographical area. Oduro et al.also affirmed the importance of using local field workers in the enrollment and recruitment procedures. The fieldworkers from the same community that are speaking the same language as the participants are able to establish an ease in the environment that eases the decision-making process of participating in a study.

Evaluating the consenting process was also conducted at a research site in Kenya. In a qualitative study, Gikonyo, Bejon, Marsh, & Molyneux (2008) examined the effect of social relationships between the community members and research on the quality of informed consent practices. Gikonyo et al. found that conducting a research study inside the community enhances the study participants' perception of their involvement in the study. In other words, the participants have more buy-in into the study and they feel more implicated since the study is being conducted in their daily environment. This particular assessment was conducted adjunct to a Malaria vaccine trial in Kenya. Gikonyo et al.

found that having local fieldworkers recruiting and enrolling in the community allowed for a decision-making that is more suitable for a collective society, such as the ones in Sub-Saharan Africa. By visiting the homes of potential participants, the field workers were able to speak to members of the household/community such as the husbands, fathers, mothers, or mothers-in-law (Gikonyo et al., 2008). These nonparticipating community members play a role that is critical in the decision-making of study participants. Gikonyo et al. also found that long-term studies such as vaccine trials have the tendency to incite rumors about the research and researchers in the community. Building a trusting relationship with the community helps to alleviate the rumors as they emerge and also to provide for an opportunity to clear-up any misconception or misunderstanding about the research in the community (Gikonyo et al., 2008). Gikonyo et al. suggested that the consent process should not merely consist of one-time information giving sessions. Instead, the researchers ought to take a continuous and community-encompassing approach to the decision-making of volunteering for a clinical research study (Gikonyo et al., 2008).

In the past few decades, accomplishments have been made in medical ethics in regards to the research participant relationship with investigators. Unlike in the past, the research participants now are given more autonomy while involved in clinical studies. The decision-making process is more shared between the medical and research staff and the volunteers (Falagas, Korbila, Giannopoulou, Kondilis, & Peppas, 2009). In keeping with the new developments, regulations, and laws that require respect for the participant's autonomy, the issue of adequate informed consent is usually raised. Falagas et al. (2009)

examined various clinical trials in order to ascertain the level of understanding in the informed consent process for research participants. Falagas et al. based their review on the basic elements of informed consent:" voluntarism, capacity, disclosure, understanding and decision" (p. 420). One of the findings from the review performed by Falagas et al. was related to the lack of understanding of the investigative nature of clinical trials. Research participants failed to acknowledge that they were participating in a research study for exploratory purposes and not necessarily for therapeutic purposes (Falagas et al., 2009). This notion is sometimes called therapeutic misconception. It should then be noted that investigators have the burden of not only ensuring comprehension of the aim of the study, but they also need to pay particular attention to assisting the participants in valuing the research study as an investigation instead of an established therapy or treatment.

Clinical trials involve notions such as randomization, voluntarism, and risks versus benefits that may not be easily understood. Falagas et al. (2009) found that randomization is only understood by half the participants in most studies. Falagas et al. suggested using novel methods of communication information in clinical trial process such as video materials. Falagas et al. also recommended that sufficient amount of time be given to research participants to ensure that the information imparted is retained in a lasting manner.

Administration of informed consent has been researched. In an effort to obtain empirical data on the informed consent process in South Africa, Moodley, Pather, & Myer (2005) studied informed consent and participant perception in an influenza vaccine

trial. In these trials, the informed consent process also took a community-wide approach combined with an individual process in the home. The informed consent assessment questionnaire was given 4 to 12 months after enrollment into the vaccine trial. Moodley et al. found that the majority of participants were cognizant that the vaccine being tested was experimental and they were aware of their freedom to withdraw from the study as they wished. However, a number of participants did not understand that their assignment to either the vaccine or the placebo group was by chance (Moodley, Pather, & Myer, 2005). Hence, Moodley et al. concluded that complex consent themes, such as randomization and placebo, were not understood in this study (Moodley, Pather, & Myer, 2005). Even though the informed consent process was extensive and involved, it is still to the researchers' best interest to expand the consenting procedure beyond information-giving and focus more on relating the consent themes in terms and circumstances best understood by research participants.

A study was conducted in Australia with aboriginals in order to test various designs of informed consent documents as well as the manner in which the information was delivered (Russell, Carapetis, Liddle, Edwards, Ruff, & Devitt, 2002). Russell et al. (2002) showed that a participatory and communal approach to informed consent was more effective than the reading of fact that Australian aboriginals come from a community where decisions are made collectively. The informed consent process was more effective when the participants were allowed to be informed as a group and discussion was encouraged among the participants (Russell et al., 2002). Researchers

such as these highlight the need to engage the participants in the process of identifying ways to improve the quality of conducting clinical trials.

Taking into account that cultural differences and traditions may impact participants' comprehension of information imparted during the informed consent process, Länsimies-Antikainen, Pietilä, Kiviniemi, Rauramaa & Laitinen (2009) aimed to assess comprehension of informed consent in older clinical study volunteers in Finland. Lansimies-Antikainen et al. also aimed to determine whether the study participant's appreciation of understanding clinical trial informed promoted his or her long-term continued involvement in the study. The participants involved in this study were originally included in a randomized controlled intervention trial "on the effects of regular physical exercise and diet" (Lansimies-Antikainen et al., 2009, p. 2). A self-administered questionnaire was used for data collection in a 23 month period. The questionnaire was focused on the following aspects of informed consent: information, understanding, competence, voluntariness and decision-making" (Lansimies-Antikainen et al, 2009, p. 2). Lansimies-Antikainen found that most participants were satisfied with the level of understandability of the information with which they were provided. Also, higher levels of education as well as being content with personal health were correlated with proper understanding of the trial information with which they were provided (Lansimies-Antikainen et al, 2009). In terms of willingness to continue to participate in clinical trial, participants who were satisfied with their own health were more agreeable (Lansimies-Antikainen et al, 2009). It was noted that particular care needed to be given to the informed consent process when participants with lower levels of education were

involved. Lansimies-Antikainen et al. (2009) highlighted the need for tailoring the informed consent process in various cultures in order to improve comprehension and promote the participants' autonomy in deciding to enroll in a clinical research study.

Some aspects of research may be difficult to explain to participants in some societies in the developing world. For example, it may be challenging to translate technical words such as "randomization" or even some concepts such as the importance of the voluntary nature of participation in a research study (Bhutta, 2004). In the developing world, it may also be difficult to ascertain a participant's real ability of giving voluntary consent if the person's autonomy in decision making is not clear (Bhutta, 2004). For example, a woman may be listening to the research staff soliciting enrollment into a study, but she may not be able to make the decision without consulting with other family members such as her husband or father. Bhutta (2004) has found that there is minimal research knowledge published in the area of consenting for research in the developing world (2004). Bhutta suggested that additional investigations should be conducted to determine "the validity of the process and the relationship of various informed consent procedures to outcomes and participants 'experience of research" (p. 775). In other words, additional research is needed to evaluate the suitability of the informed consent process and how the participants going through it.

Study Volunteers' Opinions on Participation

Lazovski et al. (2009) saw the need to explore benefits and burdens of participation in a clinical trial that are beyond the actual clinical, medical, therapeutic or research aspects of the trials. This study is another example of inquiring the participant's

point of view in order to inform the discipline of clinical research itself not a disease or health outcome. The participants surveyed were taking part in an HIV treatment study in 25 countries that included Argentina, Brazil and Thailand over a number of years. The questionnaire used was translated, back translated, and pretested before being applied in the survey study.

Study participants provide valuable opinions when inquired. In the Lazovski et al. study, the respondents identified medical and as well as non-medical benefits. In terms of health advantages from participating in a clinical trial, improvement in personal health condition was most cited (Lavoski et al., 2009) was most cited. Improved access to health care was also cited as a benefit to trial participation. In terms of nonmedical benefits cited, improved emotional conditions, time and money saved from the care received in the trial, access to quality health information were cited (Lavoski et al., 2009). The survey also identified nonmedical burdens such as problems at work for time spent in the clinical trial (Lavoski et al., 2009). The points highlighted by these participants show that understanding the participants' need adds to the research. This study provides an insight in trial's participants' perception in being involved in a clinical trial as related to non-health and non-medical aspects of the research. It is crucial to understand these other reasons in order to encourage trial participation, design studies, and conduct them in a manner that best serve the participation without compromising the scientific information that is sought.

A good number of studies soliciting the participants' point of view have been geared towards study participants' willingness to participate in clinical research. These

types of studies educate the research communication how to best find, retain, and motivate individuals that may potentially take part in clinical trials. Volkmann, Clairborne, & Currier (2009) examined the relationship between patients and their health care providers in settings that may involve HIV clinical trials (Volkmann, 2009). They inquired into the impact that this relationship would have as a potential trial participant is contemplating enrolling a study (Volkmann, 2009). The participants may be influenced by this relationship.

A self-administered questionnaire was provided to patients frequenting the Center for Clinical AIDS Research and Education (CARE) in Los Angeles. The study population included patients that had participated in trials in the past as well as those that were still enrolled in existing studies. The study by Volkmann et al. (2009) showed that a significant majority of these patients would be interested in enrolling additional studies in the future. This study also indicated that most patients are more willing to participate in clinical trial if they were contacted by their primary care provider (Volkmann, 2009). In this study, it was also found that participants were less willing to participate in a trial if they were approached by a third party such as an outreach coordinator (Volkmann, 2009). This finding may be due to the established relationship of trust that exists between the patient and the provider. The authors note that this study may be limited by selection bias since respondent were recruited from one university-based clinic and were mostly males (Volkmann, 2009).

In vaccine development, researchers need to be able to design studies that promote future optimal uptake of vaccine and they need to understand how the

community will affect certain vaccine parameters such as efficacy, dosage and access sites (Newman, 2004). Hence, engaging the community and the study participants becomes crucial in vaccine research. The community and the participants should be viewed as active partners not just in the study design to protect the statistical soundness of the data, but also throughout the clinical research study in order to improve on the study conduct and compliance with ethical and regulatory standards. The most compelling evidence of the necessity of actively engaging the community is illustrated in the case of a malaria vaccine trial site in Papua, New Guinea. Reeder & Taime (2003) worked with the community for over 25 years and spent a significant amount of time and effort in "knowing the community" and involving them as partners and not merely as "subjects" (p.281). Vaccine development at this site was greatly enhanced by the researchers' familiarity with the community and the research participants.

The same type of literature of research in TB vaccine seems to be minimal. In the present study, the aim is more focused on allowing the participants' perspective to improve the internal processes for the conduct of a TB research study. Using the "patient" perspective to improve on processes is widely used in the general health care field. In healthcare, the patient satisfaction is sought to better understand the attributes of health care processes that are important to and preferred by patients (Hunter, 2009). For the TB field, the Tuberculosis Coalition for Technical Assistance developed a guide that uses the patients' point of view for improving the quality of care in clinical settings for TB care. As long these lines, I will request the clinical study participants' perspective to

mold strategies for improving study procedures. This approach will allow for the participants to contribute to shaping research and enhancing TB vaccine research.

The premise of the study is that additional tools and strategies are required to further improve quality at clinical research sites overall and with special focus in resource limited settings. Based on Aeras' experience with capacity building and implementation of quality management at clinical research sites conducting TB studies, auditing and monitoring alone and implementation of basic quality systems has not produced the level of quality required as evidenced by serious or numerous errors, repeated deviations or quality issues, or gaps in documentation or processes. This need for additional tools and strategies for quality improvement at sites is increasingly being put forth in the literature and demonstrated in continued findings from regulatory body inspections of poor data compliance and quality and ethical violations as mentioned previously (FDA, 2007; Varsharvsky, 2004).

Evaluation of Capacity Building Efforts

Evaluation of capacity building projects are intended to appraise the progress, merit or performance of the initiative in order to inform decision-making for the future or just to ascertain a current status of the project. Since there is a significant number of health needs with limited resources to address those needs, it is important to maximize any capacity building so to make them cost effective and efficient. The benefits of capacity building are well documented in the literature. In previous experience, capacity building of health systems has been shown to improve health systems and services,

expand organizations' abilities to solve problems as well as enhance the chances for maintenance and sustainability (Smith, Coveney, Carter, Jolley, & Laris, 2004).

Once investments are made to either build or strengthen health systems for sustainable outcomes, the expected return is understandably significant. Various methods have been used for capacity building projects. For instance, a capacity building project for promoting leadership in South Australia was evaluated. The following methods were used for the study: telephone surveys, face to face interviews with key informants, focus group discussions and document review (Smith et al., 2004). For this project, the framework of capacity building was structured around three areas: "project infrastructure development, organizational problem solving capabilities and program sustainability" (Smith et al., 2004). Indicators for the status of the project were centered on these three areas. Smith et al (2004) showed that the project performed and met its capacity building goals. This is an example of successful capacity building.

In this evaluation, Smith et al (2004) chose to ascertain the performance of the project through a framework of capacity building so as to discern the value added to health systems as whole. A traditional evaluation would have taken the form of measuring the project performance against its inherent objectives such as increasing consumption of vegetable in a certain time period. However, Smith et al. (2004) chose to analyze the project outcomes in terms of the additional value that they bring to the health systems as a whole in the study area. The evaluation was useful.

Further studies have been conducted in regards to capacity building for health research. Le Thi Thu et al. (2008) opted to conduct a capacity project for improving

health outcomes by running a 5 day educational programs for community leaders in the Kim Son district of the Ninh province in Vietnam. Le Thi Thu et al. (2008) aim was to educate community leaders such as political leaders, teachers, women's group organizers and others. These leaders were expected to use their influential positions in the community in order to inspire the community at large to adopt living ideals that are beneficial to health.

Le Thi Thu et al's study took place in eight communes that were randomly selected from 14 eligible communes. The chosen communities were then randomly separated into an intervention group and a control group. In the end, 304 community leaders participated with 150 in the intervention and 154 in the control group (Le Thi Thu et al., 2008). These study participants were part of a 5 day education course with the objectives of "knowledge and skills regarding a healthy living environment, to understand potential health risks of unsanitary conditions, to provide counseling and promote a healthy living environment and apply effective health communications" (Le Thi Thu et al., 2008, p.360). The effectiveness of the educational program was evaluated with pre and posttests. Statistical analysis such as t-test, χ^2, analysis of variance and linear regression analysis were used. The 5 day educational program was successful in enhancing the community leaders' knowledge and skills as related to identified healthy living objectives (Le Thi Thu et al., 2008). This is another example of successful capacity building.

Although the educational intervention intended to improve the community's health, it would have been interesting to evaluate the impact of the educational program

within the community itself in terms of health outcomes. For example, the evaluation could have included testing the community members that were reached by the leaders that participated in the 5 day course. Or, the pre and post tests could have included random members of the community that are influenced by the leaders that participated in the program. The study could have been affected by the potential of contamination of one community from another depending on the geographical distance that separates the intervention communities from the control ones.

Process evaluation is necessary in order to better refine and troubleshoot the implementation of the health program. Assessing a program when it is active allows for an opportunity to identify problems, actual or potential, in order to better address them. In research systems, a process evaluation also gives an opportunity to determine if the research program is being conducted as it is intended or if the intended results are being collected. Tumiel-Berhalter, Mclaughlin-Diaz, Vena & Crespo (2007) performed process evaluation of a community based participatory research program that aimed to build capacity for research in a community in Buffalo, New York. The program's aim was to develop community outreach workers skills through training and education. The trained outreach workers were then able to educate the community at large and collect data for Asthma research. Tumiel-Berhalter et al (2007) presented their outcome evaluation in a descriptive manner by the number individuals that participated in the following activities: "networking, methods training, on-the-job-training and community education" (p.4). While researchers were able to implement their studies and obtain data that would combat the community's asthma problem, the community itself was able to benefit with a

well-trained research corps based within the community. The community outreach workers that were trained became empowered and had higher levels of confidence in their newly acquired skills (Tumiel-Berhalter, 2007). The trained was an avenue for performance improvement.

Although relationship-building was not quantified in this evaluation, Tumiel-Berhalter et al. (2007) noted that using community members allowed for smoother research process since the study participants were more comfortable to give information to someone that they are familiar with within the community.

An evaluation of capacity building efforts was conducted for leadership in the Public Health personnel in the United States. The program being evaluated emerged from a need of improved competencies in the area of public health in the United States. Due to recent terrorist attacks and threats, it was deemed necessary to enhance leadership capabilities for individuals in key position the field of public health (Saleh, Williams, & Balougan, 2004). It became obvious that, as a country, the United States could be vulnerable to a public health threat and that decision-makers needed to be skilled in leadership.

The Northeast Public Health Leadership Institute (NEPHLI) introduced a leadership program that aimed at improving "public health performance, developing collaborative relationships and partnerships, risk communication, team building, group problem solving, responding to the needs for cultural diversity and competence and emergency preparedness training" (as cited in Saleh et al., 2004, p. 1245).

For the program evaluation study, the leadership program was evaluated through the use of survey taken by 114 program participants (Saleh et al., 2004). The participants self-reported their competencies before and after the leadership program. There was a link between the frequency of use the skills acquired during the training and the improvement of those skills over time (Saleh et al., 2004). A significant increase in leadership competencies, it should be noted that the self-reporting aspects of the survey may well have affected the results despite the significant increase in leadership competencies.

Programs require some type of evaluation to inform decisions. However, it is necessary to design, plan and conduct the evaluation in a manner that will results in accurate and reliable evidence. Evaluating capacity building activities does not just apply to countries in the developing world. In Canada, it was noted that capacity building for health research was desperately needed in rural and remote areas (Miller, J., Mclean, L., Coward, P. & Broemeling, A-M, 2009). Miller et al., (2009) showed that if health workers and researchers are provided with an environment that fosters the conduct of research, it is likely that the amount of research undertaken will increase and evidence from research can be used in decision making. Various areas were pinpointed for the implementation of capacity building activities. Many of the stakeholders expressed a need for "enhanced communication of health results, research education, and networking opportunities" (Miller et al., 2009, p. 2).

Capacity building initiative ought to take a comprehensive approach. Miller et al., (2009) highlighted the fact that it was not sufficient to teach staff how to implement a

research study, but it was crucial to also teach how to disseminate results and use them for community health decision or policy making (Miller et al., 2009, p. 2). In other words, once the research is completed and that reliable results are obtained it is necessary to apply those results strengthening health services in the area. Capacity building has more impact when an actual champion of the project is identified and tuned into the program (Miller et al., 2009). In other words, the efforts are more effective with focused support.

Other Program Evaluation Studies In Clinical Research

There are a number of program evaluation studies in other research domains. Robinson & Trochim (2007) have recognized the importance of clinical trials in the improvement of health outcomes in the community, and pointed out that it is important to include minorities in clinical trials so as to authenticate the resulting treatments for minority populations since culture influences health behavior (Robinson & Trochim, 2007). Low rates of clinical trials participation among minority populations in the US is evident (Robinson & Trochim, 2007). The US NIH even requires that recruitment and retention of minority participants in NIH-funded clinical trials due to an enacted law (Robinson & Trochim, 2007). This policy change occurred in order to effectuate a solution t designed to solve a problem, but it is important to understand why participation rates for clinical trials are low in minority communities.

Robinson and Trochim (2007) attempted to understand the reasons for this issue from the source itself, – the community and other stakeholders. Various reasons are attributed to this problem, although the data were mostly obtained from researchers and

health professionals conducting research. Robinson & Trochim (2007) opted to study the barriers to minority participation in clinical trials (and other medical research) by investigating the perceptions of community members, researchers, and health professionals. All study participants were part of the National Cancer Institute's Special Populations Networks.

Robinson and Trochim (2007) used novel research tools such as concept mapping, a well-structured research tool that uses a participatory approach to data collection from stakeholders. Concept mapping allows for better "project planning, idea generation and structuring as well as interpretation of the stakeholder's concepts on solutions for a common problem" (Robinson & Trochim, 2007, p.531). A special software application allowed the participants to brainstorm and make various statements about their perceptions. Robinson & Trochim then sorted and rated the statements. Through concept mapping analysis, maps were generated to show how all statements from the study sample clustered by theme. Robinson & Trochim (2007) concluded that the participants perceived the design and implementation of medical research study as a barrier and study also showed that limited, with insufficient attention was paid to patients' concerns regarding their fears of clinical trials.

Robinson & Trochim (2007) reiterated the importance of taking the perceptions of research participants into consideration in order to improve the impact of clinical trials for the targeted communities. Researchers, health professionals, and policy makers may have the best intentions, but the work may not be as beneficial as intended without addressing the research participants' concerns.

Using Research to Build Capacity Strengthening Health Systems

Research systems provide the evidence that is required for justifying the needed for improving health. The global health community continuously invests into health programs due to the urgent needs for better health outcomes throughout the globe. Particularly, developing countries stand to greatly benefit from health research as their health issues keep increasing in magnitude. Hanney & Block (2006) affirmed that, by innovating and collaborating, building health systems help in the conduct and use of information so to inform policy, improve health and close the gap in health equity. Hanney & Block encouraged conducting research on research in order to show evidence of impact of research on health (p.2). In response to the demands of meeting the Millennium Development Goals (established by the United Nations), an increasing amount of funds has been invested in improve health. Conducting research on the research that has been effectuated by these funds will show cost-benefits of the work (Hanney & Block, 2006). The impact of these investments is then weighed against the outcomes.

Through an initiative led by the WHO, an international workshop on National Health Research Systems was held in Thailand in 2001 (Hanney & Block, 2006). The results of this workshop included a working definition of health research systems, potential strategies for strengthening these systems, as well as a way to evaluate their performance (Hanney & Block, 2006). Other discussions on building health research systems have included showing how evidence from health research is used and how to build a culture of research on research (Hanney & Block, 2006).

Partnerships are effective. Hanney & Block (2006) have also pointed out the need for the health communities to link up and collaborate with other sectors. For example, in order to investigate traffic accidents, it is necessary to work with transportation departments (Hanney & Block, 2006). The main area of concern in building research systems is human resources required to design, conduct, manage, analyze, and publish the studies. Recruiting, training, and retaining skilled staff is critical to building health research systems.

Conclusion of Literature Review

With the current increase in investment for capacity building in clinical research in Sub-Saharan African, the need for ethical and quality standards is being emphasized. Researchers are measuring quality assurance by collecting data against certain indicators based on GCP. Compliance with international standards is not only motivated by the need to conduct sound research, but it is also driven by the requirements to conduct research in harmony with the international health standards. However, few researchers have allowed research participants to have a say in the quality and ethics of the study, and additional research is required to explore the involvement of the participants in shaping the research and to ensure that their needs, as end-users, are being met. Involving the community in which the research is being conducted is critical to success of the study. The acceptability and longevity of the ensuing solution or intervention is also promoted when the community is earnestly involved throughout the study.

With the number of capacity building efforts in health research and programs currently in place globally, evaluations of these projects are necessary. Assuming that

capacity building projects have measurable and observable indicators, quantitative evidence can be generated to show whether or not the projects are effective, efficient and being conducted as intended.

Human research on the African continent is increasing and may be outpacing capacity building efforts. There is a need for a strategic approach in addition to the standard quality methods and tools to achieving study outcomes for large community based cohort studies and clinical trials in Africa and other parts of the developing world conducting clinical research. For the purposes of this project, the site in Kenya is conducting large-community based epidemiology studies in order to determine the incidence of TB in the target study population and/or TB vaccine trials. The next chapter includes a description of the methodological approach of this evaluation study that will utilize tools to measure the research site's performance (a GCP checklist), the level of participants, satisfaction with research procedures, and the level of informed consent comprehension through questionnaires.

Chapter 3: Research Method

This chapter provides a description of the study design as a descriptive cross-sectional study that intends to evaluate capacity -building efforts for a clinical research study in Western Kenya. The chapter includes the study site, population, and sample size considerations. It also describes methods for data collection and analysis, including the GCP checklist or GCP audit checklist, the participant satisfaction questionnaire, and informed consent comprehension questionnaire which are described as evaluation methods and tools. As for data analysis, the GCP audit checklist scoring- which scores the presence or absence of systems, processes, and documents required to conduct GCP compliant research - is used. The trending analysis that was conducted is fully described. In particular, participant satisfaction was assessed using a questionnaire to assess quality aspects of the research, such as participant-study staff interaction, usability of the documentation, physical infrastructure, convenience, accessibility, financial factors, procedures and tests, and flexibility of timing of procedures as determinants of participant satisfaction. Finally, a description of the Informed Consent Comprehension Questionnaire used in assessing the participant's ability to remember or recall basic and foundational pieces of knowledge critical to the informed consent process is also described.

General Study Design

The study is a descriptive cross sectional one, the intent of which is to gather quantitative and qualitative data. The purpose of this study is to build appreciation of the elements of quality needing to be highlighted when conducting clinical research in

resource-limited environments and to obtain the participants' opinion on the study conduct.

The clinical research site underwent a quantitative assessment of GCP compliance. The assessment of GCP compliance was conducted by collecting and analyzing data using two separate tools:

1. A GCP audit checklist scoring the presence or absence of systems, processes, and documents required to conduct GCP -compliant TB studies and covering six areas including document management, personnel and training, protocol adherence, data management compliance, monitoring, and laboratory compliance.
2. A trending analysis database was built to show a historical collection of observations and comments from various reviews and assessments of the site and the study conduct. The historical data were compiled from deviation logs, audit reports, monitoring reports, and quality control reports of study databases from initiation of enrollment of the active epidemiological study until the time of data collection for this evaluation study.

Completing the GCP checklist then provides for a means for a comparison of historical performance to the present time operations of the site and the study conduct in regards to compliance with GCPs.

Participant satisfaction was assessed using a questionnaire that is based on an adapted version of the Patient Satisfaction Questionnaire Short-Form (PSQ-18), which is used in the health care field. The PSQ-18 was adapted for this evaluation study to best

suit an environment of research as opposed to a healthcare setting. The questionnaire was modified and translated into the main local language at the study site to promote comprehension by the population in Western Kenya. The psychometric properties of the PSQ-18 were assessed and the validity and reliability of the instrument were deemed acceptable (Marshall & Hays, 1994). The main determinants of participant satisfaction are their expectations and their characteristics such as social class, marital status, gender, age, and ethnicity. For this study, quality aspects such as participant-study staff interaction, usability of the documentation, physical infrastructure, convenience, accessibility, financial factors, procedures and tests, and flexibility of timing of procedures are also determinants of participant satisfaction (Marshall & Hays, 1994). Informed consent comprehension was evaluated using an adapted version of a tool developed by Minnies et al. (2008). Some of the multiple choice questions in the assessment tool are designed to assess the participant's ability to remember or recall basic and foundational pieces of knowledge critical to the informed consent process (Minnies et al. , 2008). The rest of the multiple choice questions were used to assess the participant's understanding and its impact on the decision-making of being involved in the research. A simple scoring system was used to gauge participants' overall understanding of the informed consent procedure. The questionnaire includes 10 questions, six of which are geared towards assessing understanding while the rest are used to evaluate recall of information on the informed consent form. The participant's scored a point by choosing the correct answer in multiple choice questions. For the understanding questions, there is a maximum score of six and a minimum of zero. For the

recall questions, there is a maximum score of four and a minimum of zero. It is assumed that the concept of understanding and recall can overlap, so the questions categorized as understanding ones are those that assess the participant's ability to grasp the meaning of a particular informed consent concept, and questions categorized as recall are those that assess the participant's ability to bring back to mind or remember information provided during the informed consent process.

Sample Size Considerations

The participants in the current clinical studies and future clinical vaccine trials at the identified site in Kisumu, Kenya are minors, so the parents/guardians of study participants were approached to take part in the satisfaction and comprehension portion of the evaluation. The TB incidence study currently being conducted at the site in Western Kenya enrolls a minimum 1,500 infants participants The participants' parents/guardians were approached to complete the participant assessment questionnaire when they attended the clinic for one of the study visits (i.e., enrollment visit, follow-up visit, clinical test visit).

The sample for the satisfaction and comprehension portion of the study was drawn from the parents and guardians of the approximately 1,500 infants participating in the current Aeras Epidemiology Study. They are referred to here as participating parents and guardians. A random sample was drawn, based on every fourth participating parents or guardians whose child is attending a follow-up visit or a case verification ward visit (i.e., an enrollment visit, follow-up, or clinical test visit). This yielded at least 375

participants parents/guardians. A refusal/no-show rate of 10% was projected. Hence, 338 were expected to agree to be enrolled for the participant satisfaction assessment

At the time of data collection, the TB infant epidemiology study had already completed enrollment with a total of 2,900 participants enrolled. However, due to the sample size commitments made at the proposal stage of this evaluation study and also due to time constraints, a total of 324 participants were approached to participate in the evaluation study. Ten of them refused to participate and 17 consented but did not have the chance to have the questionnaire administered since they had run out of time from their scheduled visits. These 17 consented participants can be considered as "no-show" for the evaluation study. In the end, 297 consented participants completed the questionnaires.

Evaluation Methods and Instruments

GCP Compliance Assessment

The assessment of GCP compliance was conducted by collecting and analyzing data using two separate tools.

1. I conducted a GCP audit, an independent person/team not employed by the clinical research site. The audit included a checklist scoring the presence or absence of systems, processes, and documents required to conduct GCP compliant TB studies and covering six areas including document management, personnel and training, protocol adherence, data management compliance, clinical evaluations, and laboratory compliance. Each section was scored using a weighted score of each question/element. An overall score representing degree of GCP

compliance as measured by the audit tool was determined as well. The assessment tool was divided into six sections related to the six critical areas of compliance. A maximum score was determined for each section for each site based on applicable requirements/questions. The site was then assessed and scored based on degree of completion of each requirement/question. The scores was presented as percentages such as percent of findings related to documentation, percent of findings related to informed consent process, percent of findings related to data management and so on. There are no known researchers who have validated the GCP checklist. However, in the United States, it is a legal obligation, through the Code of Federal Regulations (21CFR312.120) to conduct clinical trials in compliance with GCP guidelines (FDA, 2006). One can thus assume that all FDA approved clinical trials have undergone a stringent GCP check such as the one proposed in this evaluation study.

2. A trending analysis database was set-up where data were compiled from deviation logs, audit and monitoring reports (internal and external), and Quality Control (QC) checks of data. Data were compiled and used for this study starting from enrollment of active epidemiology study protocol) to 3 months from initiation of GCP audit. The data elements consisted of the number and the type of findings and observations found from each evaluation and assessment of the site and study performance. For example, an audit and monitoring report of a study includes a number of critical, major, and minor findings. These findings are meant to inform the site's staff to correct deviations from guidelines and proper study conduct.

> Some examples of data found in these databases include the number of informed consent form properly completed, number of errors in data capture, number of protocol amendments and their reason, and number of training files properly maintained, and so on. These data elements were then plotted against time so to show a historical trend.

Every note of noncompliance or questionable alignment with GCP is considered either a finding or an observation. The distinction between the two is that a finding is directly related to an explicit GCP guideline and observations are thoughts or opinions of the auditor/ monitor not directly linked to a specific GCP guideline. A finding may not necessarily be negative; however, it is a point that ought to be noted by the research site. For the GCP checklist, a system of rating the seriousness of findings and observations is defined as follows:

Critical finding: Finding with a high risk of having an impact in the analysis of the trial, the data integrity, or resulting in substantial risk of regulatory authority action towards the site or sponsor.

Major finding: Finding that do not invalidate trial conduct but which represent a significant departure from the protocol or a stated ICH GCP guideline, regulation or SOP, with actual or potential effect on patient safety, data integrity or study outcome.

Minor finding: Finding that represent a departure from the protocol or a stated ICH GCP guideline, regulation or SOP, with no or minimal impact on patient safety, data integrity or study outcome.

Overall performance of the site is related to a general statement of the functioning of the site in relation to conformity to guidelines and standards such as GCP. Performance was also assessed in regards to particular categories of GCP. These categories include the following: documentation management, personnel training, data management, protocol and protocol amendments, monitoring, corrective action and preventing action (CAPA), and laboratory. The GCP checklist includes a number of items to be accomplished from each category. Each check will constitute a fulfillment of a requirement. This list was graded with a weighted score as follows: four points for an item that had absolutely no findings, three points for an item with minor findings, two points for an item with major findings, one point for an items with critical findings, zero point if the item was completely absent. The data from each method were analyzed to generate an overall performance and individual category performance scores for the site as well as ranking of low performing categories. The categories with the lowest point were considered the lowest performing.

Participant Satisfaction Assessment

Baseline demographics of the participant and parents' demographic characteristics (e.g., sex, village, age of participants, age of parents, participant's occupation,) were summarized for all participants. Figure 2 outlines the approach for assessing participants' satisfaction. This multifactorial approach is due to the various factors that may affect the participants' perceptions of study processes. These factors include aspects that are intrinsic to the participants (i.e., participant's characteristics), the study processes, the participant-staff interactions, as well as clinical settings.

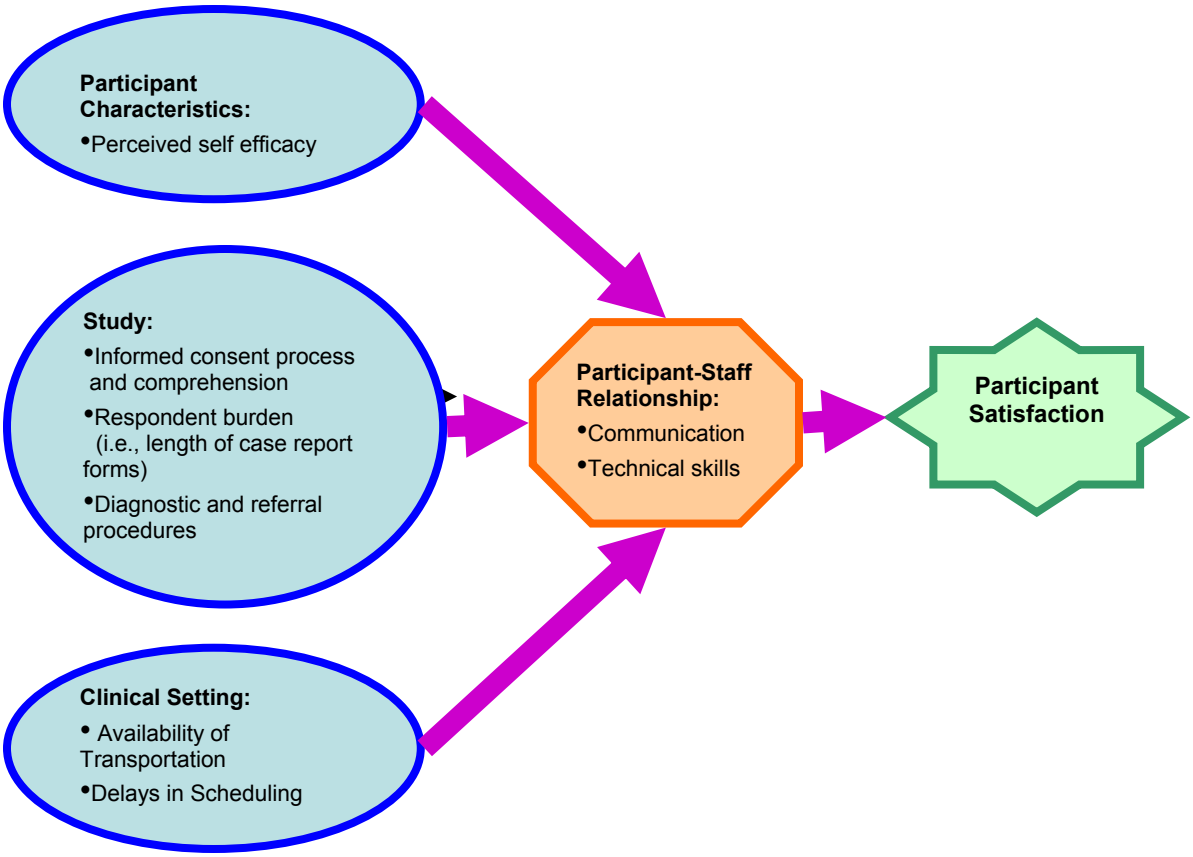

Figure 2. Illustration of multifactorial causes of participant satisfaction

A questionnaire was designed to obtain information on the experiences and perceptions of randomized study participants' parents/ and guardians and parents/guardians of study participants that were recruited to be a part of a TB incidence study (Appendix 1). The questionnaires were given to the parents/guardians of children enrolled in the TB epidemiology studies. Along with demographic information, the questions pertained to the following aspects of participant satisfaction: participant-study staff interaction, informativeness of the materials provided during the study, physical infrastructure of the facilities, convenience and accessibility of research study facilities, financial factors, procedures and tests, and flexibility of timing of procedures. These

aspects were considered as dependent variables. Validity of the data collection tools was shown by a panel of at least three experts that rated the appropriateness of the content of the questionnaires. Reliability was shown by testing and retesting a small convenience sample at the research study site. Trained independent interviewers administered questionnaire to the parents/guardians of the children enrolled into the TB epidemiology cohort study.

The following independent variables were considered primary:

- Duration of participation in the epidemiology cohort study

The following independent variables were considered secondary:

- Age
- Gender
- Occupation
- Level of education

Data on participants' satisfaction was summarized using means, medians, and percentages. Chi square tests were used to examine the relationship between satisfaction scores and participants' demographic characteristics (i.e., duration in the study, gender, age, and so on). Chi square tests were also used to compare the proportions of participants who identified with each satisfaction aspect (i.e., general satisfaction, technical quality, staff interpersonal manner, communication, financial aspects, and accessibility and convenience). For example, it may be expected that participants of different age groups will identify equally with a satisfaction as such as technical quality. By calculating a chi square statistic of the proportions of younger versus that of older

participants who identify with a satisfaction aspect such as technical quality of research activities or not, an individual will be able to determine if there is a statistically significant relationship between age and satisfaction with technical quality.

Univariate analysis was performed to determine the association of the response variables and the potential predictors (Lansimies-Antikainen et al., 2009). Univariate analysis was used to explore each variable (age, gender, duration in the study, profession, etc.) separately. The pattern of the response for each aspect of satisfaction was determined. The goal was to discern differences between the various satisfaction aspects from the variable representing the respondent. For example, the respondents with a duration of participation in the epidemiology cohort study of less than 1 year may be expected to have different score of satisfaction in some aspects than those who have participated in the study for a longer duration.

When measured on a five-point Likert scale, average individual satisfaction ratings can be calculated for each identified satisfaction aspect. These average satisfaction scores range between 1 (*all respondents rate the aspect as 'strongly disagree'*) and 5 (*all respondents rate the aspect as 'strongly agree'*). The higher the score, the higher the satisfaction level with this aspect as valued by the participant. Satisfaction scores can also be viewed by looking at the percentage of participants that rate a particular aspect as strongly agree percentage can vary between 0 and 100%.

The demographic information of the sample is presented in percentage in terms of age, gender, occupation, and level of education (See Appendix 1, Table 14).

Selected relation between participants' characteristics and the main satisfaction aspects (i.e., general satisfaction, technical quality, staff interpersonal manner, communication, financial aspects, and accessibility and convenience) was analyzed in relation to participants characteristics through chi square analysis (See Appendix 1, Table 15). Duration of participation and staff experience with research was correlated with main satisfaction aspects.

Informed Consent Comprehension

The nature of clinical trials is to find out if harm will be done by a new drug, vaccine, or treatment. With such a paradox, it is necessary to apply strict guidelines to ensure the fairness of the studies, their conduct as well as the soundness resulting data. The idea of autonomy is the bioethics principle that serves as a guideline to ensure that human rights of the volunteers are respected. The principle of respect for autonomy requires the investigator to know that the research subject has the capacity to act intentionally, with understanding, and without controlling influences that would mitigate against a free and voluntary act. This principle is the basis for the practice of "informed consent" (Oduro et al., 2008). In order to assess the quality of informed consent in the evaluation of the site's capacity to properly conduct clinical research, the participant needs to show an understanding and appreciation of the information provided to him/her during the informed consent process.

For informed consent comprehension, questions were asked covering information presented when a participant was administered an informed consent form (Minnies et al. , 2008). The questionnaire needed to ascertain whether or not the participants appreciate

the themes that are obligatory in an informed consent document for clinical research involving human beings. In order to ensure that the participant's autonomy is respected, it is critical to ensure that the participants understood the following ideas: the background of the study, the study procedures, risks and benefits, confidentiality, the voluntary nature of participation in the study, and the right to withdraw at any time. The questionnaire has a multiple choice format and choosing the correct answer will indicate comprehension of the theme of the question.

The following independent variables were considered primary:

- duration of participation in the epidemiology cohort study
- research experience of the study staff person that administered consent

As in the participants' satisfaction portion of the study, the following independent variables were considered secondary:

- age
- gender
- occupation
- level of education

On the informed consent questionnaire, participants are expected to select the correct answer from a choice of five possible answers for each of the questions. One of the answers is an exact reflection of the information in the consent document or an expected answer according ethics standards, which, if selected, was taken as an indicator of correct understanding or recall (Minnies et al. , 2008). The percent of correct answered is then used an indicator of the level of comprehension of the question from participants

(See Appendix 1, Table 4). Data on participant informed consent comprehension were summarized using percentages Duration of participation and experience of staff administering consent was correlated with the correctness of informed consent answers. Selected relation between participants' characteristics and main satisfaction aspects are analyzed using chi-square analysis (see Table 6, Appendix 1).

Data Analysis Tools

It was originally proposed that data would be entered into EpiInfo databases and analysis will be done using STATA for this evaluation study. However, on the field, these software were not available. Hence, for both the participant satisfaction and informed consent comprehension, the data management was performed with SQL server management studio while statistical analysis was done using SAS Version 9.2

Study Procedures

Study Setting

This evaluation of the capacity building program was conducted at the KEMRI/CDC Field Research Station in Karemo Division, Siaya District in Western Kenya. The site is located in rural area. The Karemo district occupies an area of 235.1 km2 with a population of 76,986 (Ministry of Finance and Planning, Republic of Kenya, 2010). This site has been involved in clinical research since 1979 in collaboration between the Kenya Medical Research Institute (KEMRI) and the U.S. CDC (2010). Although the site was originally known for its Malaria research, it has recently been involved in HIV, TB, and other research areas. In particular, the site is known for the conduct of a third phase trial of the world's most clinically advanced malaria vaccine

candidate, known as RTS,S. For preparation for the conduct of TB vaccine efficacy study, the site conducted epidemiology cohort studies in adolescents and in infants.

Inclusion/Exclusion Criteria

Inclusion criteria. The inclusion criteria for the participant satisfaction assessment and informed consent comprehension are

- Parent of a participant currently enrolled in or withdrawn from a current large-community based TB infant epidemiology study protocol at the site
- Willingness to provide informed consent

Exclusion criterion. The exclusion criterion for the participant satisfaction assessment and informed consent comprehension is an unwillingness to provide informed consent.

Participant Entry Procedures

Three hundred and twenty-four parents of baby participants currently enrolled or withdrawn from the active TB epidemiology study were approached to be administered the participant satisfaction and informed consent comprehension questionnaires. This study was nested in an active TB infant epidemiology protocol at the site and participants were randomly selected from enrollment logs and from scheduled study visits lists. The active epidemiology study consists of enrollment at Day 0 and then home visits at specific intervals for two years. Participants were recruited during the regularly scheduled study visits of the active epidemiology study at the clinic. A staff member of the active epidemiology study conducting the visits was designated as recruiter. Each recruiter was issued blocks of study identification numbers depending on the projected number to be

enrolled. During recruitment or during the visit of the active epidemiology study, participants were informed, by the active epidemiology study staff (recruiter) of the present evaluation study and were asked to participate in the present study. If the participant gave voluntary consent to be in the study, the participant satisfaction and informed consent comprehension questionnaires were administered at this point.

Ethical Considerations

This capacity building evaluation study was reviewed and approved by the Institutional Review Board (IRB) or Independent Ethics Committee (IEC) of each institution with ethical oversight on the research site, including the KEMRI and the Walden University IRB reviewed and approved this evaluation study. All participants are parents/guardians of the children that are enrolled in the TB epidemiology study that was being conducted at the site. Recruitment into the evaluation study occurred during a regularly scheduled TB epidemiology study visit. The nature of the evaluation study was explained to the participants and participants were informed that participation is voluntary and that they can withdraw at any time. Written informed consent was obtained from each participant prior to entry into the evaluation study. The consent form was translated in the local language(s) and back translated into English to ensure accuracy. A copy of the signed consent form was given to every participant and the original was maintained with the participant's records.

All study records are kept in a locked file cabinet and code sheets linking a participant's name to a participant identification number are stored separately in another locked file cabinet. Researchers also complied with all applicable privacy regulations

such as the Health Insurance Portability and Accountability Act of 1996 or the EU Data Protection Directive 95/46/EC.

Any documents that the IRB/IEC may need to fulfill its responsibilities, such as protocol amendments, and information concerning participant recruitment, payment or compensation procedures, or information from researchers was submitted to the IRB/IEC. The IRB/IEC's written unconditional approval of the study protocol and the informed consent form was in the possession of the researcher before the study is initiated.

Protocol modifications or changes could not be initiated without prior written IRB/IEC approval except when necessary to eliminate immediate hazards to the participants or when the change(s) involves only logistical or administrative aspects of the study.

Summary

Chapter 3 included the general study design as a descriptive cross sectional one that will use a GCP checklist, a trending analysis and questionnaires for both the participant satisfaction and the informed consent comprehension. GCP checklist and trending analysis were analyzed with descriptive statistics such as percentages. The participant satisfaction and informed consent comprehension assessments were analyzed with descriptive statistics. Chi square analyses were performed to evaluate the association between independent variables such as age, occupation, level of education with dependent variables such as the level of satisfaction or the level informed consent comprehension.

Chapter 4 will detail the results and present them in tabular and text form as necessary with the data analysis elements that were specified in Chapter 3.

Chapter 4: Results

In this chapter, data analysis and study findings are presented. Sections include an analysis of the study sample demographics, an analysis of the results of the GCP checklist scores, a trending analysis comparing current and historical observations and findings on compliance, an analysis of the participations satisfaction survey data, an analysis of the informed consent comprehension data, and a summary of all results.

Analysis of Study Sample Demographics

Descriptive statistics were used to describe the study sample demographics. There were 297 participants in the study. They were all females, which is consistent with the idea that, in the area where the infant TB study is being conducted, it is mothers who usually take their children to seek health care. There were no men in the study sample. As shown in Table 1, there were four age categories. Of those, 46.46% were younger than 25 years (*n*= 138), 41.41% were between 25 and 35 years old (*n*=123), 11.11% were older than 35 years (*n*= 33), and 1.01% did not mark their age (*n*=3). The mean age was 26.2 (*SD* 6.8) and the age median was 25.

Table 1

Age Distribution in the Study Sample

Age	% (n)
Less than 25 years old	46.46 (138)
Between 25-35 years old	41.41 (123)
Older than 35 years old	11.11 (33)
Unknown	1.01 (3)

Table 2 shows the occupations represented. There were eight categories: 55.56% not working-- housewife (*n*= 165), 33.67% farming (*n*= 100), 7.74% business owner (*n*= 23), 1.01% other (*n*=3), 0.67% unskilled labor (*n*= 2), 0.67% unknown (*n*=2), 0.34% salaried worker (*n*=1), and 0.34% skilled labor (*n*= 1).

Table 2

Occupation

Occupation	**% (n)**
Farming	33.67 (100)
Fishing	0 (0)
Salaried worker (e.g. teacher, nurse, office)	0.34 (1)
Business owner	7.74 (23)
Skilled labor (e.g. carpenter, tailor)	0.34 (1)
Unskilled labor (e.g. construction)	0.67 (2)
Not working (housewife)	55.56 (165)
Unknown	0.67 (2)
Other	1.01 (3)

As for the level of education in the study sample, as shown in Table 3, 85.19% had at least a primary school education (*n*=253), 9.43% had at least a secondary school education (*n*=28), 3.37% had no education (*n*= 10), 1.01% had a postsecondary education and for 1.01% (*n*=3), the education was unknown.

Table 3

Level of Education

Level of Education	**% (n)**
None	3.37 (10)
Primary	85.19 (253)
Secondary	9.43 (28)
Postsecondary	1.01 (3)
Unknown	1.01 (3)

In terms of the participants' duration into the study, 100% of the study participants had been in the study for less than 12 months and no participants (n=0) had been in the study for more than 1 year.

Analysis of the Results of the GCP Checklist Scores

The GCP checklist consisted of a list of items to be checked off if present at the site. This list was graded with a weighted score as follows: four points for an item that had absolutely no findings, three points for an item with minor findings, two points for an item with major findings, one point for items with critical findings, zero points if the item was completely absent. As a whole, the site scored had a score of 94.24 % (622/660) on the GCP check list. Details on the scores are shown in Appendix 2. There were no major or critical findings.

According to the completed GCP evaluation, the entire site is well organized, with adequately trained staffed, clean and secured facilities, up-to-date equipment and procedures, a solid quality management system, and it is mainly compliant with local and international guidelines. According to the completed GCP checklist, for practices related to document management, the study site is satisfactory. There was a document control system in place that included standard operating procedures, SOPs, in a standardized form for all functions of the clinical research study such as laboratory, clinical operations, field operations, data management, ethics, and regulatory as well as QA. Except for laboratory SOPs, original SOPs were stored in the QA office in locked cabinets. Controlled copies of the SOPs were available at each functional area work station. Each SOP included an author, a reviewer, supervisory approval, and QA review and approval.

SOPs and their related forms were uniquely numbered. SOPs that became obsolete were stored in separate binder by the QA manager. There was a change control procedure that ensured that any modification to a controlled document was captured and sent through the appropriate approval procedure prior to the implementation of the change. Archiving and storage of study document was described in SOPs. The archiving and storage procedure included identification, storage, protection, retrieval, retention, and disposition of records. All study documents with confidential study information were stored in secured areas with restricted access.

The next GCP checklist area examined was personnel and training. The site had written procedures and documentation for all staff involved in the clinical research study. Each position was depicted in the organization chart. Job descriptions were included in each staff's members training file. However, the site failed to generate and maintain a training matrix that specified details on training activities required for each study staff member. This was a minor finding. The training matrix would have allowed a way to ensure each staff member is qualified, experienced, and trained in their applicable duties. The staff was organized such that each position had at least more than one staff member capable of performing each function in the study. This redundancy prevented for gaps in case of extended absence of a staff member. Performance reviews were usually conducted annually and they seemed to occur on time since the majority of staff was on yearly contracts and their employment into the study could not continue without the results of the yearly performance review. Quality control personnel frequently monitored all study activities and their reports fed into each staff's performance review.

In the data management sections, data were mainly captured electronically, even though paper forms were used as back-up in case of failure of the electronic system. The electronic data management system ensured and documented that the electronic data processing system conformed to the established requirements for completeness, accuracy, reliability, and consistent intended performance. Although data management SOPs were still in draft form, instructions on entering and maintaining data were available. Not having finalized SOPs is a minor finding. The data systems were designed to permit data changes in such a way that changes are documented, and that there is no deletion of entered data (i.e., audit trail, data trail, and edit trail). The system was secure and prohibited unauthorized access to the data. A list of the individuals who are authorized to make data changes was maintained. The data were backed-up in a secure server on a daily basis. There were a couple of major findings related to the lack of finalized data management and statistical analysis plans. Although these plans existed and were being used, they were formally approved as required by GCPs.

In the portions related to protocol and amendments, the regulatory aspects seemed to be in order. There was an approved protocol on file that was kept by the QA department. The participant enrollment log was maintained in electronic form in the database and it was complete as it showed all 2,900 participants that had been enrolled into the study. There was also a monitoring log in place that showed that monitoring was being conducted on a quarterly basis. The delegation of responsibility was clear. All correspondence with Ethics Review Committees (ERCs) and IRBs was kept in the investigator's file. Protocol amendments and deviation reports were also on file.

Participants' recruitment procedures were detailed in an SOP, which included a description of how the potential participants were identified, how the contact was made, and who made the contact.

A review of 5% of the 2,900 (n=150) completed informed consent forms of the infant TB study was conducted as part of this evaluation. The forms themselves were valid as they were the versions included in the last protocol approved by the ERCs and IRB. The 150 informed consent forms were reviewed for authenticity of signature and validity of the consent process. In some of the forms, when the participants were not able to read, the staff printed the participant's name in the place of signature. However, the participants still have their thumb print put on the forms and a third party also witnessed the consenting procedure. Enrollment notes were written for each participant and it was documented that a signed copy of the consent form was given to each participant. The eligibility criteria (inclusion/exclusion) were defined in the protocol and set-up for entry in the electronic data entry screen.

During enrollment, a participant would have had to fulfill the eligibility criteria before being able to proceed to any subsequent data entry screens for the study. This safeguard ensured that study data were collected only on participants that met the eligibility criteria. The case report forms (data collection tools) were also electronic. Prescreening and enrollment data were collected electronically on Personal Digital Assistants (PDAs), which is a hand held small computer resembling a palm pilot. This device allowed for enrollment nurses to move around and go from house to house without being encumbered by laptops. Data from subsequent study follow-up visits, however, was

collected on laptops through software that was downloaded to a server at the main site facility. The electronic case report forms (eCRFs) contained all parameters required by the protocol. The system allowed for an electronic signature each time it was accessed by a staff member. Anytime there was change in the data, the signature feature allowed for an audit trail to be generated since each entry left an electronic record. There were defined levels of access for the relevant staff members allowed to manipulate the database. For example, the nurses were only allowed to enter data. Supervisors and the principal investigator were allowed to modify data solely after a change control was completed and approved. In case of deviations, which are departures from the agreed to procedures or the protocol, there were written procedures for CAPA that included the completion of forms for recording infringements and the ensuing corrective plan as well as a timeline for correction. The QC and QA personnel were in charge of monitoring the corrections and reporting them to the principal investigator and the ethics committees. After correcting a deviation, a paper record was kept by the QA department.

In the laboratory, the main finding was related to the actual laboratory performing the tests for study samples that had not completed the accreditation process. This is considered a minor finding since its impact does not necessarily lead to any regulatory infraction nor does it impact data integrity or study outcome. There were minor findings were related to documentation. For example, a key instrument for the epidemiology study, the Genexpert instrument, required to assess samples for the presence of mycobacterium TB, did not have its own SOP document. The calibration log did not contain a separate log for a critical instrument such as the Hain twincubator, which is the

instrument that allows for hybridization of samples suspected of infection with mycobacterium TB. In one instance, the monthly maintenance log was missing the March 2011 record for one of the autoclaves. In the SOPs, there were forms included as appendices, but the forms did not have the corresponding SOP number on them. The SOPs themselves did not have titles on each page. An SOP specifying a backup plan in case of equipment failure did not seem to exist. This SOP is expected to describe the availability and the accessibility of alternate equipment or plan for dealing for each piece of equipment. There does not seem to be health check plan for staff members who are exposed to risk of infection. For example, since staff members are handling the TB infectious agent, they should be tested for TB on a frequent basis. All findings mentioned above were considered minor.

Other findings were minor, but still had to be mentioned since they are findings nonetheless. An example of these findings is related to documentation. The SOP books all included table of contents with no page numbers. So, from the table of contents, it was impossible to easily find specific SOPs in the books. The GCP checklist was then examined in terms of percent of findings and observations related to the main areas of GCP compliance as shown in Figure 3.

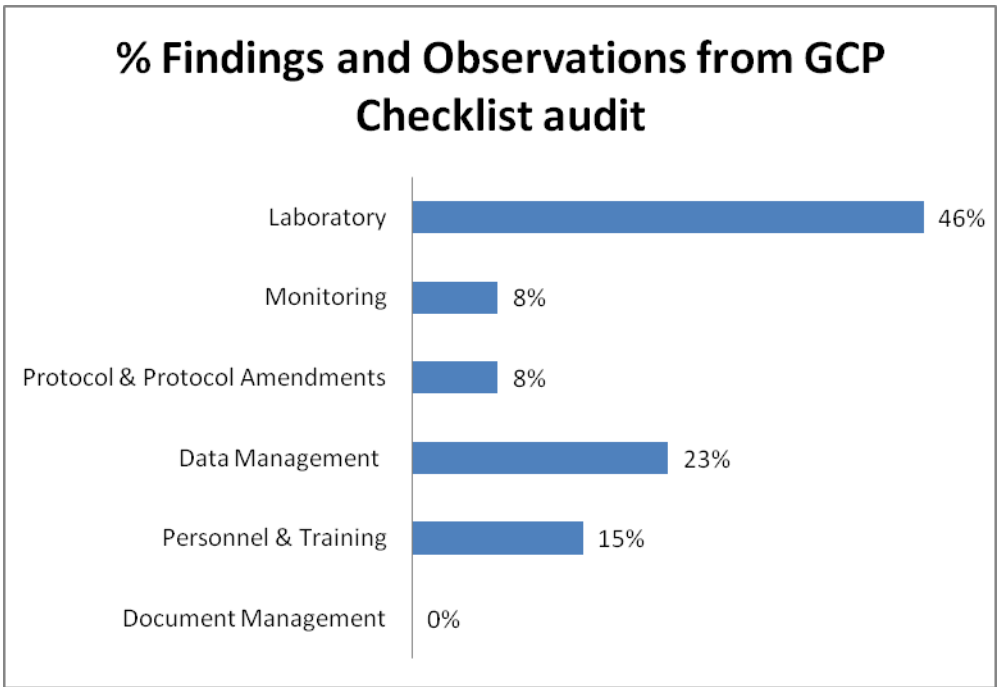

Figure 3. *Findings and observations from GCP checklist audit*

The laboratory was the study area with the most findings (46%), followed by data management (23%), personnel and training (15%), monitoring (8%), protocol and protocol amendments (8%), and document management (0%). On the GCP checklist, the laboratory had the most items to be checked which might explain the higher percentage in terms of findings and observations.

Trending Analysis on GCP Compliance

A trending analysis was performed where deviation logs, audit and monitoring reports (internal and external) were reviewed in order to identify the number of findings and observations of aspects of the study that were not compliant with GCP. In this dissertation the research question regarding trending analysis specified that only records

of the past 2 years were going to be examined. It was decided to go back to the first external GCP assessment of 2008 since, as this dissertation was being prepared, the intention was to started data collection in 2010. The 2008 report is crucial to report the actual progress of the site's performance in terms of capacity building for the proper conduct of clinical trials in compliance with GCPs.

Three past reports were found on site and they were reviewed to extract the number of findings and observations reported for the site's status of compliance with GCPs. The first report was a thorough assessment that was conducted by an external auditor in September 2008. The other two reports were prepared by an internal monitor whose responsibility was to ensure that the study protocol was being followed; that changes to the protocol were being approved by the ethics committees; that the records being maintained were current, accurate, and complete; and that the investigator was carrying out the agreed-upon activities and had not delegated them to other previously unspecified staff. The monitoring reports reviewed were from monitoring visits performed in April 2009 and January 2010. The two monitoring reports and the external assessment report were then trended against the GCP checklist audit that was conducted as part of this dissertation study in January 2012. Table 4 below, shows the number findings and observations on GCP compliance from the four reports were reviewed for trending analysis.

Table 4

Number of Findings and Observations from 2008-2012

	Document Management	Personnel & Training	Data Management	Protocol & Protocol Amendments	Monitoring	Laboratory	TOTAL
External audit Sept. 2008	6	0	9	21	5	7	48
Internal Monitoring Apr. 2009	3	3	3	5	3	3	20
Internal Monitoring Jan. 2010	5	4	1	4	0	6	20
GCP checklist Audit Jan. 2012	0	2	3	1	1	6	13
TOTAL	14	9	16	31	9	22	

Table 4 shows that the total number of findings and observations decreased by 73% (from 48 to 13) from September 2008 to January 2012 which shows significant improvement in terms of the site's performance in terms of compliance with GCPs. As shown in the Figure 4, in general, the trend of observations and findings tends to decrease from the first (2008) to the last report (2012) reviewed.

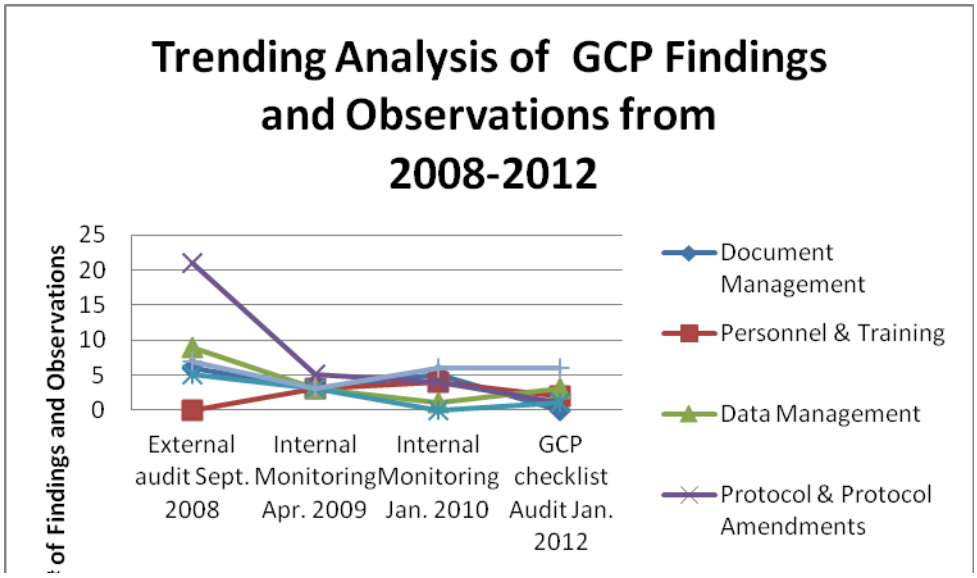

Figure 4. Trending Analysis of GCP Findings and Observations from 2008-2012

Figure 5 shows that the GCP area of protocol and protocol amendments had the most finding and observations (*n*=31), followed by the laboratory (*n*=22), data management (*n*=16), document management (*n*=14), and then personnel and training and monitoring (both *n*=9).

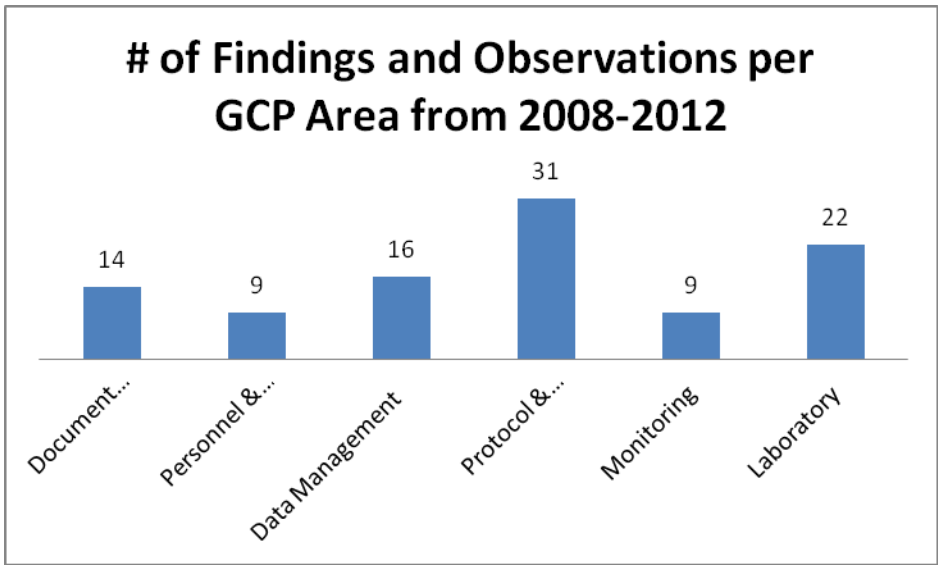

Figure 5. Number of findings and observations per GCP area from 2008-2012

Figure 5 shows that the area of protocol and protocol amendments (protocol adherence) is the one that seems to be the most noncompliant throughout the years and it should therefore be the areas with the most concentrated efforts for improvement. Altogether, the site's audit against the GCP checklist was successful; it showed that the level of compliance with international standards in the conduct of clinical research was relatively high despite a few minor findings. The site had improved in compliance level since the first assessment in 2008.

Analysis of the Participants' Satisfaction Survey

Clinical study participants' satisfaction was measured in categories related to level of contentment with various aspects of satisfaction. For the general satisfaction categories, 97.31% of the study participants either strongly agreed or agreed that the attention received from the study staff while they interact was just about perfect. In terms

of staff interaction, 78.45% of participants either disagreed or strongly disagreed that they were dissatisfied with some things about the interactions that they had with study staff. The results of the series of questions related to the technical quality of the services provided during the trial were consistent with a high level of satisfaction. For the suitability of the environment, 90.57% of the participants either strongly agreed or agreed that the study staff and their facilities have everything needed for the study. For reassurance, 91.24% either disagreed or strongly disagreed that sometimes study staff make the wonder if the study is worthwhile. For staff dexterity, 95.62% of participants either strongly agreed or agreed that the staff was careful to check that they were satisfied when they were being examined by the study staff. For the study worth, 86.19% either disagreed or strongly disagreed that they have some doubts about the need for the TB epidemiology study in the community. For clarity, 82.16% of participants either strongly disagreed or disagreed that sometimes study staff used medical words without explaining.

The results of the questions related to interpersonal manners also showed a high level of satisfaction. For those questions, 70.37% of study participants either strongly disagreed or disagreed that study staff were too businesslike and impersonal toward them; 88.56% either strongly agreed or agreed that study staff treat them in a friendly and courteous manner; 77.1% either strongly disagreed or disagreed that study staff sometimes hurry too much during the study visits; and 92.93% either strongly agreed or agreed that study staff usually spend plenty of time with me.

The next questions were related to communications and the level of satisfaction was consistently high. For those questions, 97.65% either strongly agreed or agreed that

study staff was good about explaining reasons for the research study, and 89.57% either strongly disagreed or disagreed that study staff sometimes ignore what they told them.

The level of satisfaction remained high on questions related to financial aspects. For those, 98.99% either strongly agreed or agreed that felt confident that they can complete all study visits without spending too much money; 96.3% either strongly disagreed or disagreed that they have to spend more than they can afford to be part of this study. In terms of accessibility and convenience, the study participants were still consistently satisfied, and 97.98% either strongly agreed or agreed that the study visit hours are convenient for them. Moreover, 93.26% either strongly agreed or agreed that they have easy access to study staff when they need to. And finally, 90.91% % either strongly disagreed or disagreed that they find it hard to reach the study staff right away when they need to. The participants' satisfaction data are represented in Table 5.

Table 5

Participant Satisfaction Survey Results

Participant Satisfaction Aspect *N* (%)					
	Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
General Satisfaction					
The attention that I receive from the study staff while we interact is just about perfect	173 (58.25)	116 (39.06)	0 (0)	5 (1.68)	3 (1.01)
I am dissatisfied with some things about the interactions that I have with study staff	17 (5.72)	43 (14.48)	4 (1.35)	123 (41.41)	110 (37.04)
	190	159	4	128	113
Technical Quality					
I think the study staff and their facilities have everything needed for the study	187 (62.96)	82 (27.61)	22 (7.41)	6 (2.02)	0 (0)
Sometimes study staff make me wonder if the study is worthwhile	7 (2.36)	12 (4.04)	7 (2.36}	130 (43.77)	141 (47.47)
When study staff examine me, they are careful to check that I am satisfied	167 (56.23)	117 (39.39)	0 (0)	12 (4.04)	1 (0.34)
I have some doubts about the need for this study in the community	11 (3.70)	18 (6.06)	12 (4.04)	124 (41.75)	132 (44.44)
Sometimes study staff use medical words without explaining	25 (8.42)	23 (7.74)	5 (1.68)	101 (34.01)	143 (48.15)
Interpersonal manners					
Study staff are too businesslike and impersonal toward me	37 (12.46)	48 (16.16)	3 (1.01)	93 (31.31)	116 (39.06)

(continued)

Participant Satisfaction Aspect *N* (%)					
	Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
Interpersonal Matters (cont'd)					
Study staff treat me in a friendly and courteous manner	153 (51.52)	110 (37.04)	0 (0)	26 (8.75)	8 (2.69)
Study staff sometimes hurry too much during the study visits	26 (8.75)	32 (10.77)	10 (3.37)	120 (40.40)	109 (36.70)
Study Staff usually spend plenty of time with me	154 (51.85)	122 (41.08)	2 (0.67)	17 (5.72)	2 (0.67)
Communication					
Study staff is good about explaining reasons for the research study	228 (76.77)	62 (20.88)	1 (0.34)	4 (1.35)	2 (0.67)
Study staff sometimes ignore what I tell them	8 (2.69)	21 (7.07)	2 (0.67)	110 (37.04)	156 (52.53)
Financial Aspects					
I feel confident that I can complete all study visits without spending too much money	245 (82.49)	49 (16.50)	0 (0)	3 (1.01)	0 (0)
I have to spend more than I can afford to be part of this study	5 (1.68)	4 (1.35)	2 (0.67)	73 (24.58)	213 (71.72)
Accessibility and Convenience					
The study visit hours are convenient for me	197 (66.33)	94 (31.65)	1 (0.34)	3 (1.01)	2 (0.67)
I have easy access to study staff when I need to	175 (58.92)	102 (34.34)	3 (1.01)	14 (4.71)	3 (1.01)
I find it hard to reach the study staff right away when I need to	7 (2.36)	15 (5.05)	5 (1.68)	88 (29.63)	182 (61.28)

Next, Tables 6 through 8 illustrate the relationship between participants' characteristics and the main satisfaction aspects (i.e., general satisfaction, technical quality, staff interpersonal manner, communication, financial aspects and accessibility & convenience). During data analysis, it was found that, in terms of comparing the difference in the satisfaction levels according to occupation, it was best to compare housewives vs. other occupations as opposed to farming versus other as originally proposed. This change was made due to the fact that the majority of the participants were housewives (55.56%). Table 6 shows that in terms of age, the level of satisfaction is high in both age groups (≤25 vs. > 25) in all questions. Due the high *p*-values in these data, the difference in the level of satisfaction between the age groups may not be significant.

Table 6

Management of Data for the Relationship between Age and Main Satisfaction Aspects

Satisfaction Item	Age group ≤ 25	>25	*P* value
The attention that I receive from the study staff while we interact is just about perfect			
Agree	151(51.36%)	135(45.92%)	0.8758
Disagree	4(1.36%)	4(1.36%)	
I am dissatisfied with some things about the interactions that I have with study staff			
Disagree	123(41.84%)	112(38.10%)	0.7942
Agree	32(10.88%)	27(9.18%)	
I think the study staff and their facilities have everything needed for the study			
Agree	141(47.96%)	125(42.52%)	0.7617
Disagree	14(4.76%)	14(4.76%)	
Sometimes study staff make me wonder if the study is worthwhile			
Disagree	144(48.98%)	130(44.22%)	0.8325
Agree	11(3.74%)	9(3.06%)	
When study staff examine me, they are careful to check that I am satisfied			
Agree	149(50.68%)	132(44.90%)	0.6276
Disagree	6(2.04%)	7(2.38%)	
I have some doubts about the need for this study in the community			
Disagree	132(44.90%)	132(44.90%)	0.0056
Agree	23(7.82%)	7(2.38%)	
Sometimes study staff use medical words without explaining			
Disagree	130(44.22%)	115(39.12%)	0.7939
Agree	25(8.50%)	24(8.16%)	
Study staff are too businesslike and impersonal toward me			
Disagree	104(35.37%)	104(35.37%)	0.1461
Agree	51(17.35%)	35(11.90%)	

(continued)

Satisfaction Item	Age group ≤ 25	>25	*P* value
Study staff treat me in a friendly and courteous manner			
Agree	135(45.92%)	124(42.18%)	0.5767
Disagree	20(6.80%)	15(5.10%)	
Study staff sometimes hurry too much during the study visits			
Disagree	127(43.20%)	110(37.41%)	0.5445
Agree	28(9.52%)	29(9.86%)	
Study Staff usually spend plenty of time with me			
Agree	143(48.64%)	130(44.22%)	0.6736
Disagree	12(4.08%)	9(3.06%)	
Study staff is good about explaining reasons for the research study			
Agree	148(50.34%)	138(46.94%)	0.0458
Disagree	7(2.38%)	1(0.34%)	
Study staff sometimes ignore what I tell them			
Disagree	132(44.90%)	132(44.90%)	0.0056
Agree	23(7.82%)	7(2.38%)	
I feel confident that I can complete all study visits without spending too much money			
Agree	154(52.38%)	137(46.60%)	0.4990
Disagree	1(0.34%)	2(0.68%)	
I have to spend more than I can afford to be part of this study			
Disagree	151(51.36%)	134(45.58%)	0.6135
Agree	4(1.36%)	5(1.70%)	
The study visit hours are convenient for me			
Agree	152(51.70%)	136(46.26%)	0.8927
Disagree	3(1.02%)	3(1.02%)	
I have easy access to study staff when I need to			
Agree	146(49.66%)	129(43.88%)	0.6290
Disagree	9(3.06%)	10(3.40%)	
I find it hard to reach the study staff right away when I need to			
Disagree	145(49.32%)	127(43.20%)	0.4779
Agree	10(3.40%)	12(4.08%)	

Table 7 shows that in terms of level of education, the level of satisfaction is high in both education levels (none vs. some) groups in all questions. Due the high *p*-values in these data, the difference in the level of satisfaction between the group with some education and the one with no education may not be significant.

Table 7

Management of Data for the Relationship between Level of Education and Main Satisfaction Aspects

	Formal Education		
Satisfaction Item	None	Some	*P* value
The attention that I receive from the study staff while we interact is just about perfect			
Agree	10(3.37%)	279(93.94%)	0.5925
Disagree	0(0.00%)	8(2.69%)	
I am dissatisfied with some things about the interactions that I have with study staff			
Disagree	9(3.03%)	228(76.77%)	0.4137
Agree	1(0.34%)	59(19.87%)	
I think the study staff and their facilities have everything needed for the study			
Agree	9(3.03%)	260(87.54%)	0.9498
Disagree	1(0.34%)	27(9.09%)	
Sometimes study staff make me wonder if the study is worthwhile			
Disagree	10(3.37%)	267(89.90%)	0.3874
Agree	0(0.00%)	20(6.73%)	
When study staff examine me, they are careful to check that I am satisfied			
Agree	8(2.69%)	276(92.93%)	0.0140
Disagree	2(0.67%)	11(3.70%)	

(continued)

Satisfaction Item	None	Some	*P* value
I have some doubts about the need for this study in the community			
Disagree	10(3.37%)	257(86.53%)	0.2809
Agree	0(0.00%)	30(10.10%)	
Sometimes study staff use medical words without explaining			
Disagree	8(2.69%)	240(80.81%)	0.7615
Agree	2(0.67%)	47(15.82%)	
Study staff are too businesslike and impersonal toward me			
Disagree	5(1.68%)	205(69.02%)	0.1433
Agree	5(1.68%)	82(27.61%)	
Study staff treat me in a friendly and courteous manner			
Agree	8(2.69%)	254(85.52%)	0.4124
Disagree	2(0.67%)	33(11.11%)	
Study staff sometimes hurry too much during the study visits			
Disagree	8(2.69%)	231(77.78%)	0.9695
Agree	2(0.67%)	56(18.86%)	
Study Staff usually spend plenty of time with me			
Agree	9(3.03%)	267(89.90%)	0.7132
Disagree	1(0.34%)	20(6.73%)	
Study staff is good about explaining reasons for the research study			
Agree	10(3.37%)	279(93.94%)	0.5925
Disagree	0(0.00%)	8(2.69%)	

(continued)

Satisfaction Item	None	Some	*P* value
Study staff sometimes ignore what I tell them			
Disagree	10(3.37%)	257(86.53%)	0.2809
Agree	0(0.00%)	30(10.10%)	
I feel confident that I can complete all study visits without spending too much money			
Agree	9(3.03%)	285(95.96%)	0.0038
Disagree	1(0.34%)	2(0.67%)	
I have to spend more than I can afford to be part of this study			
Disagree	10(3.37%)	278(93.60%)	0.5696
Agree	0(0.00%)	9(3.03%)	
The study visit hours are convenient for me			
Agree	9(3.03%)	282(94.95%)	0.0681
Disagree	1(0.34%)	5(1.68%)	
I have easy access to study staff when I need to			
Agree	9(3.03%)	269(90.57%)	0.6358
Disagree	1(0.34%)	18(6.06%)	
I find it hard to reach the study staff right away when I need to			
Disagree	9(3.03%)	266(89.56%)	0.7501
Agree	1(0.34%)	21(7.07%)	

Table 8 shows that in terms of occupation, the level of satisfaction is high in housewives and in participants of other occupations in all questions. Due the high *p*-values in these data, the difference in the level of satisfaction between the housewives and the participants of other occupations may not be significant.

Table 8

Management of Data for the Relationship between Occupations and Main Satisfaction Aspects

	Occupation		
Satisfaction Item	House wife	Other	*P* value
The attention that I receive from the study staff while we interact is just about perfect			
Agree	160(53.87%)	129(43.43%)	0.6886
Disagree	5(1.68%)	3(1.01%)	
I am dissatisfied with some things about the interactions that I have with study staff			
Agree	135(45.45%)	102(34.34%)	0.3323
Disagree	30(10.10%)	30(10.10%)	
I think the study staff and their facilities have everything needed for the study			
Agree	150(50.51%)	119(40.07%)	0.8243
Disagree	15(5.05%)	13(4.38%)	
Sometimes study staff make me wonder if the study is worthwhile			
Agree	155(52.19%)	122(41.08%)	0.6046
Disagree	10(3.37%)	10(3.37%)	

(continued)

	Occupation		
Satisfaction Item	House wife	Other	*P* value
When study staff examine me, they are careful to check that I am satisfied			
Agree	158(53.20%)	126(42.42%)	0.8991
Disagree	7(2.36%)	6(2.02%)	
I have some doubts about the need for this study in the community			
Agree	143(48.15%)	124(41.75%)	0.0388
Disagree	22(7.41%)	8(2.69%)	
Sometimes study staff use medical words without explaining			
Agree	134(45.12%)	114(38.38%)	0.2346
Disagree	31(10.44%)	18(6.06%)	
Study staff are too businesslike and impersonal toward me			
Agree	118(39.73%)	92(30.98%)	0.7323
Disagree	47(15.82%)	40(13.47%)	
Study staff treat me in a friendly and courteous manner			
Agree	144(48.48%)	118(39.73%)	0.5732
Disagree	21(7.07%)	14(4.71%)	
Study staff sometimes hurry too much during the study visits			
Agree	132(44.44%)	107(36.03%)	0.8188
Disagree	33(11.11%)	25(8.42%)	
Study Staff usually spend plenty of time with me			
Agree	152(51.18%)	124(41.75%)	0.5436
Disagree	13(4.38%)	8(2.69%)	

(continued)

	Occupation		
Satisfaction Item	Housewife	Other	*P* value
Study staff is good about explaining reasons for the research study			
Agree	160(53.87%)	129(43.43%)	0.6886
Disagree	5(1.68%)	3(1.01%)	
Study staff sometimes ignore what I tell them			
Agree	145(48.82%)	122(41.08%)	0.1965
Disagree	20(6.73%)	10(3.37%)	
I feel confident that I can complete all study visits without spending too much money			
Agree	162(54.55%)	132(44.44%)	0.1195
Disagree	3(1.01%)	0(0.00%)	
I have to spend more than I can afford to be part of this study			
Agree	161(54.21%)	127(42.76%)	0.4957
Disagree	4(1.35%)	5(1.68%)	
The study visit hours are convenient for me			
Agree	160(53.87%)	131(44.11%)	0.1666
Disagree	5(1.68%)	1(0.34%)	
I have easy access to study staff when I need to			
Agree	154(51.85%)	124(41.75%)	0.8320
Disagree	11(3.70%)	8(2.69%)	
I find it hard to reach the study staff right away when I need to			
Agree	151(50.84%)	124(41.75%)	0.4280
Disagree	14(4.71%)	8(2.69%)	

Analysis of the Informed Consent Comprehension Questionnaire

In the informed consent comprehension questionnaire, the questions focus on the required components of the informed consent form which are an introduction, an explanation of study procedures, risks and benefits, withdrawal, voluntary research participation and confidentiality.

Only 3.37% of the participants answered correctly that the reason their child was asked to attend the clinic so that their baby can participate in a research study. For the purpose of the study, 65.32% correctly identified it as being to find out the amount of TB disease and TB infection in children. The reason of the study, 64.98% correctly answered that the research staff wanted their child enrolled in the study so they could test them for TB and HIV. For the study duration, 83.16% correctly answered that they were expected to participate in the study is 2 years. Risks of study, 14.14% correctly identified the most common risk of being collected from their child as blistering or an open sore. Only 2.02% correctly answered that there are no immediate benefits available for the participants and their children to participate in the TB study. In terms of the ability to withdraw, 61.62% answered correctly that their child or they would suffer no loss at all if they chose to leave the study. As for confidentiality, 30.30% answered correctly that number and codes will be used to link the child to the samples. In terms of their own opinion on the reason for enrolling their child in the research study, 14.48% answered correctly that it is because they wanted to help the doctors learn more about TB. For voluntary research participation, 36.70% correctly answered that they can withdraw their

child at any time they wished. Table 9 contains the % correct responses and the number (*n*) of participants who chose the correct answer on all questions.

Table 9

Management of Data on Overall Informed Consent

Informed Consent Question	% correct	*n*=297
1. What was the reason you were asked to attend the clinic?	3.37	10
2. What is the purpose of the research study?	65.99	196
3. Why does the research staff want to enroll my baby into the research study?	65.66	195
4. What is the total amount of time my baby will be expected to participate in the study?	83.50	248
5. What is the most common risk involved when blood had been collected from my baby?	14.14	42
6. What benefits are available to me and my baby for participating in the study?	2.02	6
7. What if I didn't want my baby to participate in this study, I could withdraw	61.62	183
8. How will my baby's personal details be kept secret?	30.64	91
9. Why did I agree to enroll my child in this study?	14.48	43
10. How long do I have to keep participating in the study?	36.36	108

The results of the some of the questions showed evidence of therapeutic misconception which is the notion research participants will confuse their participation into the research study as obtaining treatment. These were shown in graphical form in Figures 6-8.

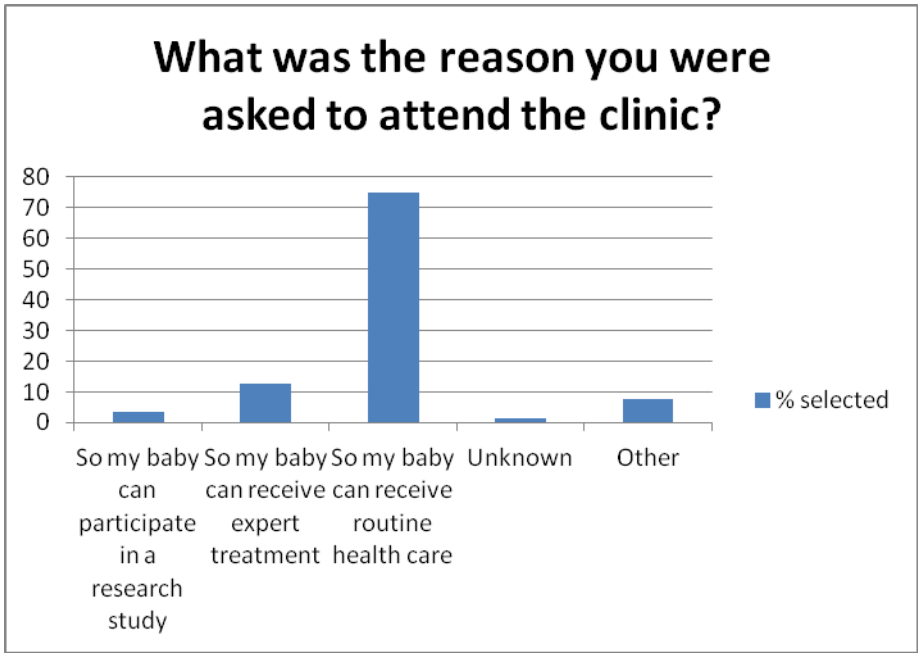

Figure 6. Percent selected on reason for attending the clinic

Erroneously, 74.75% chose that they were attending the clinic so that their baby can receive routine health care. The question on benefits also shows evidence of therapeutic misconception as shown in Figure 7.

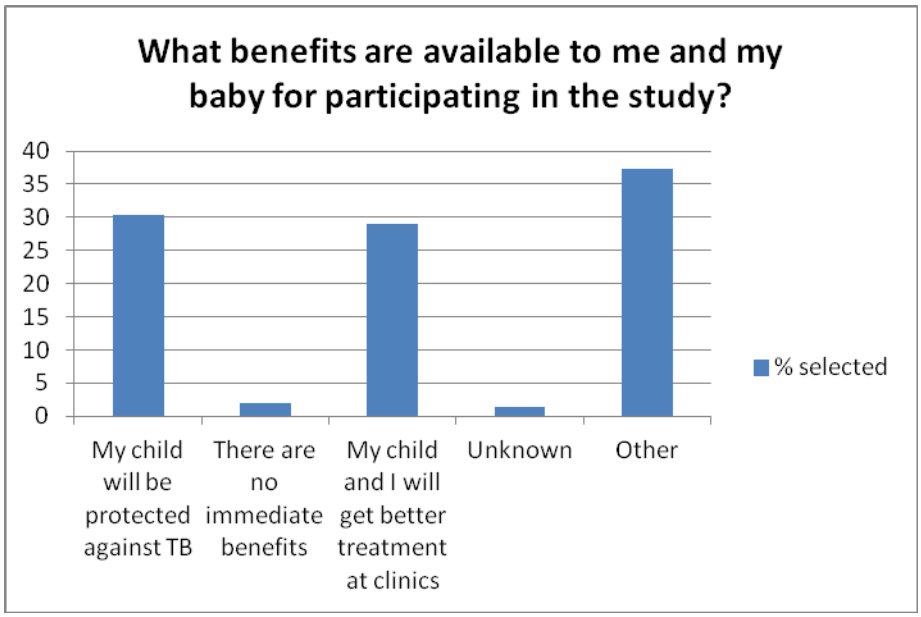

Figure 7. Percent selected on benefits for participating in the study

The same evidence of therapeutic misconception appeared on the selected benefits available to participants and their babies for participating in the study as shown in Figure 7. Of those, 30.30% thought their child will be protected against TB in participating in the study, and 28.96% thought that their child will receive better treatment at the clinic while only 2.02% correctly thought that there are no immediate benefits.

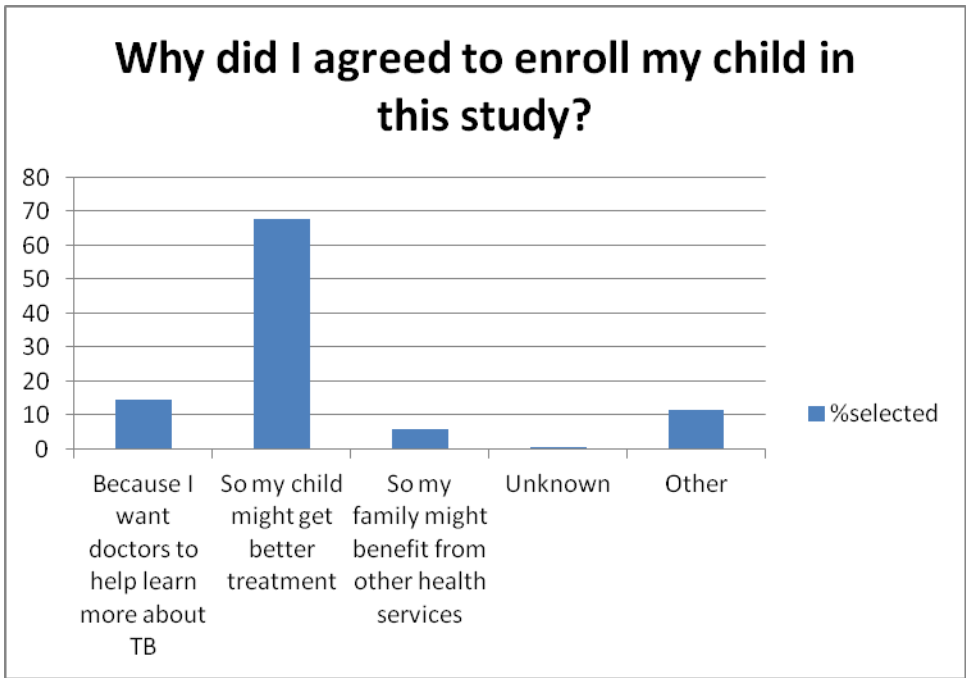

Figure 8. Percent selected on reasons for agreeing to be enroll their child in the study

The idea that there is an imbalance of power between the research participants and the study staff was also reflected in the results as shown in Figure 8. A number participants (25.59%) thought they had to stay in the study until it was completed. As for the right to withdrawal, 30.30% thought they could only withdraw if given permission and only 36.70% thought they could withdraw at any time if they wished. Table 10 shows all the answers on the informed consent questionnaire including the number of participants who chose particular answers.

Table 10

All Answers on Informed Consent

Informed Consent Question	*N* (% selected)
1. What was the reason you were asked to attend the clinic?	
So my baby can participate in a research study	10 (3.37%)
So my baby can receive expert treatment	38 (12.79%)
So my baby can receive routine health care	222 (74.75%)
Unknown	4 (1.35%)
Other	23 (7.74%)
2. What is the purpose of the research study?	
To find out the amount of TB disease and TB infection in children	194 (65.32%)
To find out if my child was vaccinated for TB	14 (4.71%)
To find out if BCG vaccination works in children	29 (9.76%)
Unknown	16 (5.39%)
Other	44 (14.81%)
3. Why does the research staff want to enroll my baby into the research study?	
So they can test my child for TB or HIV	193 (64.98%)
So they can collect blood from my child	2 (0.67%)
So they can inject my baby with BCG	32 (10.77%)
Unknown	17 (5.72%)
Other	53 (17.85%)
4. What is the total amount of time my baby will be expected to participate in the study?	
0:00:02	18 (6.06%)
0:00:03	247 (83.16%)
0:00:04	7 (2.36%)
0:00:05	25 (8.42%)
5. What is the most common risk involved when blood had been collected from my baby?	
My child may suffer from blistering or an open sore from the TB skin test	42 (14.14%)
My child can become infected with TB	26 (8.75%)
My child can lose blood	54 (18.18%)
Unknown	81 (27.27%)
Other	94 (31.65%)

(continued)

Informed Consent Question	*N* (% selected)
6. What benefits are available to me and my baby for participating in the study?	
My child will be protected against TB	90 (30.30%)
There are no immediate benefits	6 (2.02%)
My child and I will get better treatment at clinics	86 (28.96%)
Unknown	4 (1.35%)
Other	111 (37.37%)
7. What if I didn't want my baby to participate in this study, I could withdraw	
My child and I would suffer no loss at all	183 (61.62%)
My child and I will be treated differently by research and clinic staff	54 (18.18%)
My child and I would be denied access to health services at this clinic	35 (11.78%)
Unknown	11 (3.70%)
Other	14 (4.71%)
8. How will my baby's personal details will be kept secret?	
Numbers and codes will be used to keep from linking your child to the samples	90 (30.30%)
Highly trained research staff will keep information secret	73 (24.58%)
Clinic staff will be sure not to give information to the research staff	55 (18.52%)
Unknown	49 (16.50%)
Other	30 (10.10%)
9. Why did I agreed to enroll my child in this study?	
Because I want doctors to help learn more about TB	43 (14.48%)
So my child might get better treatment	201 (67.68%)
So my family might benefit from other health services	17 (5.72%)
Unknown	2 (0.67%)
Other	34 (11.45%)
10. How long do I have to keep participating in the study?	
Until the study is completed	76 (25.59%)
I can withdraw at any time if I wish	109 (36.70%)
I can only withdraw if the clinic staff give me permission	90 (30.30%)
Unknown	1 (0.34%)
Other	21 (7.07%)

The informed consent data were examined in terms of the elements of informed consent as shown in Figure 9.

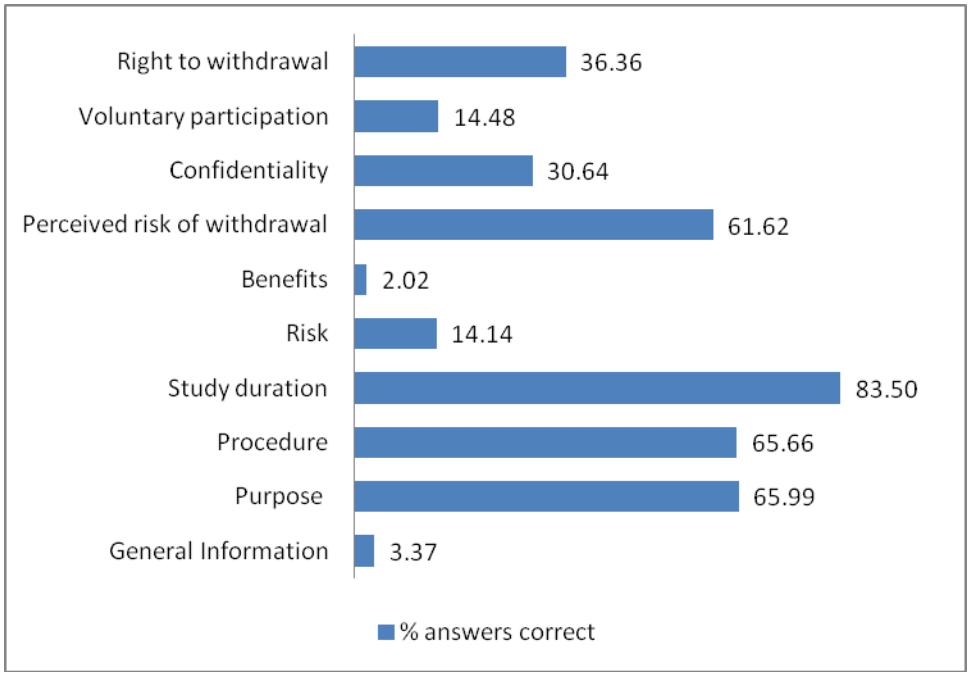

Figure 9. Percent answered correctly for each element of informed consent

The categories where most participants had correct answers were the following: perceived risk of withdrawal (61.62%), study duration (83.5%), procedure (65.66%), and purpose of the study (65.99%). In the categories, most answers were incorrect and only the following percent was answered correctly: voluntary participation (14.48%), confidentiality (30.64%), benefits (2.02%), risk (14.14%), and general information (3.37%). The benefits question had the least correct answers. In looking for correlation between the participants' duration in the study and the percent questions answered correctly, chi square analysis was performed for each informed consent comprehension question and resulted as show in Table 11. *P*-values were high in the analysis which suggests that there may not be a significant difference between the two groups (those had been in the study for < 2 yrs vs. ≥ 2 yrs) in their responses.

Table 11

Chi Square Analysis of % Correct Informed Consent Questions and Duration in the Study

% correct	Duration in the study		
Informed Consent Questions	< 2 yrs	≥ 2 yrs	*P* value
1. What was the reason you were asked to attend the clinic?			
CORRECT	9(3.03%)	1(0.34%)	0.7501
NOT CORRECT	266(89.56%)	21(7.07%)	
2. What is the purpose of the research study?			
CORRECT	177(59.60%)	17(5.72%)	0.2209
NOT CORRECT	98(33.00%)	5(1.68%)	
3. Why does the research staff want to enroll my baby into the research study?			
CORRECT	178(59.93%)	15(5.05%)	0.7438
NOT CORRECT	97(32.66%)	7(2.36%)	
4. What is the total amount of time my baby will be expected to participate in the study?			
CORRECT	226(76.09%)	21(7.07%)	0.1094
NOT CORRECT	49(16.50%)	1(0.34%)	
5. What is the most common risk involved when blood had been collected from my baby?			
CORRECT	41(13.80%)	1(0.34%)	0.1795
NOT CORRECT	234(78.79%)	21(7.07%)	
6. What benefits are available to me and my baby for participating in the study?			
CORRECT	6(2.02%)	0(0.00%)	0.4840
NOT CORRECT	269(90.57%)	22(7.41%)	
7. What if I didn't want my baby to participate in this study, I could withdraw			
CORRECT	168(56.57%)	15(5.05%)	0.5105
NOT CORRECT	107(36.03%)	7(2.36%)	
8. How will my baby's personal details will be kept secret?			
CORRECT	82(27.61%)	8(2.69%)	0.5203
NOT CORRECT	193(64.98%)	14(4.71%)	
9. Why did I agree to enroll my child in this study?			
CORRECT	38(12.79%)	5(1.68%)	0.2532
NOT CORRECT	237(79.80%)	17(5.72%)	
10. How long do I have to keep participating in the study?			
CORRECT	105(35.35%)	4(1.35%)	0.0611
NOT CORRECT	170(57.24%)	18(6.06%)	

In assessing for correlation between the experience of the staff administering consent and the percent questions answered correctly, chi square analysis was performed for each informed consent comprehension question and resulted as show in Table 12. *P*-values were high in the analysis which suggests that there may not be a significant difference between the two groups (those who were consented by staff with less than 5 years' experience vs. more than or equal to 5 years of experience) in their responses.

Table 12

Chi Square Analysis of % Correct Informed Consent Questions and Staff Experience

% correct Informed Consent Questions	Staff experience < 5 yrs	≥ 5 yrs	*P* value
1. What was the reason you were asked to attend the clinic?			
CORRECT	5(1.77%)	5(1.77%)	0.6445
NOT CORRECT	116(41.13%)	156(55.32%)	
2. What is the purpose of the research study?			
CORRECT	81(28.72%)	101(35.82%)	0.4646
NOT CORRECT	40(14.18%)	60(21.28%)	
3. Why does the research staff want to enroll my baby into the research study?			
CORRECT	76(26.95%)	104(36.88%)	0.7573
NOT CORRECT	45(15.96%)	57(20.21%)	
4. What is the total amount of time my baby will be expected to participate in the study?			
CORRECT	105(37.23%)	130(46.10%)	0.1786
NOT CORRECT	16(5.67%)	31(10.99%)	

(continued)

% correct	Staff experience		
Informed Consent Questions	< 5 yrs	≥ 5 yrs	*P* value
5. What is the most common risk involved when blood had been collected from my baby?			
CORRECT	18(6.38%)	20(7.09%)	0.5503
NOT CORRECT	103(36.52%)	141(50.00%)	
6. What benefits are available to me and my baby for participating in the study?			
CORRECT	5(1.77%)	1(0.35%)	0.0431
NOT CORRECT	116(41.13%)	160(56.74%)	
7. What if I didn't want my baby to participate in this study, I could withdraw			
CORRECT	68(24.11%)	106(37.59%)	0.0993
NOT CORRECT	53(18.79%)	55(19.50%)	
8. How will my baby's personal details be kept secret?			
CORRECT	36(12.77%)	46(16.31%)	0.8289
NOT CORRECT	85(30.14%)	115(40.78%)	
9. Why did I agreed to enroll my child in this study?			
CORRECT	22(7.80%)	19(6.74%)	0.1325
NOT CORRECT	99(35.11%)	142(50.35%)	
10. How long do I have to keep participating in the study?			
CORRECT	46(16.31%)	55(19.50%)	0.5040
NOT CORRECT	75(26.60%)	106(37.59%)	

Summary of All Results

According to the study demographics, all participants were women, the majority being less than 35 years of age, housewives with at least a primary level of education and they all have been participating in the study for less than 12 months. Research data were analyzed to answer the research questions as follows:

Research Question 1

Overall, the site's performance was in line with GCPs and with international standards since the site received an excellent score in the GCP checklist and there were no major or critical findings. The few minor findings that were observed had no or minimal impact on patient safety, data integrity or study outcome. The laboratory was the study functional area with the most findings and observations and the area of document management had the least number of findings from the GCP checklist.

Research Question 2

The historical trend comparing assessments, audits and monitoring activities since 2008 showed an upward trend in the level of compliance with GCP standards. The site showed a great deal of improvement as time went on so to have an excellent audit in the last evaluation performed in January 2012. The area of protocols and protocol amendments had the most observations and findings throughout the years and the aspects of monitoring and personnel & training had the least number of findings and observations. As mentioned in Chapter 3, every note of noncompliance or questionable alignment with GCP is considered either a finding or an observation. A finding may not

necessarily be negative; however, it is a point that ought to be noted by the research site. The difference between a finding and an observation is described in Chapter 3.

Research Question 3

The majority of study participants were contented in all aspects measuring satisfaction with their participation in the study. A high percentage of participants were satisfied in terms of participant-study staff interaction, informativeness of the materials provided during the study, physical infrastructure of the facilities, convenience, and accessibility of research study facilities, financial factors, procedures and tests, and flexibility of timing of procedures. Chi square analysis comparing the satisfaction level between different age groups (≤25 vs. > 25 years of age), between different levels of education (none vs. some education) and between different occupations (housewives vs. other) revealed no significant differences in the level of satisfaction.

Research Question 4

For informed consent comprehension, the results revealed that the components of the informed consent form most understood were related to perceived risk of withdrawal, study duration, procedure and purpose. The components that were least understood were right to withdrawal, voluntary participation, confidentiality, benefits, risk, and general information. The idea of therapeutic misconception resonated in the results since only 2.02% understood that there were no immediate benefits in participating in the research study and the rest thought that they were receiving some type of prophylaxis or treatment against TB. Chi square analysis comparing the informed consent comprehension between groups of different duration in the study (less than vs. greater than or equal to 2 years),

between participants consented by staff of different levels of experience (less than vs. greater than or equal to 5 years) revealed no significant difference in the level of comprehension.

In Chapter 5, conclusions and recommendations will be made from the data as presented. Discussion on the impact of the findings on the GCP checklist and the trending analysis will be deepened. Also, the issues that arose from the data on participant satisfaction and informed consent comprehension will be further explored.

Chapter 5: Summary, Conclusions, and Recommendations

Capacity building activities for the conduct of clinical research studies is occurring in developing countries. In Africa, the intent of building this capacity is to promote health research in the continent and to facilitate means for the highest standards of scientific research to ensure long-term health and wellbeing of its population. It is important to evaluate the impact of the capacity building activities so as to allow the researchers to learn from their own experiences, to generate evidence of transparency and accountability, as well as to reveal mistakes and offer paths for improvement.

This research was an evaluation study of capacity-building efforts for the conduct of clinical research in Kisumu, Kenya. It consisted of an assessment of the research site's compliance with GCP in performing an infant TB epidemiology study, an evaluation of the level of comprehension informed consent form and process as well as a measure of the level of satisfaction of the parents of the TB epidemiology study with their experience in the research. The study also involved a review and analysis of audits and monitoring findings from the site since 2008.

Summary of the Study

The study was conducted in two parts. First, the quality assurance aspect of the site and its conduct of an infant TB epidemiology study were assessed. Then, the 297 participants (mothers of the infants enrolled in the epidemiology) were involved in collecting data regarding their level of comprehension of the informed consent form as well as their level of satisfaction with the study procedures and study staff.

The mean age of the participants was 26.2 years of age and the median age was 25. The entire study sample was composed of females. More than 87% of them were 35 years old or younger and more than half (55.56%) were housewives, meaning that they did not have an occupation outside the home. About 88% of the participants had either none or only a primary school education and all of them (100%) had participated in the study.

According to the assessment through the GCP checklist, the site and the conduct of study were near excellent as they received a score of 94.24%. The quality assurance that was put in place functions well and the components of GCP compliance were satisfied. Although the assessment brought forth some minor findings, the level of compliance with the various components of GCP (i.e., document management, personnel and training, data management, protocol adherence, monitoring, CAPA, and laboratory) was satisfactory.

In the trending analysis that followed the GCP checklist audit, the study had made progress in terms of their compliance with GCP since their first audit in 2008. Overall, there was improvement throughout the areas of GCP. The number of observations, which are notes of noncompliance or questionable alignment with GCPs, decreased from 48 in 2008 to 12 in 2012 (73% decrease).

In general, the level of satisfaction of participants was high in all areas measured in terms of participant-study staff interaction, informativeness of the materials provided during the study, physical infrastructure of the facilities, convenience and accessibility of research study facilities, financial factors, procedures and tests, and flexibility of timing

of procedures. In correlating the level of satisfaction among different age groups (≤25 vs. > 25 years of age), different occupation (housewives vs. other), different level of education (none vs. some education), no statistically significant difference was revealed.

For the level of comprehension of the informed consent forms, the aspects of the informed consent form that were most understood were the ones concerning perceived risk of withdrawal, study duration, procedure, and purpose. Other aspects such as right to withdrawal, voluntary participation, confidentiality, benefits, risk, and general information were least understood. A correlation between groups of different duration in the study (less than vs. greater than or equal to 2 years), between participants consented by staff of different levels of experience (less than vs. greater than or equal to 5 years) showed that these groups did not significantly differ in their level of comprehension.

Conclusions and Discussions

Based the demographics of this study, the majority of the women were younger than 35: housewives with at least a primary level of education are the expected population for guardians of infants enrolled in an epidemiological study in the geographical area where study was conducted (Aeras, 2008). Since mothers are expected to be the ones taking their children to seek healthcare, the sample population for this evaluation study was exclusively female. Mothers are expected to be young and of childbearing age since the children enrolled in the epidemiology study were 2 years old and younger. As for the level of education, it was also as expected for a female population in eastern Africa.

The conclusions for this study are grouped according to the research questions that were posed in the study design.

Research Question 1

The KEMRI/CDC site in Kisumu, Kenya, conducting the infant TB epidemiology study can be deemed a suitable site in terms of performance. The assessment, through a GCP checklist, revealed an excellent score of 94.24%. The site had a few minor findings mainly related to the laboratory (46%), data management (23%), personnel and training (15%), monitoring (8%), and protocol and protocol amendments (8%). The minor findings are not consequential in terms of their impact on the integrity of the data, nor do they compromise the research participants' safety of the respect for their autonomy (FDA, 2007). Minor findings are those issues that represent a departure from the protocol or a stated ICH GCP guideline, regulation or SOP, with no or minimal impact on patient safety, data integrity or study outcome. They represent a divergence or noncompliance from the protocol or the procedures originally set for the conduct of the study. No major or critical findings were noted. Had they been present, itwould have signified major deficiencies with the site performance in terms of GCP compliance. Hence, this site can be considered more than adequate for conducting clinical research involving human participants.

This site functions in accordance to GCP as described in the guidance document from the ICH of Technical Requirements for Registration of Pharmaceuticals for Human Use. In this document, the ICH (2010) guidelines specify that it is required for a sponsor conducting clinical research to "implement and maintain a quality assurance and quality

control system for to ensure that the trials are conducted and data are generated in compliance with the protocol, GCP and the applicable regulatory requirements" (p. 13). With such an excellent score in the GCP checklist, the site is showing a high level of compliance with GCPs which leads to the conclusion that the site is committed to ensuring that they "play by the rules" and they do not take regulations and expectations of the guidelines lightly. According to the high level of GCP compliance observed at this site, the staff appreciates how failure to comply with the regulations and guidelines for clinical research can be hazardous to their success in terms of the data they generate and the ethics of conducting research with human participants.

The quality management system that the site has implemented facilitates their compliance with GCP Their quality assurance includes SOPs, a group of staff dedicated to QA, a tight system of documentation, trained staff, and a quality control system that anticipates issues and ensures that they are resolved in a manner that is least compromising to the study being conducted. This systemic approach to compliance reduces mistakes and minimizes nonconformance to specifications, standards, and expectations in the most cost effective and efficient manner.

The few minor findings that were revealed by the assessment are also an indication that the site is continuously operating and that mistakes are inevitable.

Research Question 2

It should be noted that although the research questions prescribes to analyze the historical trend of the site quality indicators for the past 2 years, it was decided to consider an assessment from 2008 as this document was the first inspection conducted to

assess compliance with GCP standards. Since the data collection of this dissertation was intended to be initiated in 2010, the 2008 report was originally meant to be taken into consideration during the data collection. Although data collection for trending analysis was initiated in January 2012, the analysis was extended to the 2008 report so to enhance the trend observed at the site.

Over all, according to the trending analysis, there was an upward trend in terms of compliance with GCP standards since the first assessment in 2008. The areas being observed, as indicated by GCP guidelines, were protocol adherence, laboratory, data management, document management, personnel and training, as well as monitoring. Since 2008, the site has made improvement in terms of total number of findings and observations with a decrease of 73%. Protocol adherence is the area most improved as it decreased the number of observation and findings from 21 in 2008 to one in 2012 (Table 9). All findings and observations are issues identified for noncompliance or questionable alignment with GCPs.

Before and during the site implementation of the infant TB data, training activities were conducted at the site. These training events were aiming to develop a cadre of professionals capable of conducting clinical research studies compliant with ethical and regulatory standards. The training was delivered in different forms such as face-to-face training, e-learning, “learning by doing” activities, and mentoring. The topics covered were GCP, GLP, research ethics, epidemiology, biostatistics, infectious disease, and other areas related to the conduct of community-based TB vaccine research in accordance with international standards. The impact of this training was revealed through the upward

trending in improvements with GCP compliance throughout the years. The decrease number of observations showed that level of site performance is increasing.

The higher levels of GCP compliance may translate to the improvement in the quality of the TB epidemiology study in terms of data integrity and protection of the rights of the study participants. Since the site is now conducting clinical trials intended for submission to the U.S. FDA, they are susceptible to an inspection by a stringent regulatory authority. With this level of compliance, it is likely that the preparation for such an inspection would be minimal since the systems and the ground work has been established to promote success if such scrutiny was to occur at the site (Axson, 2007).

In a study conducted by the Tuberculosis Trials Consortium (TBTC, 2007), an evaluation of the QA through the use of quality indicators was performed. As in this dissertation study, TBTC found that collecting quality assurance data throughout a study performance promoted the improvement in terms of quality assurance. In their study, the TBTC collected performance data real-time and compared results throughout the 28 sites involved in their study. Results from their frequent assessments were fed into a corrective action plan that allowed the site to learn and improve as time went by (Sandman et al., 2006). The TBTC study supports the idea that continuous QA checks improve a site's compliance with GCP and other standards. This improvement aspect is also evident in the Kenya site evaluated in this dissertation as, through time, a number of QA checks have propelled the site to an excellent level of compliance. As in the TBTC study, the findings and observations resulting from each quality check were subjected to a corrective action that allowed for mistakes to be corrected and the correct path to be established.

Research Question 3

As shown in Figure 2, the assessment of participant's satisfaction was based on a multifactorial approach that took into account various aspects that impact how content the participant feels with her involvement in the study. The factors are related to the participants' characteristics such as perceived efficacy, the various studies' aspects such as enrollment process, documentation to be read, and study procedures. The clinical setting itself (i.e., transportation, scheduling) was also expected to play a role in the part in the level the satisfaction. All of these aspects fed into the relationship between the research participants and research staff, which ultimately led to the degree of participants' satisfaction.

In this evaluation study, the level of satisfaction was consistently high throughout the various elements of satisfaction that were assessed. The majority of participants (no less than 70%) were always satisfied in terms of general satisfaction, technical quality, interpersonal manners, communication, financial aspects, accessibility, and convenience (Table 5). In a study conducted in 25 countries around the globe, Lavoski et al. (2009) sought research participants' opinions in regards to the medical and nonmedical benefits of participating in an HIV treatment study. As in this evaluation study, the participants themselves were given the opportunity to express their contentment with various aspects of the study. Lavoski et al. (2009) found that the results of their study were valuable in helping the researchers understand how to better design studies with the community's best interests in mind.

Chi square analysis comparing the satisfaction level between different age groups (≤25 vs. > 25 years of age), between different levels of education (none vs. some education), and between different occupations (housewives vs. other) revealed no significant difference in the level of satisfaction between the groups compared as shown by the high *p* values. Specifically, the data on each satisfaction questions were analyzed to see if, for example in the different age groups, the younger group had a statistically significant different level of satisfaction than the older age group. The high *p* values lead to the conclusion that all participants were satisfied in the same manner regardless of age, education level, or occupation. In a study conducted by Hunter et al. (2009), patient satisfaction in retail health clinics was assessed and the level of satisfaction was compared in terms of ethnicity and socioeconomic status. Hunter et al. also concluded that the level of satisfaction was "homogeneous" throughout the groups. It should be noted that the study population in the Hunter et al. study is different from those in this evaluation since the Hunter et al. study was conducted in a community in Arizona in the United States as opposed to the rural Kenyan population of this evaluation study. However, it may be possible that satisfaction in the health arena may also be consistent as the respondents are dealing with a valued human need which is the need for good health.

Research Question 4

Ethical considerations are the cornerstone of clinical research involving human participants. It is essential to respect the research volunteer's right to autonomy. Hence, the process of informed consent comprises of not only providing information on the research but also comprehension of the various elements of study (purpose, risk, benefits,

procedures, and treatment) and that of the informed consent process itself (confidentiality, voluntariness of participation, and such). In this evaluation study, questions were posed in regards to the informed consent form and process and the correct answer is considered the answer that I expected. The most understood aspects of the informed consent process were related to perceived risk of withdrawal, study duration, procedure, and purpose (Table 10). The least understood aspects of the informed consent process were related to right to withdrawal, voluntary participation, confidentiality, benefits, risk, and general information (Table 10).

Minnies et al. et al. (2008) analyzed recall and understanding of informed consent in a mother with children enrolled in a TB epidemiology study in South Africa. Due to the difference in study design between the Minnies et al. et al. study and this evaluation study, a direct comparison could not be made. However, some of the results were able to be compared due to the similarity in some of the questions that were posed. For example, in the Minnies et al. et al. study, 51.3% answered correctly on the questions regarding the benefits of study participation (Minnies et al. et al., 2008) while only 2.02 % correctly answer a similar question in this evaluation study. This difference may be inherent to the nature of the study population. In the Minnies et al. et al. study, the demographics were different as the majority (76.7%) at least reached secondary education (Minnies et al., 2008), while in the current evaluation study only 10.44 % reached the same level of education (Table 3). There were also divergent results between this evaluation and the Minnies et al. study in regards to risks of being involved in the study. In the Minnies et al. study, 79.2% answered correctly in regards to the risk of study

participation (Minnies et al., 2008) while, in this evaluation study, only 14.14% answered a similar question correctly. The difference in the level of education may explain the difference in the level of comprehension results between the two studies. Minnies et al. also mentioned that his results may have been influenced by the fact that the population in South Africa may have a heightened aware of their health rights in regards to access to healthcare, freedom of choice and freedom from harm. This high level of awareness may be due the abusive past that the people of South Africa endured such as Apartheid. Having experienced such harsh historical conditions may have made the South Africa population more alert when their rights were concerned. It is thus possible that the women in South Africa were paying more attention and were more analytical during the informed consent process so to protect themselves from any potential abuse.

The notion of therapeutic misconception occurs in clinical research when research participants misconstrue the study research procedures as provision of healthcare or treatment for the condition being studied. In other words, the research participants failed to understand that the procedures of the research are not particularly tailored to treat their own individual conditions and that due to research characteristics such as randomization; they may not automatically obtain treatment from participating in a research study. Falagas et al. (2009) conducted a systematic literature review in order to evaluate the "degree of patient's understanding of several aspects of the informed consent process for surgery and clinical research (p. 198). Falagas et al found that in one of the studies reviewed, as many as 85% of research participants gave the impression of expecting to be

fully treated as a result of participating in the trial. The notion of therapeutic misconception was apparent.

In this evaluation study, the idea of therapeutic misconception started emerging in the question regarding the reason for being asked to attend the clinic. Only 3.37% of the participants answered correctly that they were asked to attend the clinic so their baby could participate in a research study. Instead, 74.75% incorrectly answered that they were asked to attend the clinic so that their baby can receive routine care (Figure 6). The notion of therapeutic misconception continued to appear in later questions. When the participants were asked about the benefits available to them and their baby for participating in the study, only 2.02% correctly answered that there were no immediate benefits while 30.30% and 28.96% answered that their child will be protected against TB and that their child will receive better treatment against TB, respectively (Figure 7). Finally, the perception of therapeutic misconception was still apparent when, as shown in Figure 8, only 14.48% answered correctly they wanted to help doctors learn more about TB while 67.68% answered that that they thought their child would get better treatment. The results from these 3 questions tend to follow the same theme where the mothers of the infants participating in the TB study are misconceiving their child's participation in the TB epidemiology study as in means for obtaining treatment from the clinic. After an adequate informed consent process, the study participants are expected to be able to recognize that they have the right to discontinue their involvement in the study whenever they wish without worrying about losing any benefits. This point is one of the basic elements of the informed consent in research with human participants. Since most women

did not answer the “right to withdrawal” question correctly, there was likely a disconnect in their understanding of their commitment to the study. The same thoughts may apply for the reasons for the incorrect responses in the “voluntary participation” questions. Respecting the participant’s autonomy is rooted in her voluntary participation in the study. It is critical that the participant understand that she is participating in the study out of her own volition. The large number of incorrect answers of these questions suggests that the participants did not completely grasp the notions imparted during the informed consent process.

The results of this evaluation are congruent with those found by Falagas et al. in terms of the evidence that the research participants seem to believe that they will received better healthcare or treatment for taking part in a research study. This notion is dangerous as it shows that clinical care may not always be distinguished from clinical research. This confusion may due to the fact that research is being conducted in clinical settings although it is pure an academic activity. The participants may be requested to participate in research by the same medical staff that provides them with their usual healthcare. It is thus the responsibility of research staff to ensure that the research participants are aware that the intentions of clinical research are purely investigative and that they impose discomforts or risks for harm that are necessarily not rewarded by personal diagnostic or therapeutic benefits such as in clinical care.

An attempt was made to differentiate the level of comprehension between different groups in the participant’s population. Chi square analyses comparing the informed consent comprehension between groups of different duration in the study (less

than vs. greater than or equal to 2 years), between participants consented by staff of different levels of experience (less than vs. greater than or equal to 5 years) revealed no significant difference in the level of comprehension as p-values were high from the analysis. It is possible that, as in the participant satisfaction results, the level of informed consent comprehension was homogeneous between those participants who had remained in the study for less than 2 years and those that had participated in the for 2 years or more.

Recommendations

Capacity building for health programs and research is currently conducted by various organizations and institutions in Africa. While existing efforts are recognized, it is important to highlight that there is still a need for the promotion of the creation of self-sustaining institutions of excellence capable of initiating and carrying out high quality health research in Africa. The capacity that is being built should be able to translate research products into policy and practice through better integrated approaches of capacity building at individual, institutional and system levels. Opportunities for capacity building should focus on opening up discussions avenues for African researchers to share ideas among themselves and around the globe. The discussions about capacity building for heath research in Africa should be led by African researchers as they are most in tune with their own needs. At the same time any capacity building projects should pull in African national governments and civil societies (such as nongovernmental organizations and community-based organizations) in order to foster an environment that is conducive to sustainable health research growth.

The participants had a high level of satisfaction in regards to their involvement in TB epidemiology study. A follow-up qualitative study could be conducted to address the specific needs of the participants. Probing questions would be asked about the informed consent process in terms of how they understood each element of informed consent such as goal and purpose of the study, confidentiality, voluntary participation and right to withdrawal. The results of such a study may be useful in formulating informed consent documents so to make them comprehensible for this particular population. The next study should focus on the participants' experiences and expectations using a focus group format. This methodology will allow for conversation among participants which will elicit information that shows the community's perspective on participation in research studies. This follow-up study could also include individuals in the community that have never participated in research so to compare their point of view to those who are veteran research participants.

The notion of therapeutic misconception was recurring throughout the results of informed consent comprehension portion of this study. It is important to highlight the fact that recruiting research participants in clinical settings lends to confusing the goals of clinical research (which are to investigate different products or different ideas) to those of clinical care (which are to treat and provide care for health of individuals). In developing countries, the lines between clinical research and clinical practice can be blurred. Future studies should focus on understanding how misplaced trust of research participants can affect their voluntariness of participation in research studies and how this can affect the respect of participants' rights.

Implications for Social Change

One of the most significant social changes impacted by this evaluation study is related to the inefficiency of the informed consent process as it is currently being handled at the Kenya site. Although this site is perform successfully in terms of GCP audit, trend analysis and participant satisfaction, the informed consent comprehension data suggests that research participants do not fully understand the benefits of the study. This issue is not unique to the Kisumu research site. The notion of therapeutic misconception is common in Africa (Oduro et al., 2008). This evaluation study provides additional evidence and confirms that the issue should not be neglected. This data ought to lead the global research community in a quest for better methods of ensuring genuine informed consent in populations of developing countries. In these regions of the world, cultural and language obstacles may prohibit adequate comprehension of informed consent when administered as indicated in the current international guidelines and regulations.

It is doubtful that the consent provided by the research participants at the Kisimu site is truly informed and genuine. For this site, the informed consent administration is being conducted as a single event while it should take on the form of a process which starts at the time of recruitment and systematically continues for the duration of the study up to study close-out. Such a reiterative process will lessen the risk of misunderstanding and enhance the chances of genuine and true informed consent.

As the influx of clinical research studies in Africa increases, the need for high quality research sites becomes urgent. This evaluation study contributes to the growing body of knowledge showing that applying stringent quality management systems, in

resource limited environments, does in fact result in facilities, staff and an environment that is capable of conducting clinical research studies that comply with international standards such as GCP. Although the Kisumu site exists in an environment that does not benefit from resources of similar sites in the developed world, the Kisumu site was able to show improvement in quality assurance of clinical research which compares to experienced sites in affluent countries such as the United States of America.

Looking at the quality of clinical research through the eyes of participants provides for an unexplored approach for quality improvement. Research participants can take an active role in the conduct of research. Their opinion can be a determinant factor in how the study is conducted as opposed to merely being passive participants used solely for data collection. Giving the participants an active role adds to the respect for their dignity, confidence in the intent of researchers and that of the study itself.

The African continent will only be able to address its population's health problems once strong health research systems are in place. The Kisumu clinical research site is an example of a successful capacity building effort for clinical research in a resource limited environment. This site was able to capitalize on investments by upholding leadership, human and physical infrastructure, ethical practices, as well as relationships between the research staff and study participants. Nevertheless, there are multiple other existing and potential sites that will only benefit from the same investments and successes when capacity building efforts are planned with QA systems, community involvement, as well as political will of local governments.

Summary

Investing in capacity building for health research in Africa can be beneficial as shown in the Kisimu site in Kenya. This site is conducting clinical research with the same stringency as any high performing research site in affluent countries. This success can be attributed to the quality management systems implemented. The participants involved in the TB epidemiology study are content with their involvement in the study. Requiring the participants' opinion adds to quality improvement of the research study and of the site as a whole. Additional studies may be conducted to further the understanding of participants in order to determine how to best ensure continuity of that satisfaction. Although the study participants understood some aspects of informed consent, the assessment pointed to the possibility of therapeutic misconception being present in the study population. The confusion between clinical research and clinical care ought to be researched further in order to best address the problem. Social change was effected in this study through the self-reliance that the site possesses now as well as through the research participants' confidence for their involvement in the study.

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Appendix A: Management of Data for Study

Table 13

Management of Data on Participant Satisfaction

	Participant Satisfaction Aspect % (N)				
	Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
General Satisfaction					
The attention that I receive from the study staff while we interact is just about perfect					
I am dissatisfied with some things about the interactions that I have with study staff					
Technical Quality					
I think the study staff and their facilities have everything needed for the study					
Sometimes study staff make me wonder if the study is worthwhile					
When study staff examine me, they are careful to check that I am satisfied					
I have some doubts about the need for this study in the community					
Sometimes study staff use medical words without explaining					
Interpersonal Manners					
Study staff are too businesslike and impersonal toward me					
Study staff treat me in a friendly and courteous manner					
Study staff sometimes hurry too much during the study visits					
Study Staff usually spend plenty of time with me					

(continued)

	Participant Satisfaction Aspect % (N)				
	Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
Communication					
Study staff is good about explaining reasons for the research study					
Study staff sometimes ignore what I tell them					
Financial Aspects					
I feel confident that I can complete all study visits without spending too much money					
I have to spend more than I can afford to be part of this study					
Accessibility and Convenience					
The study visit hours are convenient for me					
I have easy access to study staff when I need to					
I find it hard to reach the study staff right away when I need to					

Table 14

Management of Data on Characteristics of Study Participants

Characteristics	Category	% (n)
Age	< 25	
	25-35	
	> 35	
Gender	Male	
	Female	
Occupation	Subsistence farming	
	Fishing	
	Salaried worker (e.g. teacher, nurse, office)	
	Small business (e.g. sell maize)	
	Business owner (e.g. kiosk)	
	Skilled labor (e.g. carpenter, tailor)	
	Unskilled labor (e.g. construction)	
	Commercial farming	
	Not working	
	Other	
Level of Education	None	
	Primary	
	Secondary	
	Post secondary	
Years of Education	None	
	1-9	
	>9	
Duration of participation in the study	< 6 months	
	6-12 months	
	12-18 months	
	18-24 months	
	> 24 months	
Previous personal or family experience with clinical research	yes	
	no	

Table 15

Management of Data on Relation between Participants Characteristics and Main Satisfaction Aspects

Relation Participants Characteristics and Main Satisfaction Items			
	Age group	Formal Education	Occupation
Satisfaction Item	< 25 vs. > 26	None vs. some	Farming vs. other
The attention that I receive from the study staff while we interact is just about perfect			
% Strongly Agree			
% Agree			
% Uncertain			
% disagree			
% Strongly disagree			
I am dissatisfied with some things about the interactions that I have with study staff			
% Strongly Agree			
% Agree			
% Uncertain			
% disagree			
% Strongly disagree			
I think the study staff and their facilities have everything needed for the study			
% Strongly Agree			
% Agree			
% Uncertain			
% disagree			
% Strongly disagree			
Sometimes study staff make me wonder if the study is worthwhile			
% Strongly Agree			
% Agree			
% Uncertain			
% disagree			
% Strongly disagree			

(continued)

Relation Participants Characteristics and Main Satisfaction Items

Satisfaction Item	Age group < 25 vs. > 26	Formal Education None vs. some	Occupation Farming vs. other
When study staff examine me, they are careful to check that I am satisfied			
% Strongly Agree			
% Agree			
% Uncertain			
% disagree			
% Strongly disagree			
I have some doubts about the need for this study in the community			
% Strongly Agree			
% Agree			
% Uncertain			
% disagree			
% Strongly disagree			
Sometimes study staff use medical words without explaining			
% Strongly Agree			
% Agree			
% Uncertain			
% disagree			
% Strongly disagree			
Study staff are too businesslike and impersonal toward me			
% Strongly Agree			
% Agree			
% Uncertain			
% disagree			
% Strongly disagree			

(continued)

Relation Participants Characteristics and Main Satisfaction Items

Satisfaction Item	Age group < 25 vs. > 26	Formal Education None vs. some	Occupation Farming vs. other
Study staff treat me in a friendly and courteous manner			
% Strongly Agree			
% Agree			
% Uncertain			
% disagree			
% Strongly disagree			
Study staff sometimes hurry too much during the study visits			
% Strongly Agree			
% Agree			
% Uncertain			
% disagree			
% Strongly disagree			
Study Staff usually spend plenty of time with me			
% Strongly Agree			
% Agree			
% Uncertain			
% disagree			
% Strongly disagree			
Study staff is good about explaining reasons for the research study			
% Strongly Agree			
% Agree			
% Uncertain			
% disagree			
% Strongly disagree			
Study staff sometimes ignore what I tell them			
% Strongly Agree			
% Agree			
% Uncertain			
% disagree			
% Strongly disagree			

(continued)

Relation Participants Characteristics and Main Satisfaction Items

Satisfaction Item	Age group < 25 vs. > 26	Formal Education None vs. some	Occupation Farming vs. other
I feel confident that I can complete all study visits without spending too much money			
% Strongly Agree			
% Agree			
% Uncertain			
% disagree			
% Strongly disagree			
I have to spend more than I can afford to be part of this study			
% Strongly Agree			
% Agree			
% Uncertain			
% disagree			
% Strongly disagree			
The study visit hours are convenient for me			
% Strongly Agree			
% Agree			
% Uncertain			
% disagree			
% Strongly disagree			
I have easy access to study staff when I need to			
% Strongly Agree			
% Agree			
% Uncertain			
% disagree			
% Strongly disagree			
I find it hard to reach the study staff right away when I need to			
% Strongly Agree			
% Agree			
% Uncertain			
% disagree			

% Strongly disagree

Table 16

Management of Data on Overall Informed Consent

Informed Consent Question	**% correct (n)**
1. What was the reason you were asked to attend the clinic?	
2. What is the purpose of the research study?	
3. Why does the research staff want to enroll my baby into the research study?	
4. What is the total amount of time my baby will be expected to participate in the study?	
5. What is the most common risk involved when blood had been collected from my baby?	
6. What benefits are available to me and my baby for participating in the study?	
7. What if I didn't want my baby to participate in this study, I could withdraw	
8. How will my baby's personal details be kept secret?	
9. Why did I agreed to enroll my child in this study?	
10. How long do I have to keep participating in the study?	

Table 17

Management of Data on Relation between Duration of Participation and Experience with Research and Informed Consent: % Correct Answers

	% Correct
Informed Consent Questions	**Experience of staff administering consent < 2 yrs vs. > 2 yr**
1. What was the reason you were asked to attend the clinic?	
2. What is the purpose of the research study?	
3. Why does the research staff want to enroll my baby into the research study?	
4. What is the total amount of time my baby will be expected to participate in the study?	
5. What is the most common risk involved when blood had been collected from my baby?	
6. What benefits are available to me and my baby for participating in the study?	
7. What if I didn't want my baby to participate in this study, I could withdraw	
8. How will my baby's personal details be kept secret?	
9. Why did I agree to enroll my child in this study?	
10. How long do I have to keep participating in the study?	

Appendix B: Curriculum Vitae

Sylvie Anne KWEDI, MSc., MPH

DATE [redacted]

Born on [redacted]
Marital Status : [redacted]

CONTACT INFORMATION

Business Address: [redacted]

Permanent Address: [redacted]

LANGUAGES English (spoken and written)
French (spoken and written)

Experience includes:

- **Founder and President of CLEAR, Inc which is a capacity building firm for clinical research and health programs working with the Cameroon Ministry of Health, "Chantal Biya" International Reference Centre For Research on HIV and AIDS Prevention and Management (CIRCB), Central Africa Network on Tuberculosis, HIV/AIDS and Malaria (CANTAM)**
- **Deputy Director for Field Site Development and Epidemiology at Aeras Global TB Vaccine Foundation.**
- **Setting up and managing field sites for conducting clinical trials and epidemiology studies in South Africa, Kenya, Uganda, Mozambique, Cambodia and India.**
- **More than 10 years of Project Management in new drug/vaccine development and Public Health**
- **Project Manager at the American Red Cross.**
- **Speaking appearances at the Global Health Council Policy Series in Washington, DC**

EDUCATION:

Walden University, Baltimore, MD
MD
PhD Public Health
Community Health Promotion and Education
Anticipated August 2012

Johns Hopkins University, Baltimore,

MPH International Health
May 2008

Johns Hopkins University, Baltimore, MD
M.Sc. in Biotechnology
Concentration in Biotechnology Enterprise
May 2000

Gettysburg College, Gettysburg, PA
B.S. in Biology; Minor in Chemistry
May 1994

CERTIFICATIONS

Vaccine Science and Policy

Johns Hopkins Bloomberg School of Public Health
May 2008

Project Management Professional
(PMP)

Project Management Institute
Since September 2004

Clinical Vaccine Trials and Good Clinical Practice
Johns Hopkins Bloomberg School of Public Health
October 2006

PROFESSIONAL EXPERIENCE:

Jan 2010 to Present — Founder and President
CLEAR, Inc. (Capacity for Leadership Excellence and Research)

- Provide consultancy for institutions aiming to build operational capacity of entities with health programs and research activities in resource limited settings in developing countries especially in Africa and specializing in building major systems and departments in the areas of program set-up and management, clinical laboratory design and management, regulatory compliance and quality assurance, program management, data management and information technology, as well as staff development and training. Current contracts include the Cameroon Ministry of Health, "Chantal Biya" International Reference Centre For Research on HIV and AIDS Prevention and Management, Central Africa Network on Tuberculosis, HIV/AIDS and Malaria (CANTAM)
- Built and led the design, development, launch and operation of the start-up corporation for capacity development for research and health programs in resource limited settings.
- Responsible for administration, planning and direction to company activities to obtain optimum efficiency, economy of operations, and maximize profits
- Directs and coordinates promotion of products or services performed to develop new markets, increase share of market, and obtain competitive position in industry.

May 2007 to Dec 2009 — Deputy Director, Site Development and Epidemiology
Aeras Global TB Vaccine Foundation

- Responsible for Setting up and managing field sites for conducting clinical trials and epidemiology studies in South Africa, Kenya, Uganda, Mozambique, Cambodia and India..
- Supervised the site development group with a staff of 11, 4 of which are direct reports and performed performance reviews of direct reports.
- Assisted in the identification, evaluation and selection of clinical trial sites including international field sites
- Managed field site development activities to ensure preparedness of sites for large GCP-compliant community-based Phase III clinical trials.
- Participated in networking with various collaborators on the development of international field sites for evaluation of TB vaccine candidates.
- Provided support as needed for regulatory activities, such as IND Annual Reports, and BLA submission materials related to assigned projects.

Feb 2005 to May 2007 — Senior Manager, Epidemiology and Field Sites
Aeras Global TB Vaccine Foundation

- Provided oversight and management during all phases of project to develop community-based clinical research capacity in South Africa and India.
- Generated study protocols and along with data collection forms and other source documents, submitted them for review to local and international Institutional Review Boards, collaborate with study staff in setting up databases, coordinate study monitoring activities and data review.
- Reviewed project technical status and makes decisions to achieve project goals.
- Identified contract needs, generated ensuing solicitations such as request for proposals (RFP), prepared contracts as determined by project team and provided contract administration for established contracts.
- Provided technical direction to the organization in planning, scheduling and assignment of work and resources per project management methodologies.

Mar 2004 to Feb 2005 Senior Project Planner
Aeras Global TB Vaccine Foundation

- Managed the cross functional aspects of tuberculosis vaccine development projects from vaccine discovery through preclinical manufacturing, Investigational New Drug (IND) submissions to FDA approval and clinical trials.
- Developed and maintain vaccine development Product Development Plans (PDP) to include the description of the scope, costs, resources and performance baselines

Dec 2001 to Mar 2004 Project Manager
American Red Cross, Gaithersburg, MD

- For a government contract, manage the cross functional aspects of bringing plasma based products from preclinical manufacturing through Investigational New Drug (IND) and Biological License Application (BLA) submissions to FDA approval and launch.
- Conduct meeting and teleconferences between the FDA and the American Red Cross through the FDA approval process.
- Coordinate writing and review of regulatory fillings with process owners.

Jun 1999 to Dec 2001 Project Manager
BioReliance, Rockville, MD

- Responsible for technical management of various projects for a Contract Research Organization that provides preclinical and contract manufacturing services.
- Lead project teams and collaborate on business development goals.
- Generate proposals for various projects such as product development, validation and technology transfer.
- Conduct on-site technical and quality audits by clients.

Dec 1997 to May 1999 Senior Study Systems Coordinator
BioReliance, Rockville, MD

- Provided project management support to ensure cost, schedule and quality technical performance on assay studies.
- Coordinating long term stability projects by planning and executing allocation, collection and transfer of samples to the laboratory

Jan 1995 to Dec 1997 Radiology Administrative Assistant
Clinical Radiologists, , Silver Spring, MD

- Provided patient registration for radiology exams.
- Inputted patient information into computerized billing system.
- Accomplished scheduling for various radiology procedures.

Jun 1992 to May 1994 Laboratory Assistant
Biology Department, Gettysburg College, Gettysburg, PA

- Performed an UV assay for determining the protein concentration of a protein/peptide sample by quantifying the sample's light absorption using a HP Spectrophotometer.

ACTIVE GRANTS

Project Manager for European Developing Countries Clinical Trials Partnership (EDCTP). Project Code: CB.2011.41302.021 "Documenting existing structures, processes, resources and needs of research ethics committees in Cameroon and implementing a training intervention to strengthen ethical review capacity for participating committees". 2012-2013; Total cost 49 445 €**.**

PUBLICATIONS

Kwedi, S.A.(2012). Quality Assurance And Other Critical Infrastructures For The Conduct Of Clinical Trials In Resource Limited Settings: Threats and Opportunities. *Accepted for publication by the Drug Information Association Global Forum.*

ORAL PRESENTATIONS AT INTERNATIONAL CONFERENCES/MEETINGS

Kwedi, SA. Capacity Building for Regulatory Oversight for Vaccine Clinical Trials in Sub-Saharan Africa. 4th Elsevier Global Vaccine Congress. September 2010. Vienna. AUSTRIA.

Kwedi, SA., Scott CP. Assessment of GCP Compliance of Clinical Research Sites in Developing Countries to Determine Target Areas for Capacity Building. 5th European and Developing Countries Clinical Trial partnership. October 2009. Arusha, TANZANIA

Kwedi, SA. The Impact of Weak Health Systems on the Health Care Worker Crisis. Global Health Council Policy Series. May 2008. Washington, DC. USA

SERVICE TO THE SCIENTIFIC COMMUNITY AND TO OTHER ORGANIZATIONS

Expert panel. Global Health Technologies Coalition. First annual Congressional briefing. April 2010. Washington, DC. USA

Member, Cameroon National Ethics Committee, Yaoundé, Cameroon

Member, Cameroon Bioethics Initiative, Yaoundé, Cameroon