A study of trial participants' understanding and attitudes towards randomisation, double-blinding and placebo use, and a pilot intervention in a microbicide trial in Malawi

By

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DECLARATION

I declare that the thesis titled "A study of trial participants' understanding and attitudes towards randomisation, double-blinding and placebo use, and a pilot intervention in a microbicide trial in Malawi" which I hereby submit for the degree of Doctor of Philosophy in Human Sciences at the University of KwaZulu-Natal, is my own work and has not been submitted for any previous degree at this or any other tertiary institution.

DATE November 2010

Signature : 

Name :Paul Maduba Ndebele

DEDICATION

This work is dedicated to the memory of my father, Reverend Bishop Joram Sokesi Ndebele who would have wanted to witness the fruits of his hard work and encouragement.

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ABSTRACT

This empirical study was aimed at assessing trial participants' understanding of randomisation, double blinding and placebo use as well as investigating their attitudes towards the three procedures. The study was conducted within the HPTN035 microbicide trial that was being conducted in Blantyre and Lilongwe in Malawi among other sites. The study was descriptive in nature and used a combination of qualitative and quantitative methods which included review of study documents, in-depth interviews with study staff, structured interviews with a sample of 203 participants and two focus group discussions with 18 microbicide trial participants. Overall, more than half of participants were categorised as having lower levels of understanding on the concepts under study. The study also established that the majority of participants had negative attitudes towards the three procedures. Based on these findings, a pilot intervention was designed aimed at improving understanding. The pilot intervention consisted of an information session which was delivered with the assistance of a PowerPoint. During the session, the three terms were explained using a story based on the growing of crops, as Malawi is an agricultural society. The intervention phase was delivered using a sample of 36 low scorers who were randomly assigned to the intervention and non-intervention arms. An assessment after the intervention suggested that the intervention was useful in improving understanding of the three procedures. The findings provide some evidence that research participants can understand research procedures if the procedures are explained in user-friendly terms and if information concerning their justification and personal implications is provided. The findings further suggest that the intervention was useful in changing participants' attitudes towards randomisation and double blinding. The intervention did not change attitudes towards placebo use in a statistically significant way. Theoretical and practical recommendations, as well as suggestions for further research were recommended.

Key words

Comprehension, informed consent, understanding, randomisation, double blinding, intervention, placebo, microbicide trial, trial participant

ABBREVIATIONS AND ACRONYMS

CAB	Community Advisory Board
CI	Confidence interval
CIOMS	Council for International Organizations of Medical Sciences
COMREC	College of Medicine Research Ethics Committee
DHS	Demographic Health Survey
DSMB	Data, Safety and Monitoring Board
ESC	Evaluation to Sign Consent
FDA	Food and Drugs Administration
FGD	Focus Group Discussion
GCP	Good Clinical Practice
HAART	Highly active anti retroviral therapy
HIV/AIDS	Human Immunodeficiency Virus/ Acquired Immuno-Deficiency Syndrome
HPTN	HIV Prevention Trials Network
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
IRB	Institutional Review Board
PCT	Placebo controlled Trials
PMPB	Pharmacy Medicines and Poisons Board
QuIC	Quality of informed consent
NHSRC	National Health Sciences Research Committee
NIH	National Institutes of Health (USA)
RCT	Randomised Controlled Trial

REC	Research Ethics Committee (same as IRB).
SARETI	South African Research Ethics Training Initiative
SPSS	Statistical Package for the Social Sciences
SOPs	Standard Operating Procedures
SRF	Scholars Rescue Fund
STD	Sexually Transmitted Disease
STI	Sexually Transmitted Infection
TB	Tuberculosis
UB	University of Botswana
UKZN	University of KwaZulu-Natal
UNIMA	University of Malawi
UK	United Kingdom
UNC	University of North Carolina
USA	United States of America
US	United States
WHO	World Health Organisation
WMA	World Medical Assembly

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CHAPTER 1

INTRODUCTION

1.0 BACKGROUND

The present study was motivated by the challenges that the present researcher faced in training research staff members from various clinical trials in Zimbabwe about how they explain clinical trial procedures to potential trial participants. In conducting site visits at various clinical trial sites in Zimbabwe and Malawi, the researcher also noted that there appeared to be some serious gaps in trial participants' knowledge about the trials in which they were participating. These observations stimulated a literature search which yielded several studies conducted in various countries which identified challenges in the understanding of clinical trial procedures by trial participants. This subsequently elicited questions such as the following:

- What information is provided to trial participants and how is the information provided?
- What could be missing in those interventions aimed at testing and improving understanding that have been tested in other studies?
- Can an intervention based on simple examples from daily life work in improving participants' understanding of clinical trial procedures?

These and several other questions led to the conceptualisation of this study.

The literature suggested that randomisation, blinding and placebo use seemed to be difficult concepts to understand. These three concepts are very critical in clinical trials as they form important aspects of the science of clinical trials. It could be assumed that the procedures of randomisation and double-blinding and the use of placebos in research are simple ones. This

assumption of simplicity hides the many factors and controversies surrounding these procedures, including trial participants' understanding of and attitudes towards the use of these procedures in research. While much has been written about randomisation, double-blinding and the use of placebos in research, there is still uncertainty about how these three procedures are understood, especially in an African setting. Understanding of the three concepts is compounded by the fact that research and routine care are often conducted under the same roof by the same professionals namely nurses, doctors and others (Brody & Miller, 2003).

Several authors have reported or discussed some difficulties that research participants face in understanding the three concepts of randomisation, double blinding and placebo (Brody & Miller, 2003; Elbourne, Snowdon & Garcia, 1997; Featherstone & Donovan, 1998; Kerr *et al*., 2006; Pace *et al*., 2005; Pucci, Belardinelli, Signorino, & Angeleri, 1999; Stead, Eadie, Gordon & Angus, 2004; Yuval *et al*., 2000). A contributing factor might be what has been labeled the therapeutic misconception. This is the phenomenon among research participants of confusing research with therapy (Appelbaum, 2002; Appelbaum Roth, Lidz, Benson & Winslade, 1987). Several studies have revealed that some trial participants confuse research with routine care (Belkin, 2006; Daugherty, 1999; Emanuel & Miller, 2001; Freedman, 1990; Freedman, Fuks & Weijer, 1992; Kimmelman, 2007; Lewens, 2006; Shapiro & Meslin, 2001; Molyneux, Peshu & Marsh, 2004; Spiro, 1986).

Some research might resemble medical care in various ways such as the usage of similar equipment or techiniques. While research is related to medical care in several ways, it is clearly not medical care in itself. Participants' understanding of the research procedures is very important in bringing out clearly the distinction between research and routine care. Sreenivasan (2003) notes that understanding is a very important component of informed consent and

highlights the challenges faced in trying to ensure that every individual comprehends the information that is provided by researchers. Limited understanding of trial procedures is a clear sign that there are some challenges in the way in which informed consent is understood. It may also suggest that the kind of information being received by trial participants, as well as the methods used in providing the information to study participants, may not be very useful or effective. This suggests that what is termed "informed consent" in most cases may not be truly informed

The failure to understand important clinical trial procedures as well as the distinction between research and routine care has personal implications for the research participants. If trial participants are not aware of these procedures, it implies they may not be aware that they may receive a placebo and that they are participating in the testing of a product which has not yet been proven to be effective. They may also not be aware that trial site staff are not aware which individuals are on the test product arm or on the placebo (double-blinding). This misunderstanding has serious implications, especially for the testing of products such as microbicides and preventive HIV vaccines. These products are normally tested using HIV negative individuals. The consequences of misunderstanding may be severe.

The problem of limited understanding of trial procedures has also been identified in some preventive microbicide and HIV vaccine trials conducted in various countries (Quieroz da Fonseca & Lie, 1995, 1999; Kilmarx, Ramjee, Kitayaporn and Kunasol, 2001; Ramjee *et al.*, 2000). Microbicide trials and other HIV prevention technology trials are a "special area" in that they enrol HIV negative persons. These technologies are tested on HIV negative persons in order to test for their efficacy and effectiveness in preventing seroconversions. During the course of testing these technologies, some persons become infected for a variety of reasons

including, in some cases, problems related to the technology being tested (Coggins & Elias, 2000; UNAIDS, 2007; Van Damme *et al*., 2002). In some cases, the volunteers have shown an increased probability of acquiring HIV, as was the case with the Nonoxynol-9 and Step HIV Vaccine Trial (Bernstein, 2008; Klasse, Shattock, Moore and Phillips, 2008; Robb, 2008). Once someone has been infected, there is currently no cure for HIV. Antiretroviral therapy only serves to prolong the lives of people living with HIV by suppressing viral replication (Cates & Feldblum, 2008; Feldblum, Welsh & Steiner, 2003). Because of the risks that may be associated with such trials, it is therefore critical for participants to understand that they are at risk of HIV infection and what such risk means.

Fears have been expressed that limited understanding may lead to false confidence among trial participants, which may lead participants into reducing their risk prevention behaviours, thereby increasing their chances of infection with HIV (Shuklenk & Ashcroft, 2000). There are conflicting findings from empirical studies regarding the issue of false confidence. Some studies confirmed that risky behaviours overall decreased from baseline, despite some individual and group variations (Bartholow *et al*., 2005). Several other studies also confirmed that even after spending several months participating in a microbicide or vaccine trial, there were some individuals who believed that they were being protected by the product under trial (Buchbinder *et al*., 2003; Harrison, Vlahov, Jones, Charron & Clements; 1995; McGrath *et al*, 2001; Quieroz da Fonseca & Lie, 1995; Quieroz da Fonseca & Lie, 1999). As a result of these concerns, the field of microbicide development is grappling with many ethical questions that need to be answered regarding the message that should be passed on to trial participants in order to ensure that they truly understand that they are participating in a trial to test a technology whose effectiveness is uncertain. The Alliance for Microbicide Development (2007) notes that the field of microbicide development is struggling to reach consensus on

whether it is best to provide a message that has scientific merit or one that ensures that a given message is sufficiently understood by all parties. It is obvious that while it is important to aim at achieving scientific merit, adequate understanding is also essential. They note that translation of information into local languages when providing a scientifically-based message poses several challenges, including the potential to lose some of the content during translation. This is typical when dealing with terms that are used in clinical trials such as randomised controlled trial, placebo, and standard of care, among others.

In view of the above, therefore, the study at the centre of this thesis was aimed at exploring research participants' understanding of the above concepts. The thesis examines various methods used by investigators to convey the concepts of randomisation, double-blinding and placebo to trial participants, and explores participants' understanding of the concepts. The thesis is mainly intended to test the hypotheses that trial participants do not understand the procedures of randomisation, double-blinding and placebo use, nor the implications of those procedures to themselves as individuals. The thesis also posits a theoretical model for understanding of clinical trial procedures.

1.1 STATEMENT OF THE RESEARCH PROBLEM

Studies conducted in various parts of the world have revealed that trial participants have problems in understanding the differences between research and routine care, as well as the trial concepts of randomisation, double-blinding, and use of placebos. Some illiterate or semi illiterate trial participants are unfamiliar with clinical trial methods and to make matters worse, many languages have no direct translations for words describing these key concepts which can lead to considerable confusion and controversy (Mfutso-Bengo *et al*, 2008; Oduro *et al*., 2008; Pucci *et al*., 1999. The three concepts are generally difficult to explain to study participants

because they are part of the scientific language and procedures with which the disadvantaged populations, who form the majority of research participants in developing country settings, lack familiarity (Featherstone & Donovan, 1998; Kerr *et al*., 2006; Pace *et al*., 2005; Pucci *et al*., 1999; Stead *et al.*, 2004; Yuval *et al*., 2000). Some of the studies conducted in the past have suggested that research participants misinterpret the risk/benefit ratio of participating in the research because they fail to understand the underlying scientific methodology (Brahams, 1988).

Other studies conducted on participants in microbicide trials have revealed that whilst there may not be significant increases in risky behaviour at group level, some individual participants may develop a sense of false confidence which increases their chances of infection as they begin to believe that they are protected by the product which is being tested (Kilmarx *et al*., 2001; Quieroz da Fonseca & Lie, 1995, 1999; Ramjee *et al*., 2000; Slack *et al.*, 2000, 2005). Due to this sense of false confidence, participants may adopt some risky behaviours or reduce their practice of safer sex as they begin to believe that they are protected by the product they have been provided with. This may imply that the participants may fail to understand, or may somehow choose to disregard the fact that they are participating in research which is aimed at testing the effectiveness of the microbicide and is not aimed at their own protection. An understanding of the three trial concepts is important since the three concepts are critical in distinguishing research from routine care. Most consent documents and materials may not address adequately the justification of trial procedures in use, as well as the implications of those procedures. It is possible that this may be due to an assumption that lay persons do not understand science and scientific procedures.

Ultimately, the understanding of these concepts in microbicide and other HIV prevention trials, has implications for how individual participants protect themselves from HIV infection. The false confidence that microbicide trials may create among their participants may also act as a barrier to obtaining early treatment for adverse events and side effects and therefore needs to be addressed in the interests of protecting the rights and welfare of research participants. Although most guidelines emphasise the importance of obtaining informed consent, as well as the practical steps needed to document it, there is very little emphasis on participants' understanding of the implications of research participation and trial procedures. This thesis is intended to fill this gap by focusing specifically on trial participants' understanding of research participation and trial procedures and their implications.

1.2 RATIONALE FOR THE STUDY

This study is a direct response to reports by several authors who have identified difficulties that research participants face in understanding the study procedures of randomisation, placebo use and double-blinding (Featherstone & Donovan, 1998; Kerr *et al*., 2006; Pace *et al*., 2005; Pucci *et al*., 1999; Stead, *et al*., 2004; Yuval *et al*., 2000). It is also a direct response to other studies that have found that some trial participants have problems understanding the differences between research and routine care (Emanuel & Miller, 2001; Freedman, 1990; Molyneux, *et al.*, 2004; Shapiro & Meslin, 2001; Spiro, 1986; Way, 1984).

The subject of trial participants' understanding is an important topic that needs pursuit as it relates to the ethical principles of respect for persons and nonmaleficence. Low levels of understanding imply poor informed consent and may result in the breach of the ethical principle of nonmaleficence. Research participants may be exposed to more risks as a result of having inadequate or poorly understood information about the study, including study

procedures. The belief that they are protected may actually lead some participants to engage in more risky behaviours than they would have engaged in if they were not part of the trial, thereby exposing themselves to increased chances of infection. In attempting to address this problem, this study intends to focus on trial participants and the various sources of information and the ways in which the information is conveyed to participants. The study specifically deals with trial participants from a microbicide study, as microbicide trials (and other HIV prevention technology trials) represent a high risk scenario due to concerns about a sense of false confidence that may develop among enroled, HIV negative participants. They also represent a worst case scenario because there is no cure for HIV to date. A sero-conversion which is brought about by a sense of false confidence would be an "unfortunate scenario" if better understanding might have made the seroconversion preventable.

To date few studies have been conducted to test trial participants' understanding of procedures and concepts in microbicide trials. One of the major studies that has been conducted to date evaluated trial participants from a major Phase III study (COL 1492) conducted at various sites including Durban (South Africa), Cotonou (Benin) and Hat Yai (Thailand) to evaluate the effectiveness of Nonoxynol-9 (N9) in preventing the transmission of HIV. This study was conducted as a sub-study of the microbicide trial and was conducted by some of the co-investigators of the microbicide study. An evaluation of trial participants' understanding three months after enrolment indicated that the majority of the women did not understand concepts and procedures provided during the initial informed consent process. Women with no education fared worse than those with some formal education and nearly all women believed incorrectly that the placebo, as well as the product being tested, had a protective effect (Kilmarx *et al.*, 2001). Participants were not aware of the potential implications of randomisation to placebo or N-9, nor were they aware of various clinical trial design issues and

the need to follow certain procedures in the trial. Woodsong and Abdool Karim (2005) suggest that ensuring that participants understand the contents of the informed consent form has implications for clinical trials. Hence, ways have to be found to address the challenge of low levels of understanding by developing methods to effectively measure trial participants' understanding of the study and its procedures so that more effective consent procedures can be developed and applied. This study will identify the need for such changes and will pilot an intervention to improve understanding of the three key concepts selected for this study.

The current study is a direct response to the problem of limited understanding that has been identified in earlier microbicide trials (Kilmarx *et al*., 2001; Ramjee *et al*., 2000). Limited understanding of trial procedures suggests that participants are not fully aware of the risk/benefit ratio. It is also possible that researchers may underplay the risks involved in the study and emphasise the benefits so as to ensure that they do not scare away potential research participants. Failure to deal with the false confidence that microbicide trials may create could increase distrust of researchers and the health care system in general if participants later come to feel that that have been deceived. For example, after sero-converting and then realizing at the end of the trial that they were indeed participating in a trial of a product whose efficacy was unknown, participants may feel betrayed and abused. Discussions with COL1492 participants in South Africa after the conclusion of the study and the dissemination of findings clearly confirm this possibility. Some of the participants in the study were convinced that the product which was being tested (including the placebo) had some protective effect (Mantell, Morar, Myer & Ramjee, 2006). It is possible that the publication of such experiences in newspapers or other media can further heighten public antipathy to medical research. The clinical trial method is a powerful tool for advancing knowledge but, like most scientific procedures, it has

side effects that need to be attended to, lest the benefits sought be overwhelmed by the disadvantages that accrue.

The problems and issues highlighted above are significant when considering the principles of beneficence and respect for persons. In addressing these issues, there is a need to empirically investigate research participants' understanding of the concepts of double blinding, randomisation, and placebo use, as well as the prevalence of false confidence among microbicide trial participants. Also of concern are the ways in which researchers convey the information regarding randomisation, double-blinding and placebo use, as well as the kind of information they convey (Lindegger & Richter, 2000). Information disclosure has a bearing on whether trial participants understand research participation and the trial procedures, and ultimately on the quality of informed consent.

Another issue is the "foreignness" of clinical trials to developing country settings where access to basic health care facilities is often limited. In such areas, it becomes difficult for individuals to distinguish between clinical research and routine medical care. In view of the above, this study aimed to explore research participants' understanding of the above concepts. The study also focused on the various ways used by the investigators to convey the concepts of randomisation double-blinding and placebo. The study was based on the fact that relatively little has been written on obtaining informed consent for participation in microbicide trials in African settings. Much has been written about randomisation, double-blinding and the use of placebos in medical research, yet there is little data on how adequately these three procedures are understood, especially in an African setting, and how acceptable these concepts if understood, are to research participants.

The study aims to build on previous studies by focusing on the sources of information as well as the methods that are used in conveying information. Unlike some studies which were conducted by principal investigators of microbicide studies, the current trial was conducted by an investigator who was independent of the microbicide trial. The study was also aimed at addressing the weaknesses that have been identified in previous studies. In some previous studies, the outcome of interventions to improve understanding was not tested. In this study, the usefulness of a tailored intervention will be tested. This study examined understanding from a broad and holistic perspective (including understanding of personal implications of procedures). Adequate understanding was considered using several components which all contribute towards improving understanding (such as awareness of procedure, justification and personal implications). There was recognition that all these aspects play an important role in facilitating understanding. The intervention that was designed as part of this study was based on the findings on trial participants' understanding. Recommendations will be made on how researchers can convey the concepts of double-blinding, randomisation, control groups and placebos so that the majority of research participants can adequately understand as a way of ensuring that the participants are more adequately aware of the risks involved and participate in trials with their informed consent.

The findings from this study may have implications for research participants, investigators and regulatory bodies and research ethics committees (RECs) in Malawi, other African Countries and internationally. The assessment tools that have been designed may be used by other investigators after some refinements. The study might result in publications which will add to the relatively scarce African literature on trial participants' understanding of research participation, double-blinding, randomisation, control groups and the use of placebos. As revealed by the review of literature, most studies carried out on this topic have been conducted

in developed countries, yet more and more complex clinical trials are now being conducted in Africa and other developing countries (Annas & Grodin, 1998; Cohen, 2000; Varmus & Satcher, 1997)

1.3 MAIN PREMISES AND ASSUMPTIONS OF THE STUDY

The thesis is based on the following four main premises:

1. The amount and quality of information that is disclosed through study informed consent processes have an important role in determining whether participants adequately understand the clinical trial procedures of randomisation, double-blinding and placebo use, as well as their personal implications for the participants.
2. The quality of information that is disclosed by research staff as well as the way it is disclosed, have an important role in determining whether participants understand fully the clinical trial procedures of randomisation, double-blinding and placebo use, as well as their implications for the participants.
3. Some trial participants have low levels of understanding about randomisation, double-blinding, placebo use and the personal implications of these procedures.
4. If properly explained in lay terms, trial participants can sufficiently grasp information on the purpose and personal implications of trial procedures under study.

The four major premises were further broken down into the following key assumptions:

Premise 1

- The informed consent process does not adequately explain the purpose and personal implications of randomisation, double-blinding and placebo use.

- Informed consent documents and complementary informed consent materials do not adequately explain the purpose and personal implications of randomisation, double-blinding and placebo use.
- Study documents do not require study staff to pay special attention to the justification and personal implications of randomisation, double-blinding and placebo use.

Premise 2

- Trial staff do not spend adequate time explaining the purpose and personal implications of randomisation, double-blinding and placebo use to participants
- There is a conflict in terms of the messages that reach the participants from the study staff and study documents versus the contextual message that comes from the activities and the environment at the research site. When research participants look around at the activities involved in the trial and consider the attention they are receiving and the medical inclination of the researchers, it is easy for them to infer that some kind of medical care is being extended to them. Very often the researchers use the same tools and language as that of clinicians providing routine care.

Premise 3

- Some research participants agree to participate in double blinded, randomised placebo controlled clinical trials without fully understanding the concepts of randomisation, double-blinding, and the use of placebos in research.
- Some research participants do not understand the personal implications of randomisation, double blinding and placebo use.
- If properly understood, some research participants may have a negative attitude towards randomisation, double-blinding and placebo use.

Premise 4:

- Many interventions that are developed to improve understanding are not thoroughly thought out and are merely a repetition of the information from informed consent documents-using different media.
- Trial participants can understand trial procedures and their implications if the explanations they are given about the procedures include details on how the procedure will be implemented, and the justification and personal implications of those procedures.

1.4 RESEARCH APPROACH OF DISSERTATION

A "pragmatic" approach was adopted for the present study. Pragmatism is a philosophical assumption for mixed-methods research and uses the approach of "what works" (Tashakkori & Creswell, 2007; Tashakkori & Teddlie, 1998; Teddlie & Tashakkori, 2006). The central focus of a pragmatic approach is not simply the pursuit of knowledge through inquiry but through methods that are appropriate and workable (Morgan, 2007). A pragmatic approach emphasises what is workable and takes into cognisance that researchers' values, beliefs and views are always a part of who they are, how they act and how they view phenomena. The pragmatic approach recognises that values and beliefs even impact on what researchers choose to study and how they choose to study the phenomenon.

Pragmatism offers a reciprocal approach between the quantitative and qualitative paradigms which are two diametrically opposed but potentially complementing paradigms. According to Morgan (2007), a pragmatic approach relies on abductive reasoning, which moves back and forth between deductive and inductive reasoning. Morgan notes that abduction implies moving back and forth between the separate qualitative and quantitative components in a mixed-

methods study. The researcher seeks to connect data from the two approaches in attempts to answer the research questions which were posed to guide the study.

The use of a mixed-methods approach which relies on quantitative and qualitative methods in this study was done with the awareness of the criticisms each method has attracted. The central arguments relate to the inherent assumptions about epistemology and ontology that each method purports to have as its basis. It is commonly understood that a positivist epistemology underpins the use of quantitative methods which are considered scientific, objective, reliable, valid, deductive and generalisable (Morgan, 2007). An interpretive epistemology on the other hand usually underpins the qualitative approach. Research taking a qualitative approach is considered constructivist, subjective and inductive. While the former is often associated with theory testing the latter is often associated with theory building (Spicer, 2004). It is important to note, however, that all research makes assumptions which are susceptible to dispute and contradiction and hence, no methodology is without its dangers (Charmaz, 2005). While the qualitative approach has in the past been judged to be inferior, there is increasing recognition of the value of qualitative research in answering questions that are not easily addressed exclusively by experimental methods. At the same time it is increasingly being realised that the type of knowledge generated by each method and the way it can be used are different (Robinson *et al*., 2005).

According to Hanson, Creswell, Plano-Clark, Petska and Creswell (2005) and Johnson and Onwuegbuzie (2004), there are various reasons why researchers choose a pragmatic approach which entails mixing methods. Reasons include the following:

- The two approaches may be used for complementarity. Researchers can use the findings from one method to explain the findings from the other method;

- Results from one method can be compared to results from the other method;
- The findings from several methods can also be used to expand the breadth of the study by using different method to focus on different areas of inquiry;
- After obtaining quantitative results from a sample of a population, researchers can use them to identify a few individuals who meet some defined criteria so as to expand on the results using qualitative data;
- Researchers can use mixed-methods to improve their understanding of the research problem by bringing together numeric trends from quantitative approaches and specific explanations and descriptions from qualitative approaches;
- Through qualitative approaches, researchers can identify constructs that may be measured subsequently through the use of existing quantitative instruments or the development of new ones;
- In the process of developing the research, results from one method can play an important role in shaping the research as well as in informing the other methods.

As with any design, there are strengths and weaknesses in using the mixed-methods approach. Importantly it enables researchers to combine analytical, interpretive, deductive, exploratory and experimental approaches. These approaches and methods substantiate one another to verify validity. The following strengths have been noted regarding the mixed-methods approach (Creswell, 2003; Cresswell & Plano-Clark, 2007; Greene & Caracelli, 2003; Morgan, 2007):

- Pictures, words and numbers are used to add meaning to each other. In some cases, it may not be adequate to provide only statistical data about a specific issue without adding descriptions as a way of showing how people experience that phenomenon.
- Researchers can test theories effectively by using qualitative approaches to formulate grounds for verification.

- The researcher is provided flexibility to find relations between different variables and draw conclusions.
- The researcher is provided with more space to actively participate in the generation of the data and their interpretation in a direct way.
- The use of quantitative and qualitative methods provides more insights and understanding that can be missed if only one approach is used.

The same authors point out the following weaknesses that are applicable to the mixed method approach:

- A study using a mixed method approach can be difficult for a single researcher to manage due to the quantity of work and the expertise which may be necessary.
- Research teams, including consultants, may need to be used, instead of a single individual. This has budgetary implications as well as other consequences related to team dynamics and project management.
- Mixed method research may be time consuming.
- The researcher must have sufficient knowledge and skills in both qualitative and quantitative methods, and sufficient understanding is needed to mix the data.
- Mixed-methods research is a new area which is still undergoing development. It is possible that mixed-methods researchers may encounter some difficulties which may be difficult to resolve, including some conflicts that can be brought about by the different schools of thought and underpinnings.

The combined data collection approach was deemed suitable for this empirical study as it allowed for the flexibility to pursue topics that arose during the process of data collection that would not have been anticipated at the planning stage. For this study, a quantitative approach

was specifically employed for two reasons. Firstly, the quantitative approach makes the analysis of large sets of data possible. Quantitative methods are preferred over qualitative methods especially when the proposed research is quantitative in nature (*how much* of a phenomenon) and hence involves a large number of cases. Large numbers of cases are very important for descriptive and explanatory analyses, especially where several variables are to be analysed simultaneously (Babbie & Mouton, 2001). Secondly, the quantitative approach allows for the standardisation of measures and responses.

A qualitative approach was adopted in order to complement data collected using the quantitative approach. It is often difficult to capture personal meanings and feelings adequately using quantitative methods since they emphasise numbers (Silverman, 2004; Sullivan, Monette & DeJong, 1998). Feelings and personal meaning are better captured through narrative descriptions. This study dealt with a phenomenon which is yet to be fully understood. Against this background, a qualitative approach was found to be more useful as a complementary and confirmatory tool because it is more exploratory in nature. For example, the quantitative results of this study would provide a priori information on aggregated levels of understanding of the concepts under study, while the results of the qualitative section would show how trial participants interpret the concepts. The qualitative approach was also used in pre-testing and amending the quantitative tool to help ensure correct usage of words used.

The present study benefited in several ways from the following strengths of the qualitative approach:

- Depth and detail which may not be obtained from structured approaches using tools like questionnaires

- Openness, bringing about the potential to ellicit phenomena not dealt with by previous studies
- It assists the investigator to view the phenomenon from the world view of those under study – their meaning rather than imposing meaning
- It attempts to avoid pre-judgments. The aim is to unravel what is happening rather than having preconceived ideas about what may be happening (Sullivan *et al*.,1998).

As part of the pragmatic approach, a sequential design which involves the mixing of the two approaches in a sequential manner was employed. The sequential design involves sequencing of approaches and methods in a justified manner. The sequential usage of the two approaches in the present study, while aimed at taking advantage of the strengths of both approaches, was also aimed at countering the weaknesses of both methods in an attempt to answer the research questions. The sequential design is presented in greater detail in Chapter 5.

1.5 CONTRIBUTION OF THESIS

The contributions that this thesis might make are summarised as follows:

- The thesis builds on previous studies by focusing on the sources of information as well as the methods that are used in conveying information. Unlike some of the previous studies which were conducted by the principal investigators of the microbicide studies, the proposed study was conducted by an investigator who was independent of the microbicide trial. In the majority of previous studies, the outcomes of interventions to improve understanding were not verified.
- The thesis presents a different way of looking at understanding. In this thesis, understanding was examined from a broad and holistic perspective (including

understanding of personal implications of procedures). The main difference between this and other studies which have focused on understanding is the emphasis given to the personal implications of clinical trial procedures as an important component of understanding.

- This thesis describes the design, implementation and evaluation of an intervention which was developed as part of the current study. The intervention was aimed at improving understanding.
- The thesis suggests recommendations on how researchers might convey the concepts of double-blinding, randomisation, control groups and placebos in a way that the majority of research participants can fully understand. This might ensure that the participants are more fully aware of the risks involved and participate in trials with their informed consent.
- The thesis is an addition to the relatively scarce African literature on trial participants' understanding of research participation, double-blinding, randomisation, control groups and the use of placebos.
- The thesis adds to research on informed consent in Africa. Most studies carried out on this topic have been conducted in developed countries, yet more and more complex clinical trials are now being conducted in Africa and other developing countries.
- The findings highlighted in this thesis may have implications for research participants, investigators and regulatory bodies in Malawi and other African countries. The assessment tools used in this study may be used by other investigators after refining them so that they can suit their own studies.

1.6 OUTLINE OF THESIS

This thesis is organised into twelve chapters including the introduction. Chapter 1 presents a general introduction which includes a description of the general problem area under study, an

explanation of why this topic is important, an outline of the research approach that was employed for the study, and the potential contributions made by this thesis. Chapter 2 presents a review of literature on previous studies on informed consent and understanding of clinical trial participation. The chapter illustrates that the concept of understanding is complex and needs to be viewed in a holistic manner. Chapter 3 outlines the conceptual framework that was adopted for this study. Among other things, the chapter illustrates the steps that are necessary to understand clinical trial procedures, their purpose, and their personal implications for trial participants. Chapter 4 highlights the main aim of the study, the specific objectives, research questions and hypotheses. Chapter 5 describes the methods employed for this study, including the context of the study. It provides a description of the microbicide study which hosted the study that is reported in this thesis. Chapter 6 presents the findings from the first phase of the study which was aimed at assessing trial participants' understanding of randomisation, double-blinding and placebo use. In Chapter 7, the findings that are presented in Chapter 6 are discussed. Chapter 8 presents information relating to the development and design of a pilot intervention aimed at improving understanding of the trial procedures under study. Chapter 9 describes the implementation of the intervention, as well as the findings on the implementation of the intervention. In Chapter 10, the findings from the implementation of the intervention are discussed. Chapters 6,7,8, 9 and 10 provide the bulk of the empirical evidence to the research questions. In Chapter 11, the major findings from the two phases of the study are discussed, including the study's hypotheses, responses to research questions, and clarification on research premises and assumptions. In Chapter 12, a summary of the main study findings and conclusions from the study are presented. The chapter also presents recommendations and suggestions for further research.

CHAPTER 2

LITERATURE REVIEW

2.0 INTRODUCTION

The main objective of this chapter is to present a review of literature on understanding of clinical trial procedures. The chapter is divided into various sections as follows:

- The first section reviews available literature on the need for informed consent and the need for participants to fully understand the studies they choose to participate in.
- The second section is devoted to the ethics of the clinical trial procedures under study, namely randomisation, placebo use and double-blinding.
- The third section focuses on ethical issues in HIV prevention trials, including microbicide trials. This section illustrates the need for ensuring that trial participants understand the implications of enrolling in a clinical trial.
- The fourth section reviews and discusses previous studies that have been conducted to assess HIV vaccine trial participants' understanding of research procedures are presented.
- The fifth section reviews and discusses previous studies aimed at assessing microbicide trial participants' understanding of the microbicide trials, including the study purpose.
- The sixth section reviews and discusses previous studies that assessed understanding among research participants with limited decision making capacities.
- The seventh section reviews and discusses previous studies that assessed understanding of trial participation among oncology trial participants. A separate section has been devoted to studies conducted among oncology trial participants due to various reasons. A significant volume of literature exists on studies that have been conducted in this area

due to the nature of cancer illness as well as other reasons which are explained in the section.

- The eighth section reviews and discusses previous studies that have assessed trial participants from other studies conducted in developed countries.
- The ninth section reviews and discusses studies that have been conducted in developing countries to assess trial participants' understanding.
- The tenth section critically reviews studies conducted in Africa aimed at assessing trial participants understanding of clinical trial participation.
- The eleventh section reviews and discusses previous studies that have introduced interventions aimed at improving understanding.
- The twelfth section presents a summary of the literature reviewed and some of the important lessons learned from the previous studies.

For each study, the study methods and a summary of the main findings and lessons learned are presented, including in some cases brief discussions on the strengths and weaknesses of the study methods.

2.1 INFORMED CONSENT AND THE NEED FOR TRIAL PARTICIPANTS' UNDERSTANDING

The right to self determination is one of the fundamental human rights and an established tenet of research ethics and clinical practice (Dunn & Jeste, 2001). It is generally agreed that adequate informed consent consists of three elements; namely full information, voluntary participation and capacity to make an autonomous decision (Appelbaum *et al.*, 1987). Capacity for decision making is composed of four abilities namely the ability to understand relevant information, the ability to appreciate the nature of the situation and its likely consequences, the

ability to reason with the information and weigh options logically, and the ability to communicate the choice in a clear manner (Grisso & Appelbaum, 1998). An important goal of informed consent is to present information to individuals so that they can decide which option they want to take according to their values (Ubel & Loewenstein, 1997). Lindegger and Richter (2000) note that informed consent requirements in research have been driven by two different agendas: a legal agenda and a moral agenda. While the legal requirements may be aimed at protecting human research participants, researchers and institutions may simply use these as a way of avoiding lawsuits. The moral agenda on the other hand is aimed at empowering the potential research participant so that they can make an informed decision. An informed decision is a guarantee that the likelihood of regretting after one has joined a study out of ignorance is minimised. Good quality informed consent is about ensuring that individuals' decisions to enroll or not to enroll, are based on understanding of information whilst poor quality informed consent is that which aims at getting an individual to sign a document without adequate understanding. There is therefore a difference between the information provided for reasons of legal liability and information provided for the sake of empowering an individual and facilitating informed decision making. A researcher who emphasises the legal side would ensure that he or she has included all essential elements in the informed consent document and also that the participant has signed. A researcher who strongly believes in the moral justification would try by all means to ensure that they provide information in a way that is understandable, that the individual has understood and that the decision to join is voluntary and based on the adequate understanding of the provided information.

Wendler and Grady (2008) opine that for participants to give valid informed consent, they need to understand the potential risks involved, the benefits, procedures and alternatives. The authors conducted an analysis of individuals' interests and point out that research participants

also want to know about their contribution to research – in other words, that researchers will be relying on the participants to gather generalisable knowledge, as well as the impact of the research on themselves. The authors suggest that research participants may not want to know everything about a study but may want to know about issues that are of relevance to them and their health. The authors further suggest that tests to assess understanding should include questions that focus on the participants' contributions to research, their role in generating new information, and the impact of the research on them as individuals.

A significant volume of literature has documented a variety of problems related to understanding. Some research participants may also fail to appreciate the fact that research is designed to advance the interests of others. Numerous studies have also shown that consent forms packed with technical jargon are difficult to read and participants often misunderstand the purpose of the research and the implications for their individual care (Siminoff, 2003). In these circumstances, participants are less likely to distinguish between routine medical care and medical research (Emanuel & Miller, 2001; Freedman, 1990; Shapiro & Meslin, 2001; Spiro, 1986; Way, 1984).

Another area that is identified as a problem in informed consent is that participants often do not understand key components of the studies in which they will be participating (Agre & Rapkin, 2003). The US Code of Federal Regulations specifies eight elements required in all informed consent forms and six additional requirements, where deemed appropriate. The eight elements according to 45 CFR 46 (US Department of Health and Human Services, 2009) include the following:

1. A statement that the study involves research, an explanation of the research, and the expected duration of the subject's participation, a description of the procedures to be followed, an identification of any procedures that are experimental

2. A description of any reasonably foreseeable risks or discomforts to the subject

3. A description of any benefits to the subject or to others, which may reasonably be expected from the research

4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject

5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained

6. For research involving more than minimal risk, an explanation as to whether any compensation and/or medical treatment are available if injury occurs and, if so, what they consist of, or where further information may be obtained

7. An explanation of whom to contact for answers to pertinent questions about the research and research participants' rights, and whom to contact in the event of a research-related injury to the subject

8. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

The US regulations also list six additional elements which researchers need to include in the informed consent documents as appropriate. The six elements include the following:

1. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are presently unforeseeable

2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent

3. Additional costs to the subject that may result from participation in the research

4. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject without prejudice to the subject. In all instances where abrupt withdrawal would be hazardous to the subject (e.g., medication regimens which require gradual reduction) appropriate safe discontinuation procedures will be followed and the subject advised

5. A statement that major new findings developed during the course of the research, which may relate to the subject's willingness to continue participation, will be provided to the Subject

6. The approximate number of participants involved in the study; and the number of participants planned to be involved at the local research site.

The eight elements as well as the six additional elements are aimed at fulfilling legal requirements of informed consent. This is understandable if one bears in mind the past cases involving abuse of individuals who would not have given their consent to participate in research as well as the various cases of litigation in the US (Beauchamp & Childress, 2001). Researchers and institutional review boards (IRBs) or research ethics committees (RECs) have to ensure that these eight essential pieces of information are included in informed consent documents. Yet, ethically valid informed consent demands more than just disclosure of the eight pieces of information (Flory & Emanuel, 2004). It is generally agreed that informed consent in its true sense requires more than the satisfaction of legal formalities such as the signing of informed consent forms (Lindegger *et al*., 2006). Data suggesting limited levels of understanding among trial participants have prompted calls for investigators and ethics committees to find ways to improve research participants' understanding (Lavori, Sugarman, Hays & Feussner, 1999; Siminoff, 2003).

Debates over improving informed consent have unfortunately not been guided by empirically derived information needs of potential research participants. Limited data is available concerning the type of information as well as presentation methods that are most effective in improving understanding. It is now known and agreed that while the provision of information is important, the information should not be provided in a haphazard fashion (Siminoff, 2003). Researchers should not make any assumptions about trial participants' understanding of key points in the consent document. They have responsibility to assess individuals' understanding thoroughly (Agre & Rapkin, 2003). After conducting an initial part of a study aimed at developing a model informed consent process for a genetic study, Bernhardt *et al*. (1997) concluded that research participants vary greatly in terms of their informational and counselling needs. They therefore suggested that informed consent processes should be individualized, taking into account participants' perceptions and preferences. Sreenivasan (2003) discusses the importance of comprehension in informed consent and argues that, at a minimum, prospective research participants should be able to comprehend the information that they receive. Miller and Boulton (2007) opine that the informed consent processes have to change in response to the increasing sophistication of information. Improved informed consent processes become even more important in view of the fact that risky clinical trials often rely on the socially and economically less empowered in society (Elliott & Abadie, 2008). Richter, Lindegger, Abdool Karim and Gasa (2002) emphasise culturally appropriate approaches of obtaining informed consent. They argue that for any approach to be effective, it has to be culturally appropriate to be acceptable to the community and individuals.

2.2 THE ETHICS OF RANDOMISATION, PLACEBO USE AND DOUBLE-BLINDING

At face value, the procedures of randomisation, double-blinding and the use of placebos in research are simple ones. This assumption of simplicity hides many factors and controversies surrounding these procedures, including trial participants' understanding and attitudes to the use of these procedures in research. While much has been written about randomisation, double-blinding and the use of placebos in medical research, there is still imperfect understanding of exactly how these three procedures are understood, especially in an African setting, and how acceptable these are to research participants. This is especially pertinent in HIV prevention trials (including HIV vaccine and microbicide trials) in developing country settings in which medical research is foreign and medical care not readily available. Ethical issues in HIV vaccine and microbicide trials are closely related as the trials involve HIV negative persons as participants in trying to establish the effectiveness of the new preventive technologies. For this reason, WHO/UNAIDS has published specific guidance on HIV preventive vaccine trials (UNAIDS, 2000, 2007). Some countries such as Kenya, South Africa and Uganda have also developed specific guidance (Kenya Ministry of Health, 2005; Uganda AIDS Commission, 2006; Medical Research Council of South Africa, 2003).

Placebo controls are commonly used in clinical trials of investigational treatments because they have important advantages. Supporters of placebo controlled trials (PCTs) point to the interpretive problems inherent in the use of active control equivalence trials to establish the efficacy of a new treatment (Senn, 1997). In recent years, some bioethicists have criticised the use of placebos in controlled trials, particularly where alternative therapy exists, in favour of standard treatment controlled trials (Ellenberg & Temple, 2000; Freedman, 1990; Levine, 1985, Rothman & Michels, 1994; Weijer, 1999). In 1999, the World Medical Assembly circulated a

draft version of the Declaration of Helsinki which restricted the use of placebo. The use of placebos was also widely debated during the revision of the Declaration of Helsinki in year 2000. Some bioethicists expressed concern that the use of placebos may disadvantage participants on the placebo arm and may even lead to a deterioration of their health status (Goodyear, Lemmens, Sprumont & Tangwa, 2009;Kimmelman, Weijer & Meslin, 2009; Nicholson & Crawley, 1999).

On the other hand, those who justify the use of placebos justify their use as ethical in instances where delaying or omitting available treatment has no permanent adverse consequences for the patient and for as long as patients are fully informed about their alternatives (Ellenberg & Temple, 2000). There have also been arguments that restricting the use of placebos could discourage the development of new drugs. Subsequent debates on this and other issues finally led to the 2004 and subsequently the 2008 version of the Declaration of Helsinki, which allows for the use of placebo under certain conditions, such as where no proven alternative therapy exists and where delayed treatment does not result in serious harm to the patient (WMA, 2000, 2002, 2004, 2008). Prior to year 2010, (at the time of writing this thesis) there were no comparators that could be used in HIV prevention research. No gels or vaccines had been proven to be effective by then. In 2010, there were some findings suggesting the effectiveness of tenofovir in preventing HIV transmission (Abdool Karim *et al*., 2010; Keller, 2010). UNAIDS (2007) supports the use of placebo together with voluntary counselling and testing (VCT) and condoms. Where no proven alternative exists or where no established active control exists, as in the case with microbicides, the use of placebos is routine and generally less controversial. Regardless of all the arguments against the use of placebos in research, placebos will remain in use in clinical research in future because of their advantages. Placebo controlled trials are regarded as the gold standard by most regulatory agencies and funding agencies because of their advantages, such as the conclusive nature of the results they yield within a

short period of time, thereby saving on costs (Ellenberg & Temple, 2000; Rothman & Michels, 1994).

The answer to understanding the concepts of randomisation and double-blinding lies in understanding how the scientific method is often incompatible with one of the principles of research beneficence – the obligation to do good (Beauchamp & Childress, 2001). According to this principle, the researcher is obligated to do good to the research participant's well being. The researcher is bound to maximise the chances of a successful outcome. Failure to adhere to this principle creates a potential disadvantage for the clinical research participant in a developing country setting who often opts to participate in research for the sake of accessing medical care. Even in trials comparing two treatments, it is very unlikely that the two treatments will be identically desirable for a particular patient. The physician may have reason to believe, for example, that a given treatment is more likely efficacious for a particular patient based on the physician's previous experience with a sub group of patients or even the patient's own past treatment experience or the family history of responsiveness to treatment. Participants may have had previous unsatisfactory responses to one of the medications in the trial, or may display clinical characteristics that suggest that one class of medication is more likely to benefit them than another (Rothman & Michels, 1994).

Ordinarily, the above factors would guide the therapeutic approach, but in a double blind randomised trial, the physician/researcher usually cannot allow these factors to influence treatment decisions except under exceptional circumstances. While efforts to control for such factors in the selection of research participants are possible, they are often cumbersome, expensive and may bias the sample. The reliance on randomisation and double-blinding represents an inevitable compromise of the principle of beneficence in the service of attaining scientifically valid and generalisable research results (Edwards, Lilford & Hewison, 1998;

Hellman & Hellman, 1991; Schafer, 1982). The need for control groups also produces similar effects. In a therapeutic trial, patients will rarely receive medications that are deliberately designed to be pharmacologically ineffective. Placebos are routinely employed in clinical trials without the intent of benefiting the individual participant. Double-blind procedures, on the other hand, may delay the recognition of side effects or drug interaction, and may have other adverse consequences (Brahams, 1988).

Several authors have reported some difficulties that participants face regarding the adequate understanding of the concepts of randomisation, placebo use and double-blinding to research participants (Featherstone & Donovan, 1998; Kerr *et al*., 2006; Pace *et al*., 2005; Pucci *et al*., 1999; Stead *et al.*, 2004; Yuval *et al*., 2000). This problem was also evident during the researcher's own training of research teams from various projects in Zimbabwe, including staff from a microbicide trial. Most consent documents do not address adequately the purpose and justification of the trial procedures in use, as well as the implications of those procedures (Bhutta, 2004; Stead, *et al.,* 2004). According to the same authors, consent documents and study materials mainly explain the study procedures involved as a way of promoting adherence. This may be due to an assumption that lay persons do not understand science and scientific procedures.

The apparent failure of participants to understand the use of randomisation, placebo and double-blinding in research is ethically problematic, particularly if it means that participants do not realise the implications of these procedures on themselves and their health (Dunn, Palmer & Keehan, 2006). Kilmarx *et al*. (2001) recommend that in order to ensure true informed consent, researchers need to assess comprehension before they initiate their studies. Assessments of comprehension are important as they make it possible for researchers to address potential problem areas in participants' comprehension. The authors further

recommend that research staff need to be well trained in communication and counselling and should not have substantial language or cultural barriers. Consent forms should be readable and easily understood by potential participants. Special media such as videos, flip charts, booklets or role plays should be prepared for participants and these should be reviewed by community representatives, ethics committees and other experienced members. Research staff need to facilitate participants' understanding of technical concepts and their consequences and the personal and psychosocial implications of trial participation. Research staff also need to emphasise the rights of participants to withdraw at any time and also the right for the researchers to exclude the participants if they deem it necessary through the exclusion criteria.

The problems and issues highlighted above are very significant when one considers the principles of beneficence and respect for persons. In addressing these issues, there is a need to empirically investigate the research participants' understanding of the concepts of blinding, randomisation, and placebos as well as the prevalence of false confidence among microbicide trial participants. Of concern are the ways in which researchers convey the information regarding randomisation, double-blinding and placebos, as well as the kind of information they convey (Lindegger & Richter, 2000). This has a bearing on whether trial participants understand key elements of research participation as well as the trial procedures, and ultimately on the quality of informed consent.

Several studies have been conducted to assess trial participants' attitudes towards the concepts and procedures of randomisation, double blinding and placebo use. In a quantitative study conducted by Heitenan, Aro, Holli and Absetz (2000), only 23percent of the respondents believed that their treatment had been chosen randomly. Several studies have reported that despite being aware of the use of procedures such as randomisation, trial participants found the concepts hard to understand and appreciate. This has been attributed to the expectation by

patients that clinicians would assign them to treatment based on their specific symptoms, clinical findings and age (Glogowska, Roulstone, Enderby, Peters & Campbell, 2001). In interviews with parents who had consented for their children to participate in a RCT, Glogowska *et al*. (2001) reported that some parents considered it unethical to use a placebo when there was an alternative whose value had been proven. In another study involving focus group discussions with cancer patients and women in the community, randomisation and the uncertainty in randomised controlled trials (RCTs) were considered negative aspects of clinical trials (Ellis & Butow, 1998)

Ellis, Dowsett, Butow and Tattersall (1999) found that 51 percent of their respondents agreed that RCTs were not the best way of testing new treatments. In a study by McQuellon *et al*. (1995), 95 percent of breast cancer patients reported that they would not allow the flipping of a coin to determine their treatment allocation. In a study by Snowdon, Garcia and Elborne (1998), the majority of parents in a neonatal trial found it hard to believe that chance had denied their baby better treatment when it was later revealed to them at the end of the study that their child was on placebo.

Similar findings were reported by Slevin *et al*. (1995). In a study involving cancer outpatients, respondents reported that they found randomisation and double blinding to be less appealing in clinical trials as this meant that treatment was not decided either by the doctor or the patient. In a study assessing the willingness of patients to participate in some hypothetical trials, Llewellyn-Thomas, McGreal, Theil, Fine and Erlichman (1991) reported that more than half of the respondents indicated that they would not agree to enter into a RCT and 63 percent reported that randomisation was the reason why they would refuse to join the trials. A few studies have demonstrated positive attitudes towards trial procedures. Some studies have also confirmed that provision of adequate information on the trial and its procedures increases positive

attitudes towards the trial (Kruse *et al*., 2000; Searight & Miller, 1996; Weston, Hannah & Downes, 1997). Robinson *et al*., (2005) report evidence that provision of adequate information may actually lead to greater understanding, which may ultimately lead to lower consent rates.

2.3 THE ETHICS OF HIV PREVENTION TRIALS

HIV prevention trials are a relatively new area of investigation and they present several unique ethical challenges. One of the major ethical challenges relates to the understanding by trial participants that they are participating in a research study to test the effectiveness of a particular product. Various authors have written on the possibility of creating a sense of false confidence among HIV prevention trials (Christakis, 1988; Harrison *et al*., 1995; McGrath *et al*., 2001). Concerns have been raised that the use of vaccines, microbicides or pre-exposure prophylaxis could decrease condom use, resulting in a net increase in HIV infection rates as a result of this false confidence that microbicide trials may create. In attempts to address these concerns, the Food and Drug Administration (FDA) recommended 3 arm studies to compare HIV incidence rates in the placebo arm, an active microbicide arm, and a condom only arm with no gel (Coplan, Mitchnik & Rosenberg, 2004).

The phenomenon of false confidence is related to that of therapeutic misconception, a tendency by trial participants to mistake the nature of clinical research and to confuse its aims with those of clinical care. Appelbaum *et al.* (1987) define therapeutic misconception as a wrong belief by trial participants that they are participating in research for the sake of being treated and not for the sake of obtaining new information. The authors have observed that participants in some studies develop an opinion that they are being treated with an effective product. The phenomenon of therapeutic misconception is mainly associated with clinical trials involving

therapeutic treatments, while that of false confidence is mainly associated with trials testing some preventive technologies such as microbicides and HIV vaccines. In the area of preventive HIV vaccine and microbicide trials, this phenomenon is commonly referred to as behaviour disinhibition (Abdool Karim & Baxter, 2009).

In the area of microbicide trials, there are always fears that some participants may believe that they are protected from HIV infection by the microbicide under study, thereby beginning to adopt some high risk behaviours or even reducing preventive actions (McGrath *et al*., 2001). The phenomenon of false confidence may make trial participants not consider the facts that they are going to be randomised to various groups, that there is some chance that they may receive a placebo, that a placebo does not contain the active ingredient, that the purpose of the research is to test the product, that even the researcher or staff at the clinic may not know whether they are using the placebo or the active product, and that the active product may not be at all effective.

Cassell, Halperin, Shelton and Stanton (2006) also note that, in HIV prevention programmes and research, it is possible for individuals to increase their risky behaviour as a result of a decrease in perceived risk and they raise concern that this could undermine the protective effect of a particular intervention such as circumcision, microbicides or pre-exposure prophylaxis. The authors suggest that, by so doing, such interventions may promote the spread of HIV by inhibiting the uptake of safe behaviours. The authors further suggest that the challenge of false confidence in HIV prevention research may be addressed in part by communicating clearly and broadly that the product being tested may not eliminate the risk of HIV infection. In recognition of the possibility of individuals abandoning safe behaviours such as condom use, Foss, Vickerman, Heise and Watts (2003) conducted a study which attempted to estimate the reduction in condom use that can be tolerated following the introduction of an efficacious

microbicide without increasing an individual's chance of HIV infection. They estimated that with a microbicide which is 50 percent effective, groups that use condoms with 25 percent consistency or less could stop using condoms without increasing their risk.

A study was conducted by Stolte, Dukers, Geskus, Coutinho and de Wit (2004) to investigate if men who have sex with men may change from protected to unprotected anal intercourse as a result of perceiving less need for highly active anti retroviral therapy (HAART). The study found that homosexual men were not more likely to engage in unprotected sexual intercourse under these circumstances. The findings from this study may be less applicable to HIV vaccine and microbicide trials in which the participants are individuals who are HIV negative. It is possible that the men who participated in this study were always aware of the need for continued protection as they were always reminded about their HIV status by the drugs that they were supposed to take each day. Bartholow *et al*. (2005) report on similar findings from a study which looked at men having sex with men and women taking part in a multi national HIV vaccine study. The study established that sexual risk behaviour did not increase beyond baseline levels during the first three years of the vaccine trial. On reviewing the literature, Slack *et al*. (2005) suggest that behaviour disinhibition is seldom a reality.

In microbicide trials, the possibility of behaviour disinhibition or false confidence has implications as it may leads to several questions. Some of the important questions include:

- Who may be to blame for those participants who get infected during a microbicide or HIV vaccine trial?
- Does participation in a microbicide trial increase the chances of infection by creating a sense of false confidence among participants?
- Who should be responsible for the treatment of those individuals who get infected during the course of the microbicide trial?

All these questions relate to the fact that, in microbicide trials, HIV sero-conversion is the primary end point and only HIV negative women are included in the study after some prescreening procedures. Women have to be sexually active if a microbicide is to be tested and, as such, exposure to HIV is a precondition for the successful testing of the new product. Microbicide trials are preventive trials in nature since they are mainly meant to protect uninfected women by protecting them from infection by their infected male partners. This difficult fact places a demand on the researchers to ensure that the trial participants adequately understand that they are participating in research and that they also take the necessary precautionary measures as individuals to ensure that they protect themselves from possible infection (Chistakis, 1988).

Paradoxically, just as support and scientific prospectus for microbicide development are improving, the ethical challenges in the area of microbicide research are growing. For example the issue of false confidence and the issue of post trial antiretroviral therapy for those who become infected during the microbicide trial (Coplan *et al*., 2004). A significant volume of literature exists on the debates surrounding ethical issues in microbicide studies, much of which focuses on the questions of what happens to the participants who become infected during the trial (Barsdorf, Maman, Kass & Slack, 2009; de Zoysa, Ellias,& Bentley,1998; Lange, 2005; Lavery, Grady, Wahl & Emanuel, 2007; Lindegger & Richter, 2000; Moodley, 2007; Richter, Lindegger, Abdool Karim & Gasa 1999; MacQueen, Abdool Karim & Sugarman, 2003; Saelens, 1998; Singh & Mills, 2005; Slack *et al*., 2005; Slack & Stobie, 2008; Schuklenk, n.d; Stobie, Strode & Slack, 2005; Tarantola *et al*., 2007; Tucker & Slack, 2003; UNAIDS, 2000, 2007; Wassenaar & IJsselmuiden, 2007; Weijer & LeBlanc, 2005; Wolf & Lo, 2001; Vallely *et al*., 2009). The various authors looked at this topic from various perspectives with some specifically trying to answer the question from the point of view of developing countries. The

availability of such a large volume of literature, suggests that the infection of trial participants during the course of a trial, is an important issue which needs serious attention if HIV prevention trials are to be conducted using high ethical standards. Overall, there is some level of agreement among the various authors that some level of HIV prevention efforts are necessary during the trial and some care is necessary for individuals who seroconvert during HIV prevention trials.

Preventive HIV vaccines are designed to prevent HIV infection whereas therapeutic HIV vaccines are designed to boost the immune responses of a person already infected with the virus (Esparaza, & Bhamarapravati, 2000). Several authors have argued that the commercial production and distribution of a preventative vaccine or microbicide might continue to remain an elusive dream due to the genetic mutation of the virus, which has led to failures in some of the products that appeared promising initially (Berkley, 2003; Barouch, 2008; Esparaza, & Bhamarapravati, 2000; IAVI, 2010; Johnston & Fauci, 2008). Mathematical modeling studies have established that a partially effective microbicide used in half of coital acts by 20 percent of women at risk could prevent 2.5 million infections in three years (Coplan *et al*., 2004).

The field of HIV preventive microbicides has received attention in recent times after realization that, worldwide, nearly half of all individuals living with HIV are women who have acquired the virus largely by heterosexual exposure (Blayne & Justman, 2008). With an HIV vaccine likely to be years away, topical microbicide formulations applied vaginally or rectally are now being investigated as an important strategy for HIV prevention. Importantly, HIV preventive microbicides can become an important female-controlled method that can be used by women who cannot negotiate condom use for a variety of reasons. This in itself would be a way of empowering women in the fight against HIV. A review of research on HIV preventive microbicides conducted by Blayne and Justman yielded 118 studies at the time: 73 preclinical

and 45 clinical. Clinical research included phase I and II/IIb safety studies, and phase III efficacy studies. The authors noted that while some phase I and phase II clinical trials had found some microbicide compounds to be safe and well tolerated, phase III trials completed at that time had not demonstrated efficacy in preventing HIV transmission. The findings from the tenofovir trials have brought some hope into the HIV prevention arena (Abdool Karim *et al*., 2010, Keller, 2010). Before the tenofovir success story, HIV preventive microbicide trials faced some serious scientific and ethical issues including choice of placebo gel, the potential to cause viral resistance, the potential to increase false confidence, the issue of care for those who become infected during the trial, among others (Blayne & Justman, 2008).

Previous microbicide trials conducted in developing countries have posed several complex ethical challenges. One of the microbicide studies which encountered so many ethical challenges was the Nonoxynol-9 study which was conducted in several developing countries including Zimbabwe, South Africa, Kenya, Cameroon and Thailand. Before the initiation of the major phase III study using Nonoxynol-9, some studies had already indicated that multiple use of Nonoxynol-9 had adverse effects, which were possibly associated with enhanced vulnerability to HIV infection (Coggins & Elias, 2000). One earlier trial had even shown an increase in HIV incidence among those using a 1000mg dose of N9 using a sponge as compared to those using a placebo (Van Damme *et al*., 1998). This study was dismissed for methodological reasons (Van Damme *et al*., 1998). Another study conducted among sex workers in Cameroon using a 70mg dose of N9 in a vaginal film showed no effect, either harmful or beneficial (Van Damme *et al*., 1998, 2000, 2002). However, there were already reports on genital epithelial disruption and inflammation when N9 was used frequently in high doses (Stafford *et al*., 1998). The Phase III studies confirmed all the problems documented in the earlier literature. The women in the N9 arm had a higher rate of infection compared to those in the placebo arm (Van Damme *et al*., 2002). Some authors have concluded that the

Phase III trials were conducted even after some evidence had shown that N9 was not suitable since it was reasoned at the time that microbicide studies were a matter of urgency in view of the growing HIV epidemic in Africa (Coggins & Elias, 2000; Ramjee, 2007; Wassenaar & IJsselmuiden, 2007).

The principle of nonmaleficence requires that all participants be provided with available measures known to reduce the risk of HIV infection, yet this simultaneously reduces the ability of the study to assess the protective effect of the microbicide under test. According to this principle, investigators (usually physicians) should not just watch while trial participants become infected. Instead, they are obliged to take all actions they can to ensure that those who are uninfected stay uninfected. On the other hand, providing extensive HIV/AIDS prevention services to participants as part of a microbicide trial may be construed by some critics as an undue influence, especially if the study is conducted among vulnerable populations such as sex workers and women from disadvantaged communities (Slack *et al*., 2005).

There are some reports on microbicide trials in developing countries that have targeted less educated, economically disempowered and vulnerable women. These women could have been selected for the sole reason that they are at most risk (Slack *et al*., 2005). This has implications for informed consent, as this group may have problems in understanding clinical trials and study procedures (Cohen, 2005; Moodley, 2002, 2007; Slack *et al*., 2005). In microbicide trials, at a minimum, the level of HIV infection risk should be no greater than if the participants had not participated in the trial. UNAIDS (2000) recommends that risk reduction measures such as counselling, condom promotion and training in condom negotiation skills should for part of the HIV prevention trials in order to ensure that infection risk behaviours do not increase over those reported at enrolment. These risk reduction measures should be extended to all trial arms. The same guidance is also echoed by Kilmarx *et al*., (2001) and UNAIDS

(2006). The guidance by UNAIDS is important as it is aimed at ensuring that HIV prevention trial participants are protected from obvious risk as they contribute towards the common good.

Kilmarx *et al*. (2001) note that research participants in microbicide trials are already marginalized by the very characteristics and behaviours that initially put them at risk of HIV infection, including engaging in commercial sex work and also being resident in a developing country with high HIV infection rates. As a way of taking the above into consideration, microbicide trials are moving away from concentrating only on very high risk individuals such as sex workers to also including women who may not have many sexual partners (UNAIDS, 2007; Van Damme, 2002). Microbicide trials have provided risk reduction counselling and condom promotion as part of the study procedures so that researchers are not seen as waiting for infections to happen (Hearst and Chen, 2004; UNAIDS; 2007). Some countries such as South Africa and Kenya have even gone further to provide some national guidance on the conduct of HIV prevention trials (Kenya Ministry of Health, 2005; Medical Research Council, 2003; Uganda AIDS Commission, 2006). The efforts by the three counties are aimed at supplementing UNAIDS guidance published in 2000 and revised in 2007 by providing national guidance on some of the ethical challenges that have affected some HIV prevention trials in the past. The issues discussed in this section provide evidence on the ethical challenges bedeviling HIV prevention trials. The advent of tenofovir will definitely influence the HIV prevention research landscape. The next section focuses on studies that have assessed HIV prevention trial participants' understanding of research participation.

2.4 ASSESSING HIV VACCINE TRIAL PARTICIPANTS' UNDERSTANDING

To date there are a few studies that have been conducted to test HIV prevention trial participants' understanding of procedures and concepts within the context of vaccine trials. One of the few studies that has been conducted investigated the comprehension of key trial concepts among HIV vaccine trial participants from Brazil (Quieroz da Fonseca & Lie, 1995, 1999) The study included some questions on general aspects related to the trial and attitudes towards clinical research. The study identified serious levels of misunderstanding about trial design issues even after these had been explained to the participants. Challenges in comprehension related to issues about randomisation and the unknown efficacy of the product being tested. Those who showed higher levels of comprehension were less likely to agree to participate in the study. The findings suggest that those who were agreeing to participate in the study were not agreeing on the basis of sound understanding. The study also identified some serious misconceptions about vaccines with some of the respondents believing that the test product was 100 percent effective in protecting them against HIV infection.

In a study conducted in the United States to identify injection drug users (IDUs) at high risk for human immunodeficiency virus (HIV) infection in preparation for a Phase II HIV vaccine trial, Harrison *et al*. (1995) studied willingness of drug users to enrol and their comprehension of consent. A 17-item true/false test was administered to a group of 39 IDUs and another group of 32 non-IDUs. The authors found comprehension of informed consent to be high (median score, 16 of 17 for IDUs and non-IDUs). Three IDUs were excluded from enrolment due to lack of comprehension. Follow-up rates were similar for IDUs and non-IDUs. The authors concluded that recruitment of IDUs into HIV vaccine trials was feasible, that IDUs can comprehend and complete the informed consent procedures, and that they return for follow-up

visits. This study focused on short-term recall of information and not necessarily on the processing of the information. It is important to note that while this study was conducted in the context of a developed country, it was conducted among a vulnerable population which displays some characteristics similar to those of some populations in developing countries.

In an HIV vaccine trial (AIDSVAX trial) in Bangkok, investigators assessed potential participants' understanding before the initiation of the trial (Kilmarx *et al*., 2001). They assessed potential participants' comprehension of an educational session introducing a hypothetical clinical trial as part of the willingness to participate survey. After the education sessions, they found comprehension to be high, but results indicated the need for special attention to be given to the concept of placebo as well as unknown efficacy of the vaccine under study so that the participants would understand that study participation would not confer protection from infection. In another trial in Bangkok (Carraguard vaccine trial) after an education programme and willingness to participate (WTP) survey, the most incorrect answers were about staff blinding with regard to participant active ingredient arm allocation and the concept of partial effectiveness (Kilmarx *et al*., 2001). In both the AIDSVAX and the Carraguard trials, the English language version of the consent forms were written at 8th grade reading level, translated to simple Thai and back translated to English by an independent translator. The Carraguard consent form was further adapted by a Thai behavioural scientist to make an information leaflet which was reviewed and approved by the community advisory board (CAB) for clarity (Kilmarx *et al*., 2001).

In a study comparing four measures of understanding for potential participants being prepared for enrolment in South African HIV vaccine trials, Lindegger *et al*. (2006) used detailed operational scoring criteria in the assessment of understanding of seven key trial components.

The scores for the seven components were compared via self-report, checklist, vignettes, and narrative measures. Fifty-nine participants, including members of vaccine preparedness groups and one HIV vaccine trial were recruited for this study. The authors reported significant differences across the measures for understanding of 5 components and for overall understanding. Highest scores were obtained on self-report and checklist measures, and lowest scores were obtained for vignettes and narrative descriptions. The findings suggest that levels of measured understanding were dependent on the assessment tools used. Forced-choice measures like checklists yielded higher scores than open-ended measures like narratives or vignettes. The findings further suggest that checklists and forced choice questions are good at capturing short term recall, which simply entails recalling some information without necessarily using the information in reasoning. The authors recommend that informed consent researchers should complement checklists and self-reports with open-ended measures, particularly for critical trial concepts, where the consequences of misunderstanding are potentially severe.

In a study conducted in Los Angeles, USA to assess willingness to participate (WTP) in hypothetical Phase III preventive HIV vaccine trials, and the impact of trial attributes on WTP, Newman *et al.* (2007) assessed WTP among 123 participants using eight hypothetical HIV vaccine trials. The study was conducted among low socioeconomic, ethnically diverse adults from communities at elevated risk for HIV infection Lower WTP was associated with vaccine-induced infection risk, false HIV-positives, no provision of free HIV medications and longer trial duration. The authors concluded that HIV vaccine trial attributes may strongly influence WTP. The authors noted that although the candidate vaccines do not cause HIV infection, perceptions of risk may impede WTP. They recommend that before recruiting participants for a trial, trialists need to engage in education campaigns to address issues of limited understanding and misinformed decisions. The current section has reviewed a few

studies that assessed HIV vaccine trial participants understanding of trial participation. The next section focuses specifically on microbicide trial participants.

2.5 ASSESSING MICROBICIDE TRIAL PARTICIPANTS' UNDERSTANDING

There is a small volume of literature on studies that have tested trial participants' understanding of procedures and concepts within the context of microbicide trials. One of the few studies evaluated trial participants from a major multi-site Phase III microbicide study referred to as COL 1492. The COL 1492 study was conducted in Durban (South Africa), Cotonou (Benin) and Hat Yai (Thailand) to evaluate the effectiveness of Nonoxynol-9 in preventing the transmission of HIV. The study was conducted between the years 1998 – 2000. This study which was evaluating trial participants' understanding, was conducted as a sub study of the main microbicide trial by some of the co-investigators of the main study. The evaluation included trial participants from all the three sites. An evaluation of trial participants' understanding after three months of enrolment indicated that a greater proportion of women were not able to understand concepts and procedures provided during the initial informed consent process. Women with no education fared worse than those with some formal education and nearly all women believed incorrectly that both products had a protective effect (Kilmarx *et al*., 2001).

In Thailand, testing of women's knowledge revealed that informed consent information was not understood. The same study also revealed that 58 percent of the women at the Cotonou site did not remember the name of the gel under study and 30 percent did not fully understand that the gel was being tested for preventing HIV and STDs. About 25 percent of the women could understand what a placebo was and 35 percent understood the importance of remembering their

study and randomisation number, which identified the gel they were receiving. After an intervention reiterating the informed consent procedure at each visit, 82.8 percent of the women were able to explain the notion of placebo five months later. Re-assessment of trial participants was conducted throughout the trial.

An intervention which included colourful charts with graphic presentations was said to have proven successful, but the rate of success was not quantified. At the Cotonou site, several methods were employed to promote understanding. These included role plays, using different methods to explain randomisation, placebo and double-blinding (Kilmarx *et al*., 2001). Unfortunately there was no follow-up to evaluate the effectiveness of these strategies on trial participants' understanding. However, focus group discussions at the end of the trial suggested that some women still did not understand the blinding process (Kilmarx *et al*., 2001). At the Cotonou site, several methods were employed to promote understanding, including role play and different methods to explain randomisation, placebo and double-blinding.

At the Durban site of the same microbicide trial, 70 percent of the women did not understand that they were in a trial even after three months. The women thought that the microbicide and the placebo would protect them from sexually transmitted diseases (STDs) and HIV. Asked why they liked the gel, some of the women responded that the gel protected them from STDs and this had an effect in that the women in both arms of the study reported fewer symptoms of STDs since enrolment. They attributed this to the gel rather than to the increased condom use or the syndromic standard treatment they obtained as part of the study (Ramjee *et al*., 2000). The authors therefore concluded that some of the women may have believed that the test product they were using had a protective effect and therefore minimised condom negotiation with their partners (Kilmarx *et al*., 2001; Ramjee, 2007; Ramjee *et al*., 2000,).

Kilmarx *et al*. (2001) concluded that it may take several weeks or even months before participants understand the concepts and procedures of clinical trials. They recommend that future trials should have a short run-in period prior to implementation to allow for the understanding of trial procedures. They also recommend that participants should be asked about their knowledge of the study, their reasons for participation and whether their participation was voluntary or not. Overall, Kilmarx *et al*. concluded that low education levels were associated with poor understanding

As a result of the debates surrounding the quality of informed consent, the HIV Prevention Trials Network (HPTN) has developed a conceptual framework for an enhanced informed consent process which drew upon the experiences gained during the various trials conducted by HPTN throughout the world (Woodsong & Abdool Karim, 2005). The framework is designed to ensure initial and continued understanding of research information with an emphasis on HIV prevention research. The majority of HIV prevention trials conducted by HPTN involve the testing of new methods of preventing HIV using HIV negative persons. For such trials, it is important for participants to remember that they are participating in a trial aimed at testing a product. That way they may not to adopt some risky behaviours. Attention in information provision is focused on the individual and the community, and the framework focuses on the three study phases: pre-enrolment, enrolment and post-enrolment.

During the pre-enrolment phase, researchers have to identify the best ways to convey research protocol concepts, recognise community concerns about HIV and respect community norms on decision making. During the enrolment phase, focus is on the individual and not on the community. To ensure that the researchers adequately address the information needs of the individual, this phase is further divided into smaller phases, which include information disclosure, discussion and decision making. During the post-enrolment phase, focus is on both

the individual and the community. Staff and the community monitor any issues arising in the study and work towards addressing them. During this post enrolment phase, the community advisory board (CAB) takes centre stage as the bridge between the community and the research team. During all three phases, researchers need to continuously provide information, assess understanding, and take positive steps to clarify any misunderstanding or misconception (Woodsong & Abdool Karim, 2005). This initiative by HPTN is very important as it is a clear acknowledgement that the area of informed consent needs concerted effort if informed consent is to be adequately informed.

The current section has highlighted some of the debates in the area of microbicide trials. The section has also highlighted some of the ways in which the microbicide trial community is responding to the ethical challenges. The next section is devoted to studies that have assessed trial participants with limited decision making abilities.

2.6 ASSESSING PERSONS WITH LIMITED DECISION MAKING CAPACITIES

This section reviews and discusses studies conducted to assess the understanding of patients with serious mental illnesses. While the studies focused on persons with limited decision making capacities, there are some important lessons that can be learned about assessing trial participants in general. Some of the issues that are relevant to persons with limited decision making capacities are also relevant to individuals who are not classified as such. These include how researchers can make the informed consent language simple. Decision making capacity is essential in informed consent as decisions to enrol involve the processing of information. Some of the previous studies have concentrated on patients with schizophrenia and other psychotic disorders.

One of the studies focusing on patients with limited decision making capacities was conducted by Baskin, Morris, Ahronheim, Meier and Morrison (1998). The authors conducted a quantitative study in the USA to identify barriers to informed consent for patients with advanced dementia. They were interested in patients who were above 65 years. They recruited 165 patients and their surrogates. Three percent of the surrogates understood the purpose of the study but refused for the patients to enrol their wardees. About 19 percent of the surrogates were unable to understand the research protocol and therefore they could not give informed consent on behalf of the patients. No indication was given by the authors as to how they assessed the understanding of surrogates.

Pucci *et al*. (1999) report on a study which investigated the ability of middle-aged and elderly caregivers to understand and retain information about randomised controlled trials in patients with Alzheimer's disease. They reported that 40 caregivers were given information in a semi-structured manner and were also provided with information sheets. Twenty-eight of the 40 caregivers could not explain why placebo, randomisation and double-blinding procedures were used in the trials. Eight of the forty only had a vague idea about experiment and possible use of a placebo but could not recall any other information. Twenty percent of the caregivers were not aware of the influence of chance in the process of assignment to treatment groups. The study identified a relationship between education level and understanding. Pucci *et al*. point to the complexity of methods for RCTs and the poor education of many potential participants as important factors in understanding the problem of low levels of understanding.

In a study to test a new tool to assess depressed patients capacities to consent, Appelbaum, Grisso, Frank, O'Donell and Kupfer (1999) recruited 26 women in USA diagnosed with depression and had joined a psychotherapy trial. Participants were recruited shortly after

joining the trial and having participated in the first session of the trial. They were given the MaCAT-CR, a semi-structured interview instrument which was designed to assess understanding of disclosed information about the nature of the project and the study procedures. The assessment tool was designed to assist in the assessment of competence to consent to treatment. It is administered in the form of a semi-structured interview format to assess and rate the abilities of potential research participants according to 4 components of decision making which are usually considered in clinical settings. The four abilities include understanding of disclosed information about research purposes and procedures, reasoning about participation, comparing alternatives in terms of their consequences, and appreciation of the effects of research participation.

The 26 women were administered the same MaCAT-CR tool about ten weeks later. The mean score of understanding was 23.33 out of a maximum of 26, with no volunteers scoring below 20. In this study, the authors unfortunately did not set the cut-off score judged as reflecting an adequate level of understanding. The MaCAT procedure also did not include patients' understanding of why the trial was being conducted in that particular way. In this way, the procedure did not allow the patients to reason beyond recall of disclosed information (Appelbaum *et al*., 1999).

Kitamura and Kitamura (2000) reported on a quantitative study they conducted in Japan. The study was aimed at assessing clinicians' judgement of psychiatric patients' competence to give informed consent. A total of 176 members of the Japanese Society of Psychiatry and Neurology gave clinical judgement in a questionnaire of competency. The study concluded that clinicians' global judgement of patients' competency was not reliable and recommended the use of structured interviews in improving the judgments. The findings from the study

clearly highlight the weaknesses in some studies that use self reports without conducting some tests employing valid measures.

Kovnick, Appelbaum, Hoge and Leadbetter (2003) reported on a study that was investigating competence to consent to research among long–stay patients with schizophrenia. In the study, the MacArthur Competence Assessment tool was administered to 27 patients and 24 members (normal controls) of the same age as the patients selected from the community. Significant differences were found between the patients and the control group that was made up of members from the general community. The differences related to the abilities of patients to understand disclosed information and use it to reason and appreciate the facts about the study. Consequently, the degree of psychopathology and cognitive reasoning were found to be negatively correlated with understanding and appreciation of facts among the patients. The findings highlight the difficulties that patients encounter in providing consent to research and the need for using various techniques aimed at facilitating decision making in the face of decisional impairments.

Dunn and Jeste (2003) conducted a study aimed at establishing problem areas in the understanding of informed consent among middle aged and older patients with psychotic disorders. They examined a post-consent test of comprehension given to older patients with psychotic disorders in order to identify challenges in the understanding of informed consent for research. The study was comparing the effectiveness of a routine, paper-based disclosure of study information, with an enhanced computerized slide show incorporating more information. The authors recruited 102 middle-aged and older patients with schizophrenia (and other related psychotic disorders) and 20 normal comparison participants and randomised them to the two information disclosure methods. After the information disclosure, the researchers administered a 20-item questionnaire aimed at assessing comprehension of information disclosed during the

informed consent process. They established that patients had more difficulty than normal comparison individuals regarding open-ended questions and study procedures. Among patients, the enhanced procedure was associated with better performance on questions concerning risks. They concluded that study procedures, study risks and study benefits constituted problem areas in informed consent and that these needed to be focused on if attempts to improve informed consent were to be successful (Dunn & Jeste, 2003).

In a study conducted to examine issues surrounding the obtaining of informed consent from older and frail patients, Barron, Duffey, Byrd, Campbell and Ferrucci (2004) noted that the challenges involved in obtaining informed consent from older patients include physical frailty, reduced autonomy, and impaired-decision making due to dementia, delirium or other mental illnesses that affect older persons. The authors noted that it became difficult to evaluate decision-making capacities in old-aged participants as, in some cases, the decision-making capacity may be partly impaired. The authors also singled out studies that look at end of life issues in old age. Such studies typically involve frail older participants and take place in institutions where the older patients may have neither rights nor privacy. The authors recommended that research involving older patients should use simple language in informed consent documents.

Palmer *et al*. (2005) conducted a study aimed at assessing the capacity to consent to research among older persons with schizophrenia, Alzheimer's disease or diabetes mellitus. The main aim of their study was to compare the decisional capacities of the three patient groups and to examine the effectiveness of a brief set of screening questions in detecting impaired understanding. The researchers used a 3-item decisional questionnaire and the MacArthur competence assessment tool for clinical research. They reported that patients with diabetes mellitus performed best on the capacity instruments while patients with Alzheimer's disease

had the worst performance and patients with schizophrenia were in the middle. The level of cognitive functioning as measured by the Mini Mental State Examination (MMSE) was generally the best predictor of decisional capacity. The three-item questionnaire that they were testing was found to be sensitive to impaired understanding as measured by the MacArthur Tool.

In another study aimed at assessment of therapeutic misconception in older schizophrenic patients, Dunn, Palmer, Keehan, Jeste and Appelbaum (2006) found that patients with less education or worse cognitive functioning had higher levels of therapeutic misconception. Degree of therapeutic misconception was inversely related to understanding. The authors examined the frequency of therapeutic misconception with a true/false scale among 87 middle aged and older patients with schizophrenia. They assessed the therapeutic misconception levels based on what the patients thought about a hypothetical double blind, placebo controlled trial. The patients were informed that they were going to be invited to join the hypothetical trial. Therapeutic misconception was assessed using six true/false questions; each question had a possible score of zero (0) for the correct answer and one (1) for the wrong answer. Those participants with a higher total score (closer to 6) had higher levels of therapeutic misconception. Overall, 69 percent of the participants were classified as having some level of therapeutic misconception. The majority of participants were aware that the researcher would be blind to medication assignment. The strongest correlates of therapeutic misconception were found to be lower education, severity of cognitive deficits, and worse decisional capacity.

In a study aimed at improving informed consent among patients with psychiatric conditions, Wirshing, Wirshing, Marder, Liberman and Mintz (1998) designed and evaluated a rigorous informed consent procedure for patients with schizophrenia. In their study, informed consent documents were read and explained to patients and then a questionnaire was administered to

assess their levels of comprehension. Protocol procedures were repeated until patients answered 100 percent of the questions correctly. Patients were asked the same questions 7 days later to ascertain what they could recall. Patients' median score on the first test was 80 percent. 53 percent of patients required a second trial to obtain 100 percent correct, while 37 percent required 3 or more trials. Generally, scores improved from day 1 to day 7. On the seventh day, 96 percent of patients felt adequately informed. The study demonstrated that with some effort on the part of informers, persons with decisional incapacity are able to understand and retain some critical informed consent information. The authors did not report how they tested for reliability and validity. The questionnaire used in the study included various aspects of trial information but the authors did not report the analysis of the individual responses. It is therefore not clear which aspects were better understood. Overall, the questionnaire appears to test knowledge recall and ability to learn correct answers rather than measuring understanding.

In order to investigate the perceptions of participants in depression prevention trials, Busby-Grant, Mackinnon, Christensen and Walker (2009) examined participants' motivations for joining the research and their views on randomisation. The researchers also wanted to find out if the participants understood their right to withdraw from the research at anytime. They recruited 900 adults out of a total of 105,000 that they had initially targeted, who had reported elevated depression symptoms in both urban and rural areas of Australia. Participants were required to rate their agreement or disagreement with statements in the questionnaire. The respondents expressed a variety of reasons for joining depression prevention trials including altruism. The participants were not concerned about randomisation. Over half (56 percent) of the 900 respondents did not state preference for any particular treatment arm. The findings suggest that participants indicating elevated symptoms of depression are more likely to view depression prevention trials in a positive way. This finding perhaps points to an expectation of some personal benefit in the form of prevented illness.

The current section by focusing on persons with limited decision making capacity, has highlighted challenges that researchers may face in conducting research with persons with limited decision making abilities (including both patients and surrogates). The next section focuses on participants from oncology trials.

2.7 STUDIES ASSESSING UNDERSTANDING OF CANCER TRIAL PARTICIPANTS

Much research in oncology is being conducted in countries such as the USA because of the growing magnitude of the cancer problem. Cancer illness presents some unique challenges due to its nature. Due to lack of effective treatments for some cancers and the severe nature of the disease in general, some cancer patients end up turning to phase I cancer trials as the last hope after failure of available treatment options (Daugherty, 1999; Daugherty *et al*., 2005; Morrow, Gootnick & Schmale, 1978). This presents challenges when it comes to the obtaining of informed consent. Because of the desperation dynamic, researchers are anxious to establish that cancer trial participants enroll with adequate understanding and voluntariness.

Joffe, Cook, Clearly, Clark and Weeks (2001) conducted a cross-sectional survey in the USA aimed at assessing the quality of informed consent in cancer clinical trials. The study involved a questionnaire which was sent to 287 adult patients with cancer who had recently enroled in a clinical trial; 207 of the 287 patients responded. Ninety percent of respondents indicated that they were satisfied with the informed consent and considered themselves to be well informed. However, seventy percent (70 percent) did not recognise the experimental nature of the treatment and 29 percent were not aware of the uncertainty of benefits to themselves or that trials are mainly done to assist future patients (25 percent). In multiple regression analysis,

college education, presence of a nurse and careful reading of the consent were, among others, associated with increased understanding. Only 46 percent of the respondents recognised that the main reason for clinical trials was to assist future patients. This finding may reflect the biased information that researchers may provide to potential participants during the informed consent process or the desperation of those seeking treatment for an incurable illness. The findings may also reflect a confusion between researchers' purposes and the trial participants' own purposes. The authors (Joffe *et al.,* 2001a) observed that their pilot sample scored higher on perceived understanding than on observed or measured understanding. However, when they measured the two levels of understanding using participants from various trials, they found self assessment and the measured scores were significantly correlated. The authors did not explain the contents of the template that was used in the study.

In a study conducted to assess the readability of informed consent forms that describe clinical oncology protocols, Grossman, Piantadosi and Covahey (1994) collected 137 consent forms from 88 protocols that were recruiting patients at one hospital. For each consent form, three readability indices were obtained, namely the Flesch Reading Ease score, the grade level readability score as determined by the Flesch-Kincaid formula, and the Gunning Fog index. The study concluded that consent forms for oncology trials were written at a level that was difficult for most patients to read, despite the fact that the consent forms would have been reviewed by various parties, including institutional review boards. They recommended that the informed consent needs to be strengthened by improving readability of the informed consent forms.

A similar study which focused on readability and lengths of informed consent forms was conducted by Sharp (2004). The study revealed that none of the 107 forms collected were written at below the 8th grade reading level. The study concluded that consent forms in

oncology trials were so lengthy and complex that patients are not interested in reading them or are even able to understand the concepts discussed. Sharp also reported that institutional review boards (IRBs) are not interested in lowering the readability levels of informed consent documents. This study has implications for the role of IRBs in ensuring that study participants can understand the documents that they are asked to sign.

A study was conducted with the aim of assessing willingness to participate in oncology trials by Ellis, Butow, Tatersall, Dunn and Housammi (2001). The team conducted a cross-sectional survey among women attending a breast cancer clinic for screening and treatment, to assess attitudes towards and willingness to participate in randomised clinical trials of breast cancer treatment. They found that 33 percent would consider participating in a clinical trial if they had breast cancer. Women with breast cancer (30 percent) were more likely to decline to participate than women attending for screening (15 percent) or diagnostic assessment (15 percent). Women who indicated that they would consider participation were more knowledgeable about randomised trials.

A qualitative study conducted in Australia indicated that patients who demonstrated greater knowledge about the clinical trial were less willing to participate in the trial (Ellis & Butow, 1998). In this study, 21 mothers and grandmothers were recruited in addition to 21 breast cancer patients. The study established that most women had some knowledge about randomisation but were neither aware of its purpose nor of how it was going to be achieved. The study highlights the importance of context in disclosure of information as highlighted in the conceptual framework discussed in Chapter 3. The study specifically highlights the challenge of explaining a trial to a potential participant immediately after diagnosis with a disease such as cancer. The authors call for the need to educate the public about research so as to ensure that they are aware of clinical trials and how they are conducted. With a public

sensitization programme on clinical trials in place, researchers could only concentrate on addressing issues that are specific to their study such as the procedures, risks and benefits.

In a descriptive qualitative study which was aimed at assessing knowledge and understanding of oncology trial protocol, Barrett (2005) distributed a questionnaire to 17 patients who had agreed to participate in an oncology trial. Only eight of the 17 responded. The questionnaire focused on knowledge of informed consent and the oncology protocol for which they had enroled. Results indicated that participants had a good overall understanding of the elements of informed consent as well as the trials for which they had enroled. Interestingly, half of the respondents failed to understand that treatments in these clinical trials were not standard treatments and could involve some additional risk when compared to standard treatments. The author concluded that the Quality of Informed Consent (QUiC) questionnaire may be a useful tool in providing feedback on trial participants' understanding of the elements of informed consent and that the feedback could be used in providing additional information in areas of need. Barrett recommended that there is need for more research on the development of reliable tools that can be used in assessing understanding as well as interventions aimed at improving understanding of the research process.

The current section has highlighted the effect of desperacy in informed consent, a characteristic which may be common among cancer patients. Such a characteristic may also obtain in poorly resourced communities where individuals may look up to clinical trials for some benefits. The next section focuses on studies conducted in developed countries to assess trial participants understanding of research participation.

2.8 STUDIES CONDUCTED IN DEVELOPED COUNTRIES TO ASSESS UNDERSTANDING OF TRIAL PARTICIPANTS

Whilst there is a limited amount of literature focusing specifically on assessment of microbicide trial participants, there is a significant amount of literature which exists on previous studies aimed at assessing trial participants' understanding in other contexts. Whilst a significant amount of the studies identified low levels of understanding, the researchers did not introduce interventions aimed at improving understanding A separate section has been specifically devoted to those studies in which interventions were introduced. In this section, assessment studies that were conducted in developed countries are discussed.

One of the earliest studies aimed at assessing trial participants' understanding was conducted by Faden and Beauchamp (1980). The two authors conducted an empirical study focusing on the impact of disclosed information on decision making and informed consent among patients considering consenting to the use of non-surgical contraceptive techniques. They found that disclosed information was not the sole determinant of the consent decision. This is relevant to the first premise of this study (see Section 1.3). The study revealed, however, that disclosed information has some effect on the decision making process and that the utilisation of the disclosed information was directly correlated with the quality of comprehension.

In a study which was aimed at determining whether trial participants had perceived adequate information about the trial Lynöe, Sandlund, Dahlqvist, and Jacobsson (1991) sent a questionnaire by post to 53 women 18 months after the completion of a reproductive health trial. Adequacy of the information was assessed based on the criteria set out in the Declaration of Helsinki: understanding of the aims of the study, awareness of what participation meant, and awareness of the freedom to withdraw at any time. Interestingly, 42 of the 43 respondents were

aware that they were participating in a clinical trial, seven (7) reported that they were not aware of the meaning of research participation, 17 were not aware that they had the right to withdraw at any time. The study concluded that differences in understanding were mainly a result of the variations in the way the informers provided information.

Dawes, O'Keefe and Adcock (1992) prospectively assessed the effectiveness of two structured interview techniques on patients' recall of information provided. They randomly assigned 190 cancer patients into four groups as follows: one group had no consent interview during the study period, the second had an informal interview, the third had a structured interview and the fourth had a structured interview which was supplemented with an information sheet on the procedure the patients were to undergo. Initially, all patients had higher anxiety levels but for all other groups, anxiety levels went down after seven hours with the exception of the first group which maintained a higher level throughout the study. Only 37 percent of patients recalled the operation's name and the third and fourth groups recalled a higher mean number of complications recalled per patient. The authors concluded that a structured interview when obtaining informed consent increases the amount of information recalled without increasing patient anxiety.

Some research has confirmed the need to focus on both the direct and indirect messages received during informed consent as these have some bearing on understanding. Participants can use some body language in posing questions and if the researcher is not focusing on the body language, they will not be responding to the informational need. Tomamichel *et al*. (1995) concluded that greater attention should be paid to the indirect messages and the criticisms by the patients in order to improve their participation in decision making. In their study, the authors audio recorded 32 informed consent conversations and later assessed the conversations using the Meerwein Model's three dimensions of the informing process: the

information itself, and the emotional and interactive aspects. The study revealed that the informers scored highly on the information and emotional dimensions but scored low on the interactive dimension. Doctors were specifically not aware of the indirectly expressed anxieties of the patients. The study confirmed the usefulness of Meerwein Model in identifying challenges in communication. More interaction was associated with greater understanding by trial participants. The authors recommended that researchers need to be trained in the art of communication and provision of adequate information.

For the information dimension, the study focused on the following; clear communication and comprehensibility, clear explanation of rationale of information given, clear explanation of the treatment proposed, provision of all the relevant information, avoidance of unnecessary technical terms, explaining the technical terms used, asking suggestive questions, avoiding too much information per unit of time and verifying whether the patient has understood. For the emotional dimension, scores were provided for the following; showing respect for the feelings and experiences of the patient, being friendly to the patient, treating the patient with respect, encouraging the patient and showing interest in the patient. For the interactive dimension, the authors focused on the following; criticising patient's direct statements, indirect statements, complaints and objections, reacting to patient's direct or implied criticism, discussing directly and indirectly expressed needs and anxieties of patients, allowing time for patients to react and taking full responsibility for the medical care of the patient (Tomamichel *et al*., 1995).

In order to ensure informed consent and to ensure that the participants would have understood the information disclosed, including potential benefits and risks, Melby, Mendelson and Jones (1996) administered a brief questionnaire after prospective trial participants had read the informed consent document. The participants comprised of heroin and cocaine dependent users who were potential participants in a clinical trial which was focused on addressing drug

addiction. The questionnaire allowed researchers to confirm that the participant was literate and understood the information in the document. Responses to the questionnaire also assisted the team in pin-pointing areas of the form that were unclear and needed to be revised. The questionnaire was also used for screening out those participants who were unable to comprehend or those with a different understanding of the trials. The authors confirm that due caution is necessary in dealing with groups such as hard substance abusers in addition to a clearly written and concise informed consent form. Such individuals process disclosed information in different ways depending on various factors such as whether they have taken the hard substance or not.

A study using a qualitative approach relying on in-depth interviews which carried out with 20 participants from a randomised controlled trial in the UK was conducted by Featherstone and Donovan (1998). The study was aimed at exploring trial participants' understanding of randomisation. The sample was chosen to reflect a broad range of individuals and experiences. The majority of respondents were able to recall and describe aspects of randomisation such as the involvement of chance, comparison and concealment allocation. On the whole, however, the majority found the concept of randomisation difficult to understand and developed their own explanations to make sense of their experiences in the trial. The authors identified the problem of inadequate and inaccurate patient information which led to confusion, and concluded that the provision of clear and accurate information was essential. They recommended that patients need to be apprised on the purpose of randomisation during informed consent so that they can make sense of this concept and give truly informed consent. From the report, the period between the invitation to participate in the trial and the time of the interview was not clear. The authors mentioned that they included some measures for confirming the accuracy of their data but they did not offer a description of the measures.

A structured literature review of published empirical research on informed consent with adults was conducted by Sugarman, McCrory and Hubal (1998) in order to make recommendations aimed at improving informed consent and to highlight areas needing further research. A total of 99 publications met their inclusion criteria. In the majority of studies, diminished understanding of informed consent was associated with older age and fewer years of education. They found that studies which had looked at the disclosure of information mostly suggested strategies aimed at improving understanding which included simplified forms, story book, video and others. These studies had also recommended procedures such as the use of neutral health educators, quizzing participants, multiple disclosure sessions and others. The authors concluded that various strategies should be considered when designing materials, policies and informed consent procedures.

Meade (1999) also conducted a review of literature, education and communication models. Meade concluded that information communicated during the informed consent process is difficult to understand, thereby raising ethical concerns about whether informed decision making had taken place. The strategies recommended by Meade (1999) and Sugarman *et al*. (1998) were not tested. Their studies were simply aimed at highlighting potential strategies that can be used in improving informed consent.

In an effort to find out what patients, the general public and healthcare professionals thought about trials, Edwards, Lilford and Hewison (1998) undertook a review of literature on attitudes to trials. The authors identified a total of 61 studies on attitudes to trials – 54 based on quantitative methods, six based on qualitative methods, and one employing a mix of both approaches. Twenty studies made use of hypothetical trial scenarios. From this review, the authors concluded that doctors do not seem to take informed consent from competent patients as they should. They also found that a large number of participants even in phase III trials

came out of consultations expecting to benefit personally from the trial – an indication of a therapeutic misconception.

In a study to investigate whether linguistic analysis and changes in information leaflets improve readability and understanding, Bjorn, Rossell and Holme (1999) conducted a quantitative study in Denmark. They simplified leaflets from two trials, rearranged and broke the text into smaller paragraphs with subheadings, and replaced professional language with lay language. About 235 volunteers were recruited and randomised to two groups. In each group, the individuals would be given the original leaflet and the revised one. The volunteers reported that the revised leaflets were easier to read and to understand compared to the forms that were used in the original trial leaflets. More participants perceived that they understood all the information in the revised leaflet compared to the original leaflet. For this study, the authors did not report on testing for reliability and validity of the questionnaires.

With an increase in emphasis on research ethics during the 1990s, there was a significant increase in studies focusing on trial participants' understanding in the new millennium. One of the earliest studies in the new millennium was conducted by Mason and Almark (2000). The study looked at the obtaining of informed consent from parents for clinical trials with neonates. Semi-structured interviews were conducted with 200 parents of babies who had been asked for consent to participate in neonatal trials and 107 neonatologists who were involved in seeking consent. Validity of consent was assessed using four components: parental competence, information given, parental understanding and voluntariness of consent. They found that 59 of the 200 parents (29,5 percent) had given valid consent while the rest had some problems in one of the four components. Impaired consent was more evident in research in emergency situations and for research involving risk or discomfort greater than standard treatment. In this study, 20 percent of the parents were excluded from analysis as they were considered to have

some serious difficulties with understanding. The study found that 95.3 percent of the doctors involved in obtaining informed consent had not received any formal training in obtaining consent but had learned by observing their more experienced colleagues. It is not clear how the neonatologists in the study were assessed since it was possible that those who had problems simply did not report the problems.

A study aimed at assessing the impact of information disclosed to potential participants on levels of anxiety and depression was conducted by Tomamichel *et al*. (2000). The authors found that levels of patients' anxiety and depression were not adversely affected by the information provided. In this study, 59 percent of respondents indicated the possibility of benefits as their main reason for agreeing to join the study. This was judged to be the main reason for participation by 78 percent of the study nurses and 86 percent of the study investigators interviewed. The majority of respondents reported that they found the information provided to be clear and sufficient. The findings reported by the study participants, nurses and investigators point towards a degree of therapeutic misconception since this study was a Phase I study.

In a quantitative study aimed at examining the opinions of a cohort of individuals who had participated in a randomised controlled trial (RCT) on acute myocardial infarction in Israel, Yuval *et al*. (2000) mailed a questionnaire to 360 patients. Of these, only 150 responded. Main outcome measures in this study included patient perception of informed consent procedures, comprehension of the study aims and procedures, opinion regarding participation in the study, and interest in present and future trials. Thirty-one percent of the respondents perceived that they had full comprehension while 50 percent claimed incomplete understanding and 19 percent claimed no understanding at all. Comprehension was high for patients who had an opportunity for discussion during the obtaining of informed consent. The majority of patients

recalled the oral information while a minority recalled the written information. Forty-three percent of the patients gave consent in the hope of receiving better treatment. This study relied on self-reporting for comprehension. Self-reports and tests may yield different results as individuals may even report that they understood something when in actual fact they may not have understood or comprehended.

The findings by Yuval *et al*. (2000) confirm the importance of discussing with patients and answering all their questions during the informed consent process. It also highlights the dilemma that patients commonly face in the healthcare setting. Patients in these settings may be forced by circumstances to participate in research for the sake of accessing better quality care that they cannot access through public facilities. This becomes more relevant in limited resource settings where public facilities may be overcrowded and poorly equipped as compared to research wards which may be equipped with state of the art equipment. In this study, measures of the informed consent procedure and comprehension were based on patients' perceptions and re-collections up to three months after the informed consent encounter.

In a qualitative study conducted in Sweden to investigate how patients in early phase myocardial infarction trials experience informed consent, Agard, Hermeren and Herlitz (2001) carried out semi-structured interviews with 31 patients who had consented to participate in three trials. Most participants felt that, when asked to participate, they had very low levels of understanding or they were in too much pain to bother about the information. Some participants had no knowledge at all about the trial as they did not even know that they had been included in the trial. Participants felt that they had no choice under the circumstances. While this study presents some very useful information about informed consent practices, the authors did not state how long the consent process was and at what point the respondents were interviewed. They did not report on how the analysis and findings were validated.

A team of researchers reported on a study in which they designed a brief questionnaire which they have termed the Quality of Informed Consent (QUiC). Joffe, Cook, Cleary, Clark and Weeks (2001b) report that the QUiC is a tool aimed at measuring participants' actual and perceived understanding of clinical trials. The QUiC questionnaire incorporates the basic elements of informed consent specified in US regulations and also assesses therapeutic misconception. After pilot testing for validity, the questionnaire was mailed to 287 adult cancer patients in Phase I, II and III trials. Two hundred and seven (72.1 percent) of the 287 patients responded and the questionnaire was re-tested with a random sample of 32 of the 207 patients for reliability. The questionnaire was further edited and the final version had 20 questions for objective understanding and 14 questions for subjective understanding. For each question, a correct answer is assigned a score of 100, a wrong answer a score of "0" and "unsure" a score of 50. Scores for each domain are obtained by averaging the scores for all completed question in that domain. Joffe *et al.* (2001b) concluded that the QUiC is a brief, reliable and valid questionnaire that can be used as a standardised tool in assessing the outcome of informed consent in cancer clinical trials. While the QUiC that they developed was specifically meant for cancer clinical trials because of their uniqueness, it could be edited to be usable as a robust and flexible tool that can be used for any kind of clinical trial.

Loh, Butow, Brown and Boyle (2002) report on a study aimed at assessing the effectiveness of using a third party such as a research nurse or a data manager in obtaining informed consent, instead of the study clinicians. Four focus group discussions were held in four hospitals with 21 data managers who were involved in cancer clinical trials. While the data managers indicated that they were happy to take part in the informed consent process, they indicated that they confronted some ethical dilemmas which put them in very difficult positions. They pointed out that, in some cases, the patients asked for medical information that the third parties were not familiar with – information that could only be provided by clinicians. At times they found

themselves dealing with patients who would have agreed to join the trial for the wrong reasons due to misunderstanding or need. This study illustrates some of the dilemmas that relate to efforts aimed at reducing conflict of interest in the situation in which study clinicians are involved in obtaining consent for their own trials. Furthermore, the data managers used in this particular study may not qualify to be labeled as third parties because they were already part of the research team. This compromises their stance as they play a role in meeting the targets set for the study team.

In a study that was conducted to examine how and why patients decided to participate in research and how much they understood about trial design, Featherstone and Donovan (2002) recruited 33 middle-aged and older men with lower urinary tract infection symptoms related to benign prostate cancer. Twenty two of the men had agree to participate in a trial testing the effectiveness of new laser technology compared with standard surgery while 11 had refused to participate in the trial. Data was collected through in-depth semi structured interviews. Most participants recalled various aspects of trial design, including the involvement of chance in assigning treatments. Participants indicated that they struggled to make sense of randomisation as they trusted that the clinicians were acting in their best interests. This study findings suggested that patients have challenges in understanding RCTs because of the way they look to clinicians for assistance. This buttresses the need for clear information and adequate time to discuss the trial with individuals who require more information. The authors recommend efforts aimed at improving public understanding of trials.

The question about the amount of information that needs to be provided in order to ensure adequate understanding, is a difficult one. Ferguson (2000) conducted a study aimed at exploring trial participants' views on the amount of information provided and of their own understanding of that information. Structured interviews were conducted with patients

participating in clinical trials of interventions for chronic medical conditions. Patients generally perceived that they were provided with an adequate amount of information, and that they were able to understand much or all of it. They felt they were given adequate time to ask questions before making a decision to participate. Patients felt that more information was provided in the trial environment than in the hospital environment. It is important to note that this study did not assess the participants' understanding but simply sought their perceptions of the amount and quality of information provided and their own perceptions of their own understanding. It is possible that the study could have suffered from a social desirability effect. With the social desirability effect, people report opinions that they think the questioner is expecting. Similar findings were reported by Abebe (1996) and Taylor (1999a) in Ethiopia and the USA respectively. The two authors found that patients often report that they have been provided with adequate information as they are not prepared to ask questions of the study clinicians.

The question of unblinding of treatment allocations at the end of the trial has received attention through a study conducted by Di Blasi, Kaptchuk, Weinman and Kleijnen (2002). The authors report on a study that they conducted to assess whether and how investigators of placebo controlled trials (PCTs) inform participants of their treatment allocation at the end of the trial, as well as to assess barriers to feedback. The authors mailed a semi-structured questionnaire to approximately 120 investigators that had published findings on PCTs in five leading medical journals during the course of one year. About 45 percent of the investigators reported that they informed all or most of their participants about the treatment arm they had been assigned to during the trial. The rest (55 percent) did not inform the participants or only informed those who enquired. Forty percent of investigators indicated that they never considered this option and 24 percent that they did not want to bias results during follow-up. This study presents some evidence that investigators may want participants to have enough knowledge for them to

participate in a trial but not complete knowledge about the trial, as complete knowledge may make recruitment and retention difficult (Morreim, 2009).

A quantitative study conducted in the United Kingdom aimed at ascertaining the views of researchers regarding the amount of information they provided to patients and whether this information was understood (Ferguson, 2003). The study found that researchers generally felt that they were required to give trial participants an appropriate amount of information and that the majority of patients had an understanding of the information that they provided. Investigators' opinions differed regarding the level of information they felt patients themselves wanted. The majority of researchers thought that the informed process remained important, even though some patients could not understand some of the information provided. These findings support the need for further research into effective ways of disclosing information so that the informed consent process may become more meaningful.

In studies that involve children or infants as participants, parents' understanding is crucial as the parents are the ones who have to make the ultimate decision about their child's involvement in the study. Mortensen, Kiyak and Omnell (2003) conducted a study which examined patient and parent understanding of children's Phase I orthodontic treatment trials. Interviews were held with 29 children aged 6-12 and their parents or guardians. Before the orthodontic treatment, the orthodontist explained the proposed treatment, reasons for the treatment, procedures to be used, risks and benefits, alternatives, and parents' responsibilities during the treatment. After the session, interviews were held with the children and parents or guardians. These were audio taped so that they could be compared with the orthodontist's presentation. The study established that both children and parents or guardians recalled very little about reasons for treatment, procedures and risks associated with the treatment. Such low recall rates raise concerns about treatment compliance, success, and ultimately the validity of informed

consent processes. It should be noted, however, that the study did not assess the effect of children's age on understanding in view of the large age range and that the study was about informed consent for treatment, not for research.

Various challenges have been noted in empirical research on informed consent. Sachs *et al*. (2003) studied the challenges that researchers face in conducting empirical research on informed consent. The authors noted several design issues that researchers have to consider. One of the challenges is that some investigators use hypothetical situations or vignettes to study decision making. The authors noted that while this is a noble approach, in some cases the responses may not reveal how real trial participants make decisions in a real situation. Some researchers choose to witness the informed consent process by sitting in during the interview. This may introduce bias as the participants could become conscious of being observed. This also affects the behaviour of the informer as he or she tries to ensure that they are unusually thorough in informing the participant, knowing that they are being watched.

The same authors also point out that informed consent studies are problematic in that one researcher would be asking another researcher and their participants to become participants in another study (Sachs *et al*., 2003). They suggest that informed consent researchers need the cooperation of the investigators they will be studying. Bias may also undermine the findings because of the selection of the projects. Investigators who are confident about their informed consent procedures will agree to have another researcher studying how informed consent was obtained, while those who are not confident will simply refuse to cooperate. Sachs *et al*. also noted that researchers studying informed consent may find themselves in a dilemma when they come across violations in informed consent processes. The researchers have to ask themselves whether to intervene or not, as well as question the effects of such interventions on their findings. The issues that these authors raise are real and yet difficult to address in the field. It

is important for informed consent researchers to be aware of these ethical issues as they have important implications on the findings as well as other aspects.

In an effort to compare original written forms, forms written in simple language, narrated videos, and self-paced computer based presentations of informed consent information, Campbell, Goldman, Boccia and Skinner (2004) conducted a study which examined the amount of information that is orally recalled from the different presentations of the same information. This study involved a simulation of the recruitment of children into two trials. The study used a non-clinic sample in order to ensure that the parents would not have been exposed to information related to the disease and the study at clinics. The parents were also not given an opportunity to discuss the two studies amongst themselves. No format-related differences in recalled information were found among the four groups. One would have expected the video narrative to lead to some improvements in information recall. These findings emphasise the necessity for researchers to not only repackage the same information into different formats but to think of how the concepts and procedures can be better understood.

Lay conceptions of the ethical and scientific justifications for trial procedures are important as they influence the type of information that researchers need to prepare. Robinson *et al*. (2004) were specifically interested in establishing lay conceptions of the ethical and scientific justifications for randomisation in clinical trials. Around half of the respondents found it difficult to accept the fact that a clinician could be completely uncertain about which of two treatments was better. The majority of participants found randomisation to be unacceptable as it did not clearly demonstrate which treatment was better than the other. The results suggested that participants did not understand the assumptions underlying randomised controlled trials (RCTs). The authors recommend that researchers should identify better ways of explaining randomisation to participants, including the reasons why it was important for establishing

clarity in results. Robinson *et al*. further observe that informed consent documents simply describe what will happen, without offering some accessible explanations. As a result, patients may create their own explanations of those procedures and, as such, consent or refusal may be inadequately informed.

A similar study which focused on the understanding and acceptability of randomisation by potential trial participants was conducted by Kerr *et al*. (2004). The authors recruited 130 adults attending further education colleges covering a wide range of ages, education levels and occupations. The 130 participants were given five pamphlets which had different hypothetical scenarios and asked whether these constituted random assignment and whether they found them to be acceptable. The scenarios ranged from assignment using a computer, tossing a coin, picking small numbered pieces of paper from a hat or box, allocating each person in turn as they arrived, or asking each person what they preferred. The majority of respondents judged correctly that asking respondents about which group they preferred was not random. Judgments were split over assigning of individuals in turn as they arrive. The authors found that providing the scientific justification for randomizing significantly increased the acceptability of the process of randomizing using a computer. This was perhaps the result of the fact that this is now the most commonly used method of randomising. This finding demonstrates the importance of providing complete information to participants which promotes informed decisions.

In a study aimed at exploring how prospective trial participants interpret and understand the science of clinical trials using information provided through study information sheets, Stead *et al.* (2004) found that respondents had difficulty comprehending the meaning of concepts such as randomisation and double-blinding. The authors used focus group discussions to hear, in the patients' own words, how they interpreted the information. The authors also wanted to find

out if there were differences in interpretation among the various individuals. While respondents were aware of the usage of a placebo, they were not aware of the reasons for its use, and some respondents even argued that there was no point for one to take part in a study if they were going to receive a dummy pill. Some participants were even of the opinion that it was immoral for the investigators to withhold treatment and give other individuals placebos. This implied a misunderstanding of the scientific need for these procedures, as well as therapeutic misconception - a widely held belief that they key reason for participating in a trial was for therapeutic benefit. The respondents indicated that these concepts were not in tandem with their expectations regarding medical care. The study established that the technical language in the informed consent forms was a barrier to communication.

Stead *et al*. (2004) also found that participants had some ideas about randomisation as the process of assignment using a computer or small pieces of numbered paper from a hat, but they were not aware of the reasons why individuals were randomised in research. Only a handful of respondents acknowledged the fact that randomisation was necessary so as to avoid biasing of results through biased assignment by research staff. Regarding double-blinding, some respondents were concerned that the clinicians' ignorance could result in inappropriate prescribing or otherwise negatively affect their care. As with randomisation and placebo use, only a few respondents could explain why double-blinding was used in clinical trials. This study confirms the challenges that trial participants face in understanding the concepts of randomisation, double-blinding and placebo use and clearly demonstrates how individuals end up agreeing to participate in research even if they do not agree with the study procedures to be used in that study.

In order to examine how consent forms for early phase trials address equipoise (scientific uncertainty) and describe potential benefits, King *et al*. (2005) analysed 321 consent forms for

gene transfer research. The goal was to assess how the language used in the informed consent form may promote or reduce therapeutic misconception, including overestimation of potential benefits in early phase clinical trials. Almost all the consent forms mentioned potential for direct benefits to participants. Some consent forms used some indeterminate language on the issue of benefits, such as stating that benefits were not guaranteed. In 16 percent of the forms, the words 'treatment' and 'therapy' were used inappropriately in the title of the study to refer to the experimental intervention. In 39 percent of consent forms, the word "treat" was used to refer to the implementation of the intervention, while the word "patient" was used in 49 percent of the informed consent documents to refer to the participants. The findings confirm that many individuals who participated in research were not well informed about their role in clear and unambiguous terms. The findings confirm that there is often vagueness and inconsistency in consent forms, which may contribute to therapeutic misconception. King *et al*. therefore recommended that researchers need to keep the terms clear and simple, describe potential direct benefits consistently, limit variation in use of terms, avoid misleading 'treatment' implications, and avoid vagueness about potential benefits.

A literature search in electronic databases for articles published from 1980 to 2004 which described structured assessments of adult capacity to consent to clinical treatment or research participation was conducted by Dunn, Nowrangi, Palmer, Jeste and Saks (2006). The literature search study was aimed at critically reviewing existing measures of decisional capacity for research and treatment. The authors identified 23 decisional assessment instruments and evaluated each of them in terms of format, content, administration features and psychometric properties. Six of the 23 instruments focused on understanding disclosed information, 11 tested for understanding, appreciation, reasoning and expression of a choice. They found that the instruments varied in terms of format, degree of standardisation of disclosure, and scoring procedures.

Dunn *et al*. (2006) found that all 23 of the instruments had some limitations, some of which were related to reliability and validity. The authors found the MacAthur Competence Assessment tool for clinical research and Treatment to be stronger empirically than most others. A similar study was conducted by Redman (2006) who reviewed 65 measurement instruments reported in literature between 1999-2003. The author found that only 10 of the 65 had minimal psychometric data. Dunn *et al*. (2006) and Redman (2006) concluded that decisional capacity assessment tools need further refinement for them to be usable in various contexts. Wendler (2004), on the other hand, suggests that the focus on individuals' capacity to consent is too narrow. He recommends that future research should be directed at developing a post-decision questionnaire that can be adapted to individual studies and used to assess voluntariness and the understanding of study information.

In cases where informed consent documents are developed in a foreign language, the issue of language translation assumes paramount importance. Hunt and de Voogd (2007) thus conducted a study that aimed at examining research informed consent procedures with limited English proficiency individuals in the absence of trained interpreters. They observed the informed consent processes involving 30 non-English speaking participants. Using content analysis, they examined whether the basic criteria for informed consent had been fulfilled. The authors identified some serious communication challenges. In some cases, study staff relied on the clinicians' limited foreign language. The participants were disadvantaged in terms of the disclosure of adequate information, understanding of the information, and therefore the voluntariness of their decisions. The authors concluded that, in the absence of trained interpreters, it was obvious that the non-English speaking participants were not provided with quality information during informed consent.

In a qualitative study conducted in the United Kingdom (UK) by Madsen, Holm and Riis (2007) aimed at examining research participants' attitudes towards research, the majority of respondents expressed positive attitudes towards research. However, most participants expressed discomfort with randomisation. Morris and Balmer (2006) conducted a study to understand how research participants understood their own participation in experimentation. They were specifically interested in finding out how the volunteers viewed their own role, the experimental setting, and how they understood the relationship between themselves and the researchers. They found that the majority of participants understood themselves to be playing a range of roles and identities. They looked at themselves as givers, clients, collaborators, and in some cases as guinea pigs. This study illustrates the importance of the social setting in determining the relationship between the researcher and the participant, and how this may affect the informed consent process. In the report, the method of qualitative analysis and reliability were not reported.

In order to investigate how often participants' comprehension or decisional capacity was assessed in the consent process, and the rate at which investigators were using validated tools to assess decision making capacity, Kon and Klug (2006) conducted a quantitative study in which questionnaires were mailed to investigators. Responses were received from 102 researchers, representing a 56 percent response rate. About 66 percent of respondents reported that they assessed comprehension and decisional capacity prior to accepting consent. Nine researchers used a formal questionnaire and three used a validated tool. These findings suggest that not all investigators are interested in assessing comprehension and decisional capacity. Henderson *et al*. (2006) conducted a study that was aimed at examining the content of gene transfer research informed consent documents. They analysed the content of informed consent document and then held interviews with researchers and participants in early phase gene

transfer trials. They found level of education, type of disease under study, and communication by study personnel to be important predictors of therapeutic misconception.

Lansimies-Antikaiken *et al*. (2007) conducted a qualitative study aimed at describing and analysing the use of informed consent in adult clinical research. They intended to use the data to develop and test an interview schedule for the evaluation of informed consent. The majority of the 32 participants were aware of the key elements of informed consent; information, understanding, competence, and decision making. The authors found the interview schedule they had developed to be useful in the investigation of informed consent. Similar findings were reported from a quantitative study by Lansimies-Antikainen, Laitinen, Ruaramaa and Pietila (2009). Resnick *et al*. (2007) conducted a similar study which was aimed at evaluation of the validity and reliability of a five item Evaluation to Sign Consent (ESC) as a measure that can guide determination of an adult's capacity to consent for research. Using various methods, including statistical tests and replication, the authors found some evidence of validity and reliability with the measure.

In an opinion piece on informed consent in research, Landro (2008) opines that participants do not read the forms that they sign before going into surgery or medical treatment. The author notes that with increased lawsuits arising from poor communication, doctors and other medical personnel have to ensure that they redesign their informed consent procedures. Health institutions now offer some videos, pamphlets and other tools aimed at ensuring that patients understand what they are agreeing to participate in. Some institutions have even resorted to hiring some specialist translators in order to improve the communication between the patients and medical personnel. Some health institutions have adapted informed consent forms that are easy to read and patients are required to repeat to the healthcare professionals in their own words what they understand from the disclosed information. The author notes that health

professionals now realise that they cannot just walk to a patient's bed and inform them about the procedures that they need to go through. Health institutions in the past used to treat informed consent as just an administrative procedure but they now realise that it is an important opportunity to establish a meaningful relationship with the patient. The author reports that some companies have taken advantage of the need for proper documentation of informed consent and have developed various types of software that are used for taking patients through the informed consent procedures. Whether these methods have been evaluated and validated however remains unclear.

In order to understand the discussions which take place between investigators and study participants, Jefford and Moore (2008) conducted a qualitative study which involved both analysis of the written consent documents and the discussions between the investigators and potential participants. They identified several areas of deficiency, including technical language, which served as a barrier for communication. They recommend simplification of the language which is used in informed consent, as well as the creation of an environment which is conducive to discussion during the informed consent process. Brehaut *et al*. (2008) propose the use of decision aids during the informed consent process in order to promote comprehension of informed consent information.

A qualitative study aimed at investigating what occurs during the research informed consent process was conducted in the United Kingdom by Wade, Donovan, Lane, Neal and Hamdy (2009). The study explored what occurred during the informed consent process and was specifically aimed at investigating how study staff disclosed study information, how well participants were informed, and what aspects of the communication process can assist in enhancing informed consent. The authors audiotaped 23 informed consent discussions and found some variations in content and structure of informed consent conversations. Some

appointments were recruiter-led, while some were participant-led. Some recruiters employed some communication techniques which facilitated systematic and detailed discussion. The authors concluded that the focus on covering the elements of informed consent should be broadened to include considerations on how the information is best conveyed to potential participants. They proposed that staff should take their time in answering participants' questions adequately and addressing concerns. This requires some training of staff members involved in obtaining informed consent. While this study identified obstacles to understanding, it did not test any intervention.

Hochhauser (2008), a readability consultant, noted that in many interventions aimed at improving comprehension that that have been tested, the tests used have not been psychometrically sound and have failed to produce consistent results as they miss measurable definitions of comprehension. It is important for individuals who intend to test comprehension to become conversant with psychometrics, which is the psychological study of test construction and measurement. Researchers also need to be aware that comprehension tests can be affected by other environmental or contextual factors such as anxiety, age, literacy, memory and cognitive functions. Some tools have also been lacking in terms of validity and reliability, administration, standardisation, scoring and interpretation. The author notes that the recommendation to reduce readability to lower levels has often not been accompanied by improvements in comprehension. Clinical trials are becoming more and more complex and this may serve as an impediment to the improvement of comprehension.

Hochhauser (2008) also notes that in the majority of studies assessing comprehension, researchers have not bothered to conceptually and statistically define comprehension before conducting the assessment. This therefore means that one cannot necessarily conclude that those individuals who scored poorly did not understand the materials. Some studies to improve

comprehension have been weakened by the fact that they did not obtain baseline data before the intervention so as to check on the usefulness of the interventions. The author also noted that real and simulated studies cannot be compared since simulations do not fully represent reality. Studies which enquire about perceived understanding can suffer from the desirability bias as perceived understanding is not the same as real understanding. In some studies, researchers have measured comprehension using inconsistent definitions, which also makes comparisons impossible. The author also points out that readability formulas that are still being used today were developed some decades ago and may be less meaningful in present day complex trials. This therefore means that readability alone may not guarantee understanding

2.9 STUDIES CONDUCTED IN DEVELOPING COUNTRIES TO ASSESS TRIAL PARTICIPANTS' UNDERSTANDING

With the increasing amount of research being conducted in developing countries, it becomes imperative for research around ethical standards and practices to be conducted in these contexts. In this section, studies conducted in developing countries outside Africa and those dealing with developing countries in general, are reviewed.

In a study of HIV-1 transmission in Haiti, participants were required to pass an oral examination on the contents of the consent form with a passing score of 12 out of 15 (80 percent) before enrolment. Fitzgerald, Marotte, Verdier, Johnson, and Pape (2002) conducted a small study involving 35 individuals to compare two methods of disclosing information. Fifteen individuals were given information during a single meeting with a physician, and 30 other volunteers were given information by a counselor during three meetings. Three of the 15 (20 percent) got high scores of 80 percent and above, compared to 24 of the 30 (80 percent). The findings suggest that interactive and flexible methods of disseminating information,

including the repetition and reinforcement of the information during various sessions, may lead to improvements in recall. The authors recommended that formal assessment of research participants' comprehension of provided information should be considered as a routine step in the informed consent process in HIV prevention research among illiterate populations.

In a pilot qualitative study to learn how participants in international clinical trials define research and why they choose to enrol in research, Kass, Maman and Atkinson (2005) interviewed 26 participants from three developing countries who were participating in six different international studies. The participants were referred to the authors by study staff. The study revealed that participants generally understood the purpose of the clinical trials that they had chosen to participate in. However, respondents generally did not understand randomisation and treatment allocation. The authors found that most of the participants had agreed to join the clinical trials so as to access better quality medical care. A significant number of the respondents were not aware that they could withdraw from the study at any time. The authors recommended that formative research should guide the development of messages to be disclosed to participants so that the messages are relevant and meaningful within the specific communities in which the research is conducted. It is possible that the referral of participants by the study staff could present a selection bias, as study staff may only have referred those participants that they were confident would answer the questions correctly.

In a study conducted in Peru to examine challenges in obtaining informed consent among indigenous peoples, Creed-Kanashiro, Ore, Scurrah, Gil and Penny (2005) reported the complexities of obtaining informed consent among individuals that live in close-knit societies and the need to involve significant others in the informed consent process. They note that, while this may be a noble gesture, it may inadvertently lead to an individual agreeing to participate in research as a result of pressure from others and not as a result of understanding

about the research aims and procedures. The authors discuss the role of verbal consent in illiterate populations, where written documents may not be very meaningful. They also discuss the importance of formatting and presenting information in a way that is meaningful to a specific target audience, and recommend that, in international trials, investigators at specific sites should take positive steps to adapt generic informed consent documents and information so that these become more meaningful at their specific site.

Dawson and Kass (2005) conducted a study with US researchers doing research in developing countries to investigate the ethical issues they confronted during informed consent as well as in conducting their research. Findings revealed that researchers' experiences and beliefs about informed consent could be categorized into three categories: regulatory, community and individual. US researchers were mainly interested in fulfilling regulatory requirements that are emphasised by IRBs, while at the same time trying their best to fulfill the expectations of the communities, and also individual information requirements. Researchers described community influence on individual decision making but stressed the need for comprehension and voluntary decision making at individual level. About 52 percent of the researchers stated that the legal language in their informed consent documents was meaningless to participants, and 23 percent believed that the informed consent focused too much on the individual while ignoring the individuals' social context. About 54 percent of the researchers believed that participants did not understand placebos. The authors recommended that more studies to look at how culture and community affect individual decision making need to be conducted.

In a study conducted in Thailand to assess the quality of information provided during the informed consent process, Pace *et al*. (2005) interviewed 141 individuals immediately after they had consented to participate in a randomised HIV study in Bangkok. The survey looked specifically at individuals' experiences with the informed consent process, their understanding

of the information provided, and the voluntary nature of their decisions. The authors note that in Thai culture it is common for individuals to defer to the authority of healthcare professionals. The informed consent in the HIV study was divided into two parts: a group discussion led by trained study nurses, followed by individual interviews. The Thai language protocol was read through page by page, followed by questions and discussion. The instrument that was used consisted of 67 multiple-choice questions designed to elicit information on the individuals' experience with informed consent as well as their comprehension of the information disclosed to them.

About 98 percent of study participants reported having read the informed consent document adequately and 77 percent found the form to be moderately easy to understand (Pace *et al*., 2005). About 21percent of the respondents found the discussion to be more useful than the informed consent form. All respondents except for one reported that they felt well or moderately informed and yet, only 31 percent were aware that only half of the study participants would receive the test drug. One-third of the respondents were aware of the randomisation procedure. Eighty-eight percent (88%) of respondents identified the test drug as an experimental therapy for HIV, while nine percent identified it as routine treatment. About 56 percent believed that their own chance of developing AIDS might decrease. This finding presented some evidence of therapeutic misconception. Some study participants indicated that they had some issues they had not understood but that they did not ask questions as they could not find the best way of asking the questions. This finding suggests that researchers should not take silence on the part of potential research participants as a sign of understanding as it may be a sign of confusion (Pace *et al*., 2005).

Hyder and Wali (2006) conducted a survey of developing country researchers involved in human subjects research. They distributed a questionnaire with 169 questions to the

researchers. They found that about 40 percent of the researchers did not use written consent in their most recent studies. Eighty-four percent of respondents acknowledged that measures of understanding should be incorporated into informed consent processes. The majority of respondents recommended that regulations should allow for some flexibility in the methods that are used in documenting informed consent. These findings suggest that researchers from limited resource settings have an interest in ensuring that trial participants' decisions to participate are based on adequate information.

A study was conducted in India to assess comprehension and recall of informed consent after the closure of a birth cohort study on diarrhoea (Sarkar, Grandin, Gladstone, Muliyil & Kang, 2009). In this study, a structured questionnaire was administered to 368 respondents. About 329 of these reported that the study had been adequately explained to them. However, only 43,5 percent of respondents could recall that the study was on diarrhoea. About 46 percent of the respondents stated that they would not have joined the study if it was not for free medical care which was offered at enrolment. The authors concluded that, in a typical rural Indian setting, medical doctors are respected as authority figures and this could have led to some individuals agreeing to join the research so as to please the researchers. The authors found that, despite high levels of compliance with the protocol, retention of study information was low over a long period of time such as one year. The finding relating to free medical care is very important, especially in limited resource settings, and demonstrates the influence of contextual factors in the making of decisions to participate in research.

The current has reviewed some studies assessing trial participants in the context of developing countries outside Africa. Factors such as illiteracy, culture and limited resources are critical in one's decision to enroll in research. The next section is devoted to studies conducted in African countries.

2.10 STUDIES CONDUCTED IN AFRICA TO ASSESS TRIAL PARTICIPANTS' UNDERSTANDING

Some assessment studies conducted in Africa have been identified. One of the early studies in Africa was a qualitative study conducted by Preziosi, Yam, Ndiaye, Simaga and Simondon (1997). The authors reported their practical experiences in evaluating the informed consent processes adopted during the implementation of a new pertussis vaccine trial in a rural community in Senegal. During the pilot test for obtaining individual informed consent for the pertussis study, some women reported that they were confused by being asked to give their consent as they believed that they had already consented during the group meetings prior to one-on-one conversations for obtaining individual consent. Many mothers asked which vaccine their children would get, as well as why the study was blinded. Of 55 women in the pilot session, 50 agreed to enrol their children on the basis that they trusted the team of medical doctors and also that they wanted to follow what their colleagues were doing. The majority of mothers who attended the monthly vaccination sessions indicated that they did not know the details of the study. This study reflects the communal life in some settings and the effects of trust on the informed consent process.

Abdool Karim, Abdool Karim, Coovadia and Susser (1998) conducted a quantitative study aimed at evaluating the consent process for testing for HIV in an ongoing study in an antenatal clinic in South Africa. The study involved the administering of a questionnaire to 56 women attending antenatal care before and after a counselling session. They found that despite the fact that researchers were following the standard procedures for obtaining informed consent, including assurances that participation was voluntary, 88 percent of participants thought that it was compulsory to participate in the HIV surveillance study which was part of an HIV perinatal transmission study. The study included a control group of 56 who completed the

post-counselling questionnaire. The pre-counselling questionnaire covered questions relating to HIV/AIDS, while the post-counselling one included questions relating to the women's participation in a perinatal HIV transmission study. Close to 30 percent of the respondents believed that the care they received at the hospital would change if they did not participate in the perinatal HIV transmission study.

In a study evaluating the informed consent process used in a major efficacy trial of a haemophilus influenza vaccine in the Gambia, Leach *et al*. (1999) noted that 93 percent of the participants interviewed stated that they joined the study as they wanted to get the HIB vaccine. The placebo design was understood by only 10 percent of the participants. Thirty-five percent (35%) of refusers gave the reason that they did not want to participate in the research as the vaccine was experimental and 29 percent indicated that the vaccine might have unknown side effects. It is interesting to note that the majority of those who agreed to join did so for mistaken reasons, while a significant proportion of refusers (35 percent) were aware of the experimental nature of the vaccine. This study further confirms the challenges that researchers face in trying to inform prospective participants about research. For reliability and validity, during interviews for this study, the interviewers were writing the responses directly onto the questionnaire, while the interviews were also being taped. A 25 percent subset of the interviews were checked afterwards by retranslation of both questions and answers by a second study worker for accuracy. The authors however did not report the percentage of accuracy.

Yoder and Konate (2002) evaluated the informed consent processes used for obtaining blood samples for HIV testing during a demographic health survey (DHS) held by the National Statistical Office of Mali. Their study involved observing the disclosure of information, assessing the respondents' understanding of the information disclosed, and establishing the reasons for accepting or refusing to participate in the blood testing component of the DHS.

About 88 percent of respondents recalled that the DHS included a test for HIV, and 60 percent also mentioned that the HIV test results were anonymous. The authors reported that the majority of respondents had agreed to donate blood specimens for testing because they were aware that the staff administering the DHS survey were from the Ministry of Health. Nationally, the refusal rate for HIV testing during the DHS was 11 percent. All participants who agreed to the anonymous blood testing were given a green card that they could take to the hospital for a free HIV test. Only a few dozen out of 6,800 persons tested during DHS used their cards for the free HIV test at the hospital. The findings from this study have implications for the data collection activities of government departments. The study findings suggest that it is possible and desirable for government agencies can respect the rights of citizens and still collect data that is needed for planning purposes.

In a study that focused on the understanding of informed consent in studies in Kilifi in Kenya, Molyneux, Peshu and Marsh (2004) identified the presence of therapeutic misconception among some of the participants that they interviewed. This was because most of the research that they looked at was hospital-based. They also found out that some research activities were sometimes misunderstood by the community members. For example, there were rumours to the effect that some blood samples that had been collected through some of the studies were being pooled for blood transfusions. They found that many community members were not familiar with the concept of research, while researchers and community members tended to use various words interchangeably to refer to research. Fieldworkers regularly reported some challenges in relating consent information to community members. In another paper reporting on other findings from the same study, Molyneux, Wassenaar, Peshu and Marsh (2005) report that the study revealed the community's difficulties in differentiating research from routine clinical investigations that are conducted in clinical settings). Community members had the general belief that the research unit which was conducting the trials in the area was actually

there to provide health services or assistance as opposed to research. This was explained by the provision of ancillary care or trial-related care by a well equipped unit based in a limited resource setting.

In an effort to ensure that researchers take the local context into consideration, some researchers in Africa have focused on procedures that are important in obtaining informed consent. Doumbo (2005) reports on the procedures adopted for obtaining consent for malaria research in Malian communities with predominantly illiterate persons. The team developed a stepwise process which involved holding a discussion with the community elders and getting permission from them to proceed. Next, they convened focus group discussions with the heads of extended families, then with mothers of the children they wanted to recruit. Finally, they obtained the consent of the individual families involved in their cohort. This process reportedly generated more confidence by the villagers in the research project and led to a better understanding among researchers of the village behaviours and cultures. Unfortunately, the informed consent processes were not evaluated for their effect in enhancing understanding of research participation. The author points out, however, that the process does not always achieve what it set out to achieve and requires the dedication of a significant amount of time for discussion.

Krosin, Klitzman, Levin, Cheng and Ranney (2006) conducted a study in Mali which was aimed at identifying deficits in comprehension during the informed consent process. The authors administered a nine-item questionnaire to individuals who had agreed to participate in a malaria vaccine trial. They found that participants had difficulty understanding various components that were covered during informed consent. About 90 percent of respondents were not aware of their rights to withdraw, while 93 percent were not aware of the potential side effects of the vaccine. About 74 percent were not aware that they were participating in a trial

but thought that they were receiving therapy. The authors found that those who lived near the main road were most likely to give correct answers compared to those who lived far away from the road. This suggests the important role of proximity to communication infrastructure such as road networks in the dissemination of information.

In a study focusing on informed consent in the rural District of Kassena-Nankana in Northern Ghana, Tindana, Kass and Akweongo (2006) elicited the views of research participants about how informed consent for participation in research was obtained and what participants thought about the informed consent processes. The qualitative study found that most of participants were of the opinion that the Ministry of Health had always brought interventions aimed at assisting them. They therefore assumed that anything proposed by the Ministry, including clinical trials, were in their best interests. The study also revealed that some community members agreed to join some research studies as a way of gaining access to good quality care, while some agreed to join because they thought they could not refuse to participate in programmes that had been granted permission by the chief. It emerged that trust in researchers and community chiefs rather than information provided by researchers was a good predictor of members' decisions to participate in research in rural settings.

In an effort to improve understanding of trial participants within the context of an intervention trial aimed at reducing vertical transmission of HIV in Malawi, Cornelli, Bentley, Sorenson and Henderson (2006) conducted research which was aimed at exploring the community's understanding of medical research, as well as how to explain research using local terms and meanings. The formative research was part of efforts aimed at incorporating the local social context into the informed consent processes. The team identified some analogies that were meaningful in Malawian communities to explain consent information. They used the formative data to develop some counselling cards that were culturally appropriate for the trial in Malawi.

The authors recommended the adoption of a formative research step before embarking on a major study in an effort to come up with messages that are culturally appropriate and acceptable.

In a qualitative study conducted in Egypt to examine attitudes, understanding and concerns regarding research, Khalil, Silverman, Raafat, El-Kamary and El-Setouhy (2007) found that many participants had discomfort with or difficulties in understanding the concepts of randomisation, placebo and double-blinding. The majority of participants did not understand the need for randomisation and were of the opinion that they should be allowed to choose which arm they wanted to join. The idea that the physician-researcher in a double-blinded study would not know what treatment they were taking was also not understood. Trust in the physicians conducting the research was an important predictor of the decision to participate. This study only looked at the views of those who had agreed to participate in research. The researchers recommended enhanced educational efforts aimed at improving general understanding of research procedures in order to enhance the validity of the informed consent process. However, the research did not test such efforts.

Molyneux, Gikonyo, Marsh and Bejon (2007) report on a qualitative study conducted in Kenya to document community reactions to an informed consent quiz. The quiz was administered to 189 mothers through a semi-structured questionnaire after they had consented to have their children participate in a malaria vaccine study. Once the vaccine study was under way, focus group discussions were held with some of the mothers and community based staff attached to the vaccine trial. In-depth interviews were also held with some of the vaccine trial staff members. The authors found that the quiz prompted members to voice concerns about blood sampling and side effects that could be associated with the trial. Some of the quiz questions

appeared to fuel fear and suspicion, with potential negative consequences for both the study and the community.

The findings showed that the quiz was useful in increasing the trial participants' knowledge and awareness. The mothers ended up asking some questions that they could not have asked if they had not participated in the quiz. The findings also showed that the mothers had agreed to participate in the study not based on adequate information but on trust of the researchers. The authors recommended that formal assessments of understanding should be employed with sensitivity and caution as they may lead to some complications, such as difficulties in both recruitment and retention. They encourage researchers to consider the social contexts in designing methods for assessing trial participants' understanding (Molyneux *et al*., 2007). What is clearly emerging from these findings is the suggestion that friction between the research study and the community will be reduced if the community and the potential research participants are well informed about the study in the first place, and decisions to join are not based only on trust but are based on adequate understanding.

Manafa, Lindegger and IJsselmuiden (2007) report on a study which examined the informed consent processes in an antiretroviral trial conducted in Nigeria. In this study, a semi-structured questionnaire was administered to 88 of the 180 individuals participating in an antiretroviral study. The questionnaire covered aspects of the information that was disclosed in the leaflet of the trial. The authors found that 85 percent of respondents knew that the purpose of the research was to test a new drug. About 14 percent thought that they were receiving free treatment for HIV/AIDS. The participants' understanding of potential trial risks and the right to withdraw was poor. The authors concluded that a signed informed consent document is not evidence that participants have understood the information that has been disclosed. They recommended that researchers have to make sure that participants' decisions are based on

adequate information, especially in limited resource settings were people may join clinical trials because of limited access to health care.

In a quantitative study conduced in South Africa to evaluate the quality of consent in a tuberculosis (TB) case control study and to identify factors that may influence the quality of consent, researchers administered a questionnaire to 192 participants from a study which was studying the correlates of TB (Minnies *et al*., 2008). The questionnaire contained questions covering the major elements of informed consent and tested for recall (defined as success in selecting the correct answer) and understanding (defined as correctness in the interpretation of statements presented). The majority of the respondents obtained scores greater than 75 percent for both recall and understanding. About 79 percent were aware of the risks and 64 percent were aware that their participation was voluntary. Participants who had seven or more years of education were more likely to score higher than those with fewer years of education. The fact that the questionnaire was testing for simple recall suggests that success in selecting the correct answer implies that not much was expected of the participants in processing the information so as to come up with an adequately informed decision. Nonetheless, the findings suggest that, with proper training of staff in information disclosure, participants from communities that are classified as illiterate can understand research participation.

Gikonyo, Bejorn, Marsh and Molyneux (2008) report on a qualitative study aimed at exploring community understanding and perceptions of a malaria vaccine study which was being conducted in a rural setting in Kenya. The study confirmed the importance of providing information to the whole community before initiating recruitment so as to ensure that all members in the community are aware of the trial and the purpose of the trial. On the basis of their findings, they suggest that during the disclosure of information, researchers should not only focus on fulfilling the informed consent requirements, but should take into consideration

the social context as well as the relationship between themselves and the community to ensure that this relationship does not necessarily influence individuals to participate without adequate information. The authors noted that the current guidelines do not adequately address the social realities that researchers face when they work in the field in developing world settings.

In a study conducted in Ghana, Hill, Tawiah-Agyemang, Danso and Kirkwood (2008) sought to find out how participants in a placebo-controlled vitamin A supplementation trial perceived the trial. They also wanted to establish whether the women knew that not all the capsules were the same and to identify factors associated with this knowledge. The study found that the majority of women knew that they were participating in research (75 percent) and yet a greater majority thought that they were receiving an active and beneficial medication (93 percent). The women reported that the capsules they were being given were good for strength and protected them against illness and assisted them during delivery. Some of the women who were taking part in the trial knew nothing about the purpose of the trial. The investigators found that education and district of residence were important predictors of this understanding. The authors recommended the urgent need for research focusing on developing interventions aimed at improving understanding.

Chingono, Lane, Chitumba, Kulich and Morin (2008) reported on how they successfully demonstrated the process of randomisation in a community based intervention trial in a rural area in Zimbabwe. The authors noted that randomisation of communities to control and intervention groups may create a perception of service denial to those in the control group. The researchers engaged in a process of randomisation which involved community members and elders. To explain the concept of randomisation, the group used a supplementary feeding scheme analogy that the communities were already familiar with. They discussed with community members how they could randomise a pair of twins to two different schools. One

school offered some supplementary food while the other offered no food to pupils. To explain chance, they used local language idioms that would explain chance or luck. Once the committee's concerns about randomisation had been addressed, the researchers then proceeded to randomise the communities using small pieces of paper that were picked by the leaders of all the communities who were participating in the intervention trial. They found the approach to be useful as communities understood randomisation and eventually participated in the randomisation exercise.

Oduro *et al*. (2008) report on a quantitative study conducted in Northern Ghana in order to assess the retention of disclosed information. They recruited 270 mothers who had consented for their children to participate in a malaria cohort study. A semi-structured questionnaire which covered the information provided during the informed consent process was administered to the women. About 90 percent of the women were aware that their children were participating in a study that was not related to medical care, and 66 percent confirmed that the study procedures had been adequately explained to them. About 95 percent were aware that study participation was voluntary and yet only 21 percent recalled that they had the right to withdraw their children at any time. About 37 percent of mothers indicated that they had agreed to participate in the study so they could access free medical care, and 19 percent indicated that they joined so that they could access better quality care.

The findings by Oduro *et al*. (2008) are important in limited resource settings where there is limited access to good quality care. These findings suggest that the researchers had engaged the community before initiating research to explain the research to them. The findings may also be a reflection of the ways in which the questions on those variables were asked. About 47 percent of the parents suggested that the researchers needed to devote more time to explaining study procedures, and 16 percent recommended that researchers needed to communicate in the local

language so that they could clearly understand the information being disclosed. In the study, the recall of information was positively associated with the increasing age of the parents.

In a study conducted in Nigeria to assess the post-consent understanding of study participants in an oral health research study, Taiwo and Kass (2009) interviewed 113 individuals who had just consented to participate in an oral health study. They found that there was poor understanding of key elements of informed consent such as involvement in research. They concluded that factors such as poverty, illiteracy and confusion about the dual role of the dentists as both researchers and clinicians were contributing towards therapeutic misconception. The authors recommended that dentists should be trained in health research and research ethics during their professional training so that they can conduct ethical research upon completion of their studies.

In order to investigate the existence of therapeutic misconception, Wazaify, Khalil and Silverman (2009) conducted a qualitative study in Egypt. They administered a semi-structured questionnaire to individuals who were attending outpatient departments at a university in Cairo. In their study, therapeutic misconception was defined in two ways: either as inaccurate beliefs about how individualized care can be compromised by the procedures in research, or as inaccurate assessment of benefits obtained from the research study. Evidence of the therapeutic misconception defined using the first criterion was found in the majority of their small sample (11 out of 15) and therapeutic misconception as defined using the second criterion was evident in five of the 15 respondents. While the authors were cautious about the generalisability of their findings due to the small sample size they used, they concluded that there was some evidence of therapeutic misconception amongst Egyptian patients. It is important to note that the patients that they interviewed were not research participants.

2.11 STUDIES AIMED AT IMPROVING TRIAL PARTICIPANTS' UNDERSTANDING

Various studies have been conducted globally aimed at improving trial participants' understanding of research participation, including clinical trial procedures. Most of these studies have been conducted in developed countries. Simes *et al*. (1986) conducted one of the earliest interventions aimed at improving informed consent. In their study, 57 patients were randomised to an individual approach in which each doctor had discretion in determining the information that the individual wanted, or the uniform approach in which there was total disclosure of all relevant information. Comprehension was assessed qualitatively by asking questions which were aimed at establishing comprehension. Overall, patients' understanding of both treatment and research aspects of the trial were significantly better in the total disclosure group than in the individual approach. A reassessment of comprehension four weeks after the initial assessment revealed no significant differences between the two arms. This suggests that the total disclosure approach was important only in improving short-term recall. It is possible that the two approaches were simply providing the same kind of information using two different approaches. This is evidence that the study was looking at simple recall. However, the findings from this study are difficult to interpret as the authors did not define the cut-off criteria for an acceptable recall score.

Fureman, Meyers, Mclelan, Metzger and Woody (1997) conducted a study aimed at evaluating a video tape specially produced to supplement written information about preventive HIV vaccine trials. The study involved 186 drug users randomly assigned to reviewing a pamphlet or watching a video prior to reviewing the same pamphlet. The video programme was modeled in the form of a talk show involving a panel of experts as well as some potential vaccine study participants, and was aimed at covering important information that trial participants were

supposed to be aware of concerning HIV vaccine trials. The effect of the two methods was assessed qualitatively by asking some questions aimed at eliciting recall of the information that had been provided. The findings suggested that the video/pamphlet combination was superior in improving retention of information one month later as compared to the pamphlet alone. The authors highlighted the challenge of communicating facts to a socially marginalized group and suggested that researchers should provide technical information in an understandable manner. The participants in this study had been enroled in a longitudinal study for several years. It is possible that they may have received useful information informally about HIV vaccines. This information might have contributed to their high levels of knowledge about HIV vaccine trials.

A similar study conducted by Jimison, Sher, Appleyard and Le Vernois (1998) concluded that it was feasible to adapt a structured multimedia informed consent system to a specific trial and to incorporate techniques aimed at improving understandability of informed consent content. In this study, the authors tested a prototype multimedia informed consent tool against a routine informed consent form. The prototype included information on clinical trials in general and information specific to the trial at hand. Prospective participants felt that the multimedia prototype gave them a greater sense of self control as they could proceed at their own pace. They also liked the modular and hierarchic approach to presenting information and felt that this made the information more understandable. Institutional Review Board members, while finding the system valuable, expressed concerns about how to review the system for potential biases in presentation and also about legal issues relating to the replacement of the paper consent document.

Standard informed consent forms were tested against simplified forms in a study conducted by Davis, Holcombe, Berkel, Pramanik and Divers (1998). This study was based on the realization that a high level of reading skill and comprehension are necessary to understand the

contents of the informed consent documents. In the study, 183 adults were randomised to read either the standard informed consent document which was written at sixth grade level, or a simplified form written at seventh (7^{th}) grade level. Participants were then assessed to determine their comprehension levels and were then given the alternative form and asked which one they preferred and why. The majority of participants (62 percent) preferred the simplified form and 97 percent of the participants confirmed that the simplified form was simpler to read compared to the standard one. Surprisingly, the degree to which the two groups understood the contents of the two forms was the same. The average score for the simplified form was 58 percent while that for the standard form was 56 percent. The scores of the ten comprehension questions were reported, but there was no indication of what the response options were, thereby giving no information about the wrong answers that the respondents were selecting. The findings raise some serious questions regarding the adequacy of the design of informed consent forms for persons with low to marginal literacy skills. The study dealt with oncology patients and it is possible that they already knew about the oncology trial from their hospital visits or past experiences with trials. The findings suggest that that simplifying the informed consent materials is an important strategy in efforts aimed at improving participants' comprehension. Researchers need to explore combinations of various methods to complement the simplified forms.

Dunn and Jeste (2001) reviewed various interventions aimed at improving trial participants' understanding. They reviewed a total of 34 studies which included interventions aimed at improving understanding by participants. In 25 of the 34 studies reviewed, patients' understanding showed improvement with a variety of interventions. Some of the successful interventions were based on the following characteristics: better organized processes, shorter and more readable informed consent documents, simplified and illustrated formats, and corrected feedback. Eleven studies compared simplified with standard (complex) forms.

Studies which involved the augmentation of the informed consent process with a video tape showed significant promise. In some of the studies reviewed, education and age were identified as predictors of understanding. The authors point out the challenge of distinguishing between understanding and recall in some of the studies and suggest the use of various interactive multimedia technologies in efforts aimed at improving understanding.

In a study aimed at evaluating the impact of an educational booklet on women's knowledge of and willingness to participate in a randomised clinical trial of a breast cancer treatment, Ellis, Butow and Tattersall (2002) randomised 83 women to either receive standard information or standard information plus booklet. The booklet contained information on the need for clinical trials and the manner in which randomised controlled trials (RCTs) are conducted. The researchers concluded that educating women using an educational booklet was not effective in improving recruitment of women to the RCT. It is important to note that the study was aimed at assessing the impact of the educational booklet on recruitment and not specifically on their understanding of clinical trial procedures, so its relevance to this study is limited.

In a study aimed at improving the understanding of informed consent among middle aged and elderly patients with psychotic disorders, Dunn *et al*. (2002) randomised 80 patients and 19 normal comparison participants to receive a routine consent or enhanced consent. The enhanced consent consisted of a computerised slide show incorporating more structure and review of important information. A comprehension test was administered after the consent procedure. The normal comparison participants scored better than the patients overall. The patients who received the enhanced consent scored better than those who got the routine consent. Patients on the enhanced consent did not differ from the normal comparison participants who received routine consent. Comprehension was reported only in terms of how many achieved 100 percent. The questionnaire was not included in the report and so it was

difficult to understand the areas of comprehension that were tested or answered wrongly. The study established, that among patients, comprehension test scores correlated with levels of education and cognitive performance. The findings suggest that structured presentation of information may help patients with cognitive impairments to understand information concerning research and research related procedures.

In a study aimed at comparing the usefulness of various sources of information, Agre and Rapkin (2003) compared the effectiveness of information provided through videotape, computer and booklet against the standard written consent form. All three methods had been demonstrated to be effective in separate studies and yet no study had been conducted comparing the three methods. The study involved patients, family members and surrogates who were waiting for patients. The study observed that there was no evidence of significant differences in patient knowledge related to any of the alternative consent tools. It was observed, however, that computer and video formats produced slight improvements in understanding over booklet and standard formats. Interestingly, the study found that no one in any group or age group answered more than two thirds of the knowledge questions correctly. The authors therefore concluded that there was a need for more research on this issue. Such research could focus on the types of questions that were asked and even the contents of the various interventions used in the study. The authors have also suggested that instead of having detailed and longer informed consent documents, it might be better to have a form covering key facts accompanied by appropriate resources that provide more details. They concluded that media consent tools should not be considered a panacea for improving informed consent and that these tools cannot simply be a conversion of standard consent information to another format.

The reading level of documents is important in the informed consent process as it contributes in a significant way towards understanding of the information presented in the documents. Coyne *et al*. (2003) conducted a randomised controlled study that assessed the effectiveness of an easy-to-read consent statement when compared with a standard consent statement. The authors hypothesised that the easy-to-read statement would result in higher levels of comprehension, lower patient anxiety, higher levels of patient satisfaction, and higher patient accrual. Patients in the easy-to-read arm demonstrated lower levels of anxiety and higher satisfaction compared with patients who received the standard package. Patient comprehension and accrual were not affected by the intervention. This study confirmed that trial information can be simplified without omitting useful information. The authors caution, however, that the generalisability of the findings from this study may be limited by characteristics of the patient sample.

Agre *et al*. (2003) reported on eight studies that involved interventions aimed primarily at impacting on decision making, knowledge and therapeutic misconception. The interventions used included video and computer based programmes aimed at providing information, modified consent forms for low literacy populations, role plays, and decision aids. Six of the studies were randomised controlled trials (RCTs). To their surprise, most of the interventions did not significantly improve knowledge of consent information. The majority of participants in one of the studies incorrectly described therapeutic aims as a purpose of the trial, even after viewing the intervention video. It is not clear what type of information was provided through the various interventions. The interventions could simply have been attempts to package the same information from consent documents into different formats. For all eight studies, there was no gold standard for maximizing understanding. The authors pose various questions including: what should be the gold standard for maximizing understanding? What should we expect people to know? Do scores on knowledge quizzes actually reflect an understanding of the information? Are all the elements of equal importance?

In a study to evaluate a prototype informed consent process, Colletti *et al*. (2003) concluded that participation in the prototype informed consent process was associated with substantial and sustained improvements in knowledge. Baseline data on knowledge levels was obtained before the implementation of the prototype. Participants from the intervention group were given a booklet that described a hypothetical HIV vaccine trial. The low literacy participants were offered an audiotape recording of the informed consent form. Immediately after reading or listening to the tape, participants were allowed to discuss any questions with trained study staff and they were encouraged to take the booklet or tape home to read and to discuss with others. Participants were invited to come back to the clinic after one or two weeks to discuss with a trained staff member. After discussions, the trained member would then ask questions aimed at assessing the trial participants' understanding of key concepts. Participants were then requested to complete a self-administered questionnaire to assess their understanding of the hypothetical situation, as well as their willingness to join the hypothetical study. Significant improvements in understanding were observed among the low literacy participants. The findings from this study demonstrate the importance of giving potential participants time to read and discuss information provided in a simple way.

Sastry *et al*. (2004) report on a study they conducted in India, aimed at optimizing informed consent among low literacy populations. They assessed pregnant women's understanding of group education and counselling about HIV/AIDS provided at an antenatal clinic. They then enhanced the group education and counselling process with the use of culturally appropriate visual aids, and assessed the subsequent changes. They found that the use of visual aids improved women's understanding from 38 percent to 72 percent. They also found that when the same visual aids were reinforced during individual counselling, women's overall comprehension rose to 96 percent. This study confirmed that complex information can be

clearly conveyed and understood even in populations of low literacy and even within busy and limited-resource government hospital settings. The study also confirmed that the standard model of conveying information may not be sufficient to ensure understanding of participants. This approach has been used successfully in developing countries in the areas of public health, nutrition, sanitation, health and family planning (Howze, 2009; Olatoye, 2005). The important issue to note is that such visual aids should be developed with the specific population in mind in order to ensure their positive impact. The study has successfully demonstrated that, with some effort, it is possible to improve understanding about research and research procedures.

Flory and Emanuel (2004) reviewed research on interventions aimed at improving research participants' understanding of information disclosed during informed consent. They did a Medline search covering studies conducted between 1966 to March 2004 and they identified 42 studies that met their inclusion criteria. They found that out of 12 trials that used multimedia interventions, three showed significant effectiveness, and of 15 trials that used some enhanced informed consent documents, six showed significant improvements in understanding. Five of the 6 studies were unfortunately of limited quality, thereby limiting their conclusiveness. Lower education was associated with limited levels of understanding in the majority of trials. This review concluded that efforts to improve understanding through the use of multimedia and enhanced informed consent forms have had only limited success. Flory and Emanuel (2004) further concluded that having a team member or a neutral educator who spends more contact time with participants appeared to be the most effective way of improving research participants' understanding, but that this needed further research.

A study was conducted to assess the usefulness of a 20-minute video which was developed for use in recruitment for a microbicide study (Friedland *et al*., 2004). The video was developed as an intervention aimed at improving comprehension in the microbicide trial. The team also

developed a booklet that was used as a supplement for the video. The primary purpose of the video was to introduce the trial and to explain the concepts of microbicide, randomisation and blinding. The video also addressed other issues such as HIV testing and voluntary participation. The video, which was filmed in three South African languages, was pilot-tested through focus group discussions and local community advisory groups. The video was revised and finalized based on the feedback from the focus group discussions. The authors found that the combination of presenter, interviews and animation which was used in the video held viewers' attention. Furthermore, the video encouraged people to discuss issues openly and to ask questions. Unfortunately, the team did not formally test the effectiveness of the video and the booklet as their main aim was simply to assist in the microbicide study recruitment efforts.

Wray, Stryker, Winer, Demetri and Emmons (2005) conducted a pilot study aimed at assessing the effectiveness of trial-specific tailored materials in improving understanding of research. They recruited 118 candidates from oncology trials and randomly assigned them to tailor-made materials or to a generic booklet about clinical trials. Participants rated tailor-made materials as a useful reference, but there were no major differences between the two groups in terms of understanding. This finding could have been influenced by factors such as length, complexity and readability of the tailor-made materials. The investigators did not control for participants duration of trial experience.

In order to promote understanding of HIV preventive microbicide trials, a team developed a booklet which explained the basic elements of informed consent with simple language and illustrations (Woodsong, 2005). Based on review of literature and her own studies, Woodsong suggested that investigators conducting HIV prevention research in developing countries need to use creative approaches in improving comprehension. The author confirmed that concepts associated with research such as randomisation, placebo and double-blinding are difficult

concepts to convey to illiterate persons. However, the effectiveness of this booklet has not been assessed in a systematic way.

In an effort to improve understanding of microbicide trials by potential participants, Woodsong and Abdool Karim (2005) proposed a conceptual framework for an enhanced informed consent process. The framework consists of three stages, namely pre-enrolment, enrolment and post-enrolment stages. The pre-enrolment phase includes a community engagement process, during which researchers work with community representatives and community advisory boards in developing a message that is culturally appropriate. In the enrolment phase, the researchers deal directly with the potential participants in conveying information in a way that is meaningful and acceptable to the individual. In the post-enrolment phase, the researcher continually checks on the willingness of the individual to continue in the study and also conveys any new information they would have found out about the study or the product being tested. This conceptual framework is based on the authors' field experience and appears useful, but was not tested to confirm its effectiveness.

More and more, children are taking part in research which is frequently aimed at addressing problems specific to them. There is therefore the need to conduct research which looks at ways of obtaining informed consent from children. Barnett, Harrison, Newman Bentley and Cummins (2005) conducted a study which looked at the impact of different styles of informed consent documents for children. The authors concluded that a story format was clearly superior in maximizing children's understanding. However, it should be noted that this study has been criticised for failing to provide information on what types of questions were included in the assessment questionnaire and how the validity of the assessment questionnaire was assured (Cracowski & Paris, 2005). The study has also been questioned on the use of a prompting questionnaire, as well as for the effect of the environment in which the intervention

was implemented (Cracowski & Paris, 2005). Environmental factors such as noise, light, set-up of room, friendliness of the environment and many others may have an impact on the intervention.

Eriksson and Helgesson (2005) observed that potential research participants have different information needs. They suggest that researchers should not force information on potential participants if the potential participants are not interested in the additional information. They suggest a tool for identifying those research participants who want limited information. The tool consists of some questions around appraisal of the research, priority of time and privacy, and perception of duty to participate. Unfortunately, effectiveness of the tool that was proposed was not evaluated.

In a study which sought the opinions of parents of children with leukemia on how informed consent can be improved, Eder, Yamokoski, Wittman and Kodish (2007) established that parents needed more time to consider information provided to them. Furthermore, they established that the amount and type of information should not be excessive, and additional materials should be provided. This research marked an important step in efforts to improve informed consent as it elicited the voices of important stakeholders in the informed consent process. The authors' recommendations were not evaluated as their research was only aimed at eliciting the views of the children on how informed consent could be improved.

An intervention study conducted by Dunn, Palmer and Kehaan (2006) aimed at improving participants' understanding of the use of placebos in research established that participants who received the intervention obtained higher scores on the placebo post-test compared to those who received standard information alone. In this study, 49 schizophrenic patients were randomised to either a routine explanation of placebo or a routine explanation plus a brief

educational module explaining placebo in greater depth. This information was presented in the context of a hypothetical double-blind placebo-controlled trial. It was observed that some participants related the term "sugar pill" to diabetes. This term is often used in clinical trials to refer to placebo tablets. This finding confirms the need for discussions with participants aimed at clarifying any points of misunderstanding.

Juraskova *et al*. (2007) reported on a decision aid kit that they developed aimed at improving women's understanding of breast cancer trials. The kit included graphical information, text and tables relevant to the decision whether to participate in a trial. The investigators observed that after exposing 37 women to the aid kit, 31 agreed to participate in the study. They reported that they had a very good understanding of the trial. At the time of reporting, the authors were planning to conduct a randomised controlled trial to test the effectiveness of the decision aid kit against standard information provided through the informed consent document and routine processes.

Ryan, Prictor, McLaughlin and Hill (2008) conducted a review of studies which compared the effects of providing audio-visual information alone or in conjunction with standard forms of information provision. They identified four studies that fitted their inclusion criteria. Of the four, three were randomised controlled trials while one was a quasi-randomised trial. A review of the four studies as found by Flory and Emanuel (2004), showed that considerable uncertainty remains about the effects of audio-visual materials. Audio-visual materials did not consistently increase participants' levels of understanding. The authors caution that the heterogeneity of findings may be a reflection of differences in design as well as content of the audio-visual interventions.

In order to improve informed consent in illiterate populations, Kripalani, Bengtzen, Henderson and Jacobson (2008) conducted a study aimed at testing the usefulness of different approaches of disclosing informed consent information among low literacy populations. They provided verbal information as well as visual aids and asked patients to teach back main points. Approximately 40 percent of the patients were able to teach back the eight items initially. Those with higher levels of education faired better. Despite the use of simplified consent documents, the study concluded that literacy remains an independent predictor of comprehension. The authors further concluded that additional measures were necessary to promote informed consent among low literacy populations. Some of the weaknesses of this study include the fact that the same information found in informed consent documents was repackaged and complemented by visual aids. The study also focused more on recall than on broader understanding of the information as the participants were assessed for understanding based on the eight points that are emphasised by US regulations.

Kass *et al*. (2009) reported on a study in which they compared an enhanced informed consent process against a standard process involving use of an informed consent form and a meeting with an oncologist in a cancer trial. In the enhanced process, participants watched a 20-minute computer-based presentation on early phase cancer clinical trials. Participants in the control arm received an information pamphlet on taking part in clinical trials. The intervention was self-directed and participants viewed it in a private area before meeting the oncologist. Respondents in the intervention group were found to be more likely to state correctly the purpose of an early phase trial (34.4 percent) compared to those on the control arm (16.7 percent).

Kass *et al*. (2009) found that the majority of participants on both arms continued to report a belief that the purpose of an early phase trial related to efficacy. This was not surprising since

this study was conducted using cancer patients who had very limited treatment options and would thus look forward to clinical trials as a source of hope. Some of the weaknesses of this study included the fact that the oncologists were not blinded, and that participants in the control arm were provided with a pamphlet on cancer clinical trials on the insistence of the IRB which reviewed the study. The pamphlet could have led to the small differences that were observed between the two arms. The study focused more on recall as it did not ask some questions that would show whether the participants were able to use the information disclosed in a meaningful manner.

2.12 SUMMARY OF LITERATURE REVIEW

From the review of literature, it is evident that a significant amount of literature exists on the subject of trial participants' understanding. Studies assessing trial participants' understanding have attracted increasing attention over the past decades due to the importance that is now placed on informed consent as a result of the changes in the international research landscape. A significant number of studies have confirmed the challenges that participants face in understanding research and specific trial procedures such as randomisation, double-blinding and placebo use. There are various barriers to obtaining better informed consent. Taylor (1999b) has ably summarized some of the barriers. These include patient-centred barriers such as age, education, cognitive ability and severity of illness. Process-centred barriers include content, readability, terms used, framing of information provided, timing of discussion, source of information, educational programmes aimed at improving understanding, and amount of time allotted to discussion of information.

The studies that have assessed understanding have used various methods for assessing participants' capacities to comprehend informed consent information. Methods include

questionnaires, interviews and other specific tools. There are variations across studies in terms of time of assessment and how comprehension is measured. Some studies rely on self reports, others use real world trials and others use hypothetical trials. Various weaknesses have been identified in some of these studies. Some of the tests that have been employed by researchers in assessing understanding are more appropriate for assessing short term recall, which is not an adequate indication of understanding. It is also evident from the review of literature that, in some of the studies assessing comprehension, researchers have not developed conceptual and operational definitions of comprehension before conducting the assessment. Some studies have not obtained baseline data before the intervention so as to provide a clear picture of the situation before and after the intervention, while some have relied on simulations and perceived understanding, which may not approximate reality. Some of the tools that have been used have been lacking in terms of validity and reliability, administration standardisation, scoring and interpretation. The review has further revealed that comprehension tests can be affected by other environmental or contextual factors such as anxiety, age, literacy, memory and cognitive functions.

From the review, there are various lessons that can be learned. The lessons learned can be categorized into "outstanding" lessons and "other" lessons. The outstanding lessons are that personal contact improves comprehension and also that narrative measures best assess comprehension. There are various other lessons learned; it is important to note that while improving informed consent may not necessarily reduce the risks involved in a particular study, it helps to ensure that individuals are responsible for their participation, as well as for their health. Assessments of comprehension are important as they make it possible for researchers to address potential problem areas in participants' comprehension. Research staff need to be well trained in communication and counselling and should not have substantial language or cultural barriers. Consent forms should be readable and easily understood by potential participants.

Special media such as videos, flip charts, booklets or role plays should be prepared for participants and these should be reviewed by community representatives, ethics committees and other experienced members. Research staff need to facilitate participants' understanding of technical concepts.

In the present study, an attempt has been made to take into consideration the various weaknesses and strengths that have been identified through the review of literature. This study therefore aims to build on previous studies in terms of assessing understanding, as well as in developing an intervention aimed at improving understanding if indicated. It was evident that, in most of the studies reviewed, the authors made recommendations based on interventions that have not been empirically tested. The current study is aimed at bridging this gap by testing an intervention if limited understanding is identified.

CHAPTER 3

CONCEPTUAL FRAMEWORK

3.0 INTRODUCTION

The main objective of this chapter is to present the conceptual framework developed and adopted for this study. The study is grounded mainly on the psychosocial schema developed by Faden and Beauchamp (1980) and the Meerwein model of the informing process (Tomamichel *et al*., 1995, 2000).

3.1 FADEN AND BEAUCHAMP'S PYCHOSOCIAL SCHEMA

The psychosocial schema developed by Faden and Beauchamp (1980) views informed consent as comprising three sequential behavioural steps which include (a) reception, (b) comprehension and (c) utilisation of the comprehended information in reaching a decision whether or not to participate in a study. The schema as presented in Figure 3.1 postulates that, for consent to be informed, a prospective trial participant has to go through the three main steps, namely disclosure of information, comprehension of information and utilisation of the information in making a decision (Faden & Beauchamp, 1980). Beauchamp and Childress (2001) provide further refinement of the schema as they address the distinction between understanding and acceptance. Acceptance is viewed as an agreement which is not based on the disclosed information. Such agreement may be based on other factors such as trust, expectation of benefits and others.

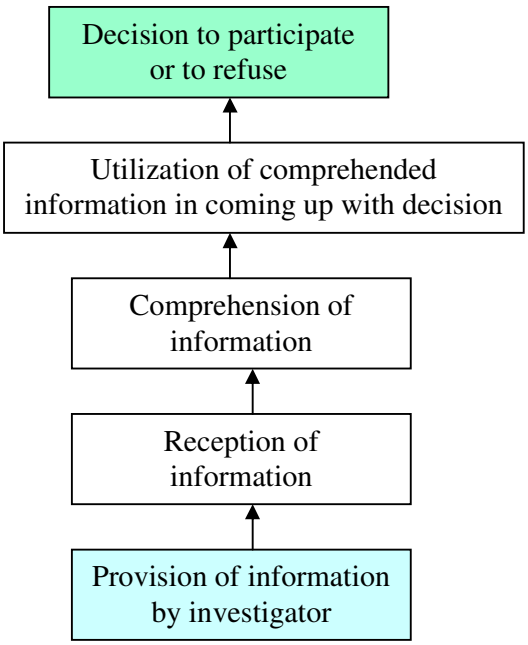


Figure 3.1 Faden and Beauchamp's psychosocial schema of informed consent (modified)

3.2 MEERWEIN MODEL OF THE INFORMING PROCESS

On the other hand, the Meerwein Model of the informing process concentrates only on the aspect of how a prospective trial participant processes the information he or she would have received from the investigator in arriving at a decision on whether to participate in a study or not. Figure 3.2 presents a diagrammatic representation of this model. The model defines three main dimensions of the informing process. These include (a) the information itself, (b) the emotional dimension concerned with rapport between the researcher and the participant, and (c) the interactional dimension which is concerned with the capacity and willingness of the research staff to perceive and discuss emotional needs, concerns and complaints of trial participants and to deal with these (Tomamichel *et al*., 1995). The Meerwein model has been utilised for this study because it deals with important aspects of the researcher-participant relationship that impact on informed consent, namely, communication of information, negotiation skills and the environment in which the information is conveyed.

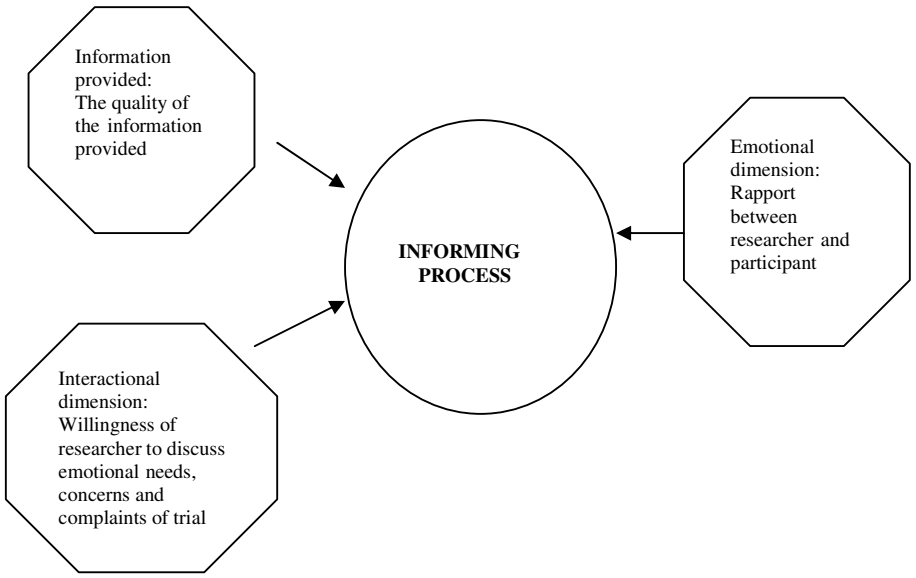
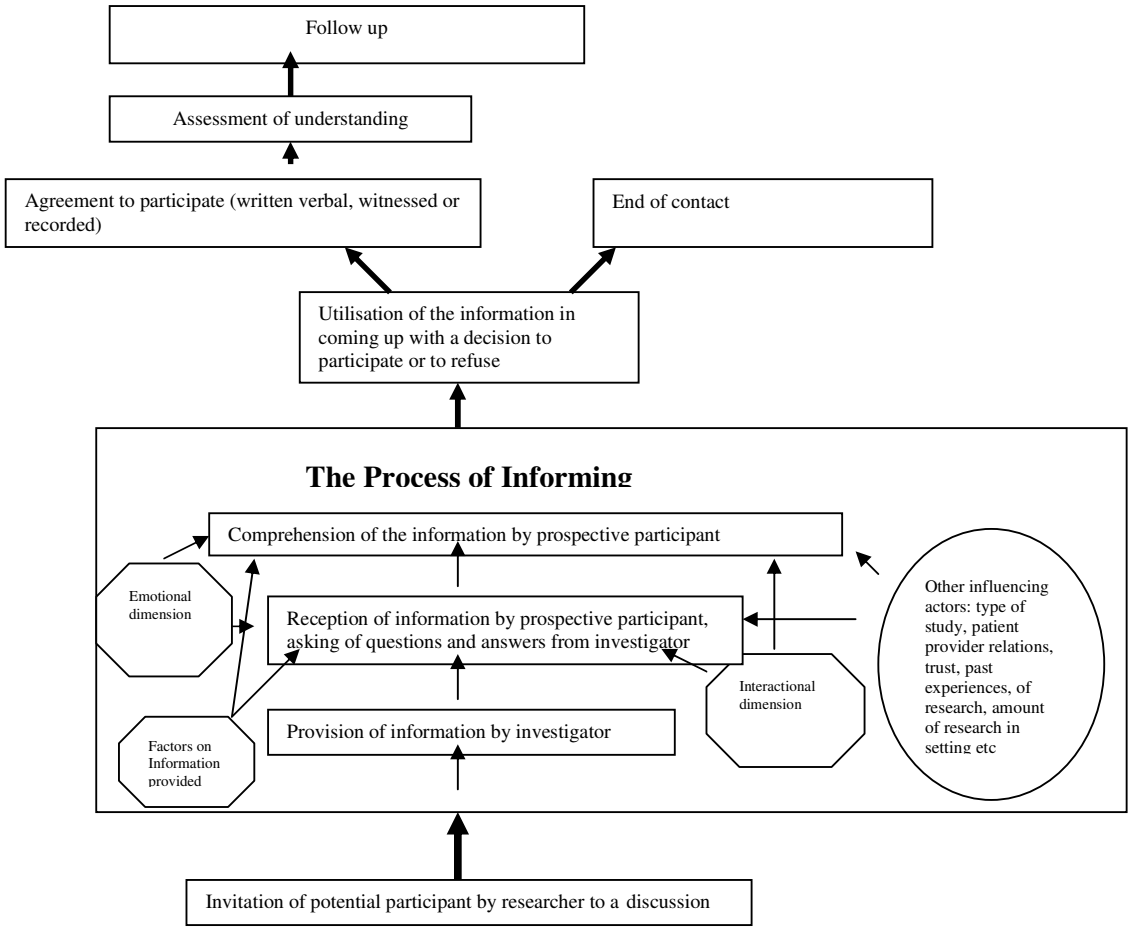


Figure 3.2 Meerwein Model of the informing process

Based on the Psychosocial Schema and the Meerwein Model of the process of informing, a conceptual framework has been developed for this study which incorporates aspects from both. This study has further adopted a framework presented by Bhutta (2004) and modified it so as to present a more detailed conceptualisation of the informed consent process. The conceptual framework adopted for this study takes cognisance of the behavioural steps as outlined in the psychosocial schema and the important dimensions that impact on the decision to participate in a study, as outlined in the Meerwein Model of information processing. Figure 3.3 below shows the conceptual framework that has been adapted for this study. The framework shows that informed consent is a process that includes various steps and key elements of the information to be shared by the researcher with the potential participant in a manner that can be adequately grasped and acted upon (Bhutta, 2004). The various stages and key elements are detailed below.



Adapted from Bhutta, 2004: The framework combines Faden and Beauchamp's pychosocial schema and the Meerwein Model of the informing process.

Fig 3.3 Conceptual framework for the process of obtaining informed consent.

In the first stage, the researcher invites the potential participant to a discussion. Once the potential participant accepts this invitation, the investigator then proceeds to the second stage of informing the participant. This stage is viewed as a process in itself as it is composed of various mini-steps. The informing stage needs adequate time on the part of the potential participant to process the information without duress. The Meerwein Model of information processing assumes importance at this stage as it illustrates the factors that play an important role at this stage of informing the potential participant.

As the first mini-step at this stage, the researcher provides sufficient and clear information to the potential participant about the research and the participant's rights in a way that can be understood by the potential participant. Such information includes the purpose of the study, the procedures involved, the risks and benefits, issues such as maintenance of confidentiality, and other important elements that are emphasised by all the international ethical codes and regulations. Participants also need to be adequately informed of the purposes of the study procedures as well as the implications of the procedures on themselves as persons. They also need to be clearly informed that this is research and not routine care, and have the differences between research and routine care explained to them as necessary. The information has to be clear, and sufficient (Tomamichel *et al*., 2000). Where possible, the potential participants may request more time to process the information and even to consult other persons. Such requests need to be granted as a way of showing respect for the potential participant.

In the second mini-step at the informing stage, the potential participant receives the information and is given the opportunity to ask questions and has the questions responded to adequately. In the third mini-step, the potential participant should have reached a state of comprehension. He or she has understood what is being asked of him or her. This state may result from the fact that the information was presented in a way that is simple and yet conveys the essential information that is essential for the potential participant to research an informed decision. This stage is probably one of the most important as it plays a crucial role in determining whether one comprehends or not. Among other things, comprehension can be assured through several factors including the simplicity of the information, the discussive nature of the conversation as well as a conducive and friendly environment. The environment should be such that the potential participant feels at ease, he or she is satisfied with the discussion, and he or she is not worried after the discussion (emotional dimension). Whether the potential participant understands or not also depends on the interaction with and the researcher. The potential

participant needs to be satisfied with answers to their questions, they should be able to express their worries, fears, objections and concerns, and feel that these have been addressed adequately. The potential participant also needs to feel that they have found the discussion helpful (interactive dimension). This stage is influenced by the broader context which is made up of various factors such as type of study, patient provider relations, trust, past experience of research, amount of research in that setting and other factors.

The third stage is crucial in the informed consent process. This stage involves the utilisation of all the information that has been provided by the researcher. This stage is very dependent on the previous stages. Having processed the information received, the potential participant now moves to the next stage, which involves making a decision about whether to participate in a study or not. If the potential participant refuses to participate, then the researcher terminates the contact without use of coercion or undue inducement. The next stage involves the reaching of an agreement between the researcher and the participant. This agreement can be in writing, verbal, witnessed or recorded.

After this agreement, it is crucial for the researcher to assess that the participant has adequately understood that they have agreed to participate in a study and not in a programme that is providing routine care. The researcher can achieve this through various ways including administering a short questionnaire or asking the potential participant to explain in their own words. The researcher also needs to determine whether the participant is aware of the study procedures that are being used in the study, the purpose of those procedures as well as the personal implications of those procedures. If the researcher identifies some areas that need reinforcement, he or she can assist the participant accordingly. The next stage is that of follow-up, which involves reminding the participant that they are participating in a study and that they are free to withdraw at any time. Some of the aspects of the above framework were used to

guide the development of the tools and the pilot intervention and also in the discussion of findings.

3.3 TAXONOMY FOR ANALYSING UNDERSTANDING OF CLINICAL TRIAL CONCEPTS

A taxonomy for analysing understanding of clinical trial concepts/procedures has been developed for this study. The taxonomy borrows from Bloom's Taxonomy of Educational Objectives (Hochhauser, 2005) and the Psychosocial schema proposed by Faden and Beauchamp (1980).

Level of understanding	**Actions associated with level of understanding**
1. Awareness about study procedure ↓	**Recall** – basic awareness about a procedure and how it is implemented.
2. Awareness about justification of study procedure ↓	**Interpreting**- why a procedure is important is important
3. Awareness about the personal implications of procedure ↓	**Analysis, synthesis and evaluation** - information on how the procedure is implemented as well as the reasons for adopting the procedure in the trial are used to have an understanding of the personal implications of the procedure.
4. Making an informed decision which is based on adequate information.	**Informed decision** - The synthesised information is then used meaningfully to make judgments and decisions. Judgment also includes attitudes towards that procedure.

Figure 3.4 Proposed Taxonomy for analysing understanding of clinical trial concepts

The taxonomy for analysing understanding of clinical trials (see Figure 3.4) postulates that, decisions to join clinical trials should be based on adequate understanding of the study and its

procedures such as randomisation, double-blinding and placebo use. According to this taxonomy, for potential participants to be classified as having understood, they should have reached the third level of understanding, which can then lead to the making of an informed evaluation and ultimately a decision whether to join a study or not. The usefulness of the taxonomy is tested in this study.

3.4 SUMMARY

The above section has illustrated how the process of obtaining informed consent can be conceptualized. The key players, as well as the factors that contribute to understanding, have been indicated. Informed consent is a process that should be viewed more as a conversation or negotiation between the researcher and the potential participant, culminating in either participation in a study or refusal to participate. Most guidelines emphasise the documenting of consent and do not emphasise the participant's understanding or the assessment of this understanding. During the documentation of the agreement, there is no evaluation of the participant's understanding of the nature of the study, as well as the personal implications of participating in the study (Bhutta, 2004). By following up on all the above steps, including assessment of trial participants' understanding, the researcher ensures that participants' decisions to participate in research are well informed.

This thesis, like much of the literature on informed consent, emphasises the fact that informed consent is not an event but a process. Furthermore, illiteracy in and of itself should present no problem in the informed consent process, which, if conducted properly, entails a discussion rather than reading from the informed consent document. This thesis further argues that the informed consent process should show respect to the potential participant and foster their interests by empowering them to pursue and protect their own interests. Informed consent is not necessarily there to protect the interests of the investigators and their institutions against

criminal liability (Levine, 1991). This study examines the information that is conveyed to the potential participants and determines how much of this information the potential participants retain, comprehend and use in making their decision to participate in the research.

CHAPTER 4

STUDY AIM AND OBJECTIVES

4.0 INTRODUCTION

This chapter highlights the main study aim and specific objectives of the study. The chapter also presents the study questions that the study sought to answer, as well as the hypotheses that were tested as part of the study.

4.1 MAIN STUDY AIM

The primary aim of the study was to assess microbicide trial research participants' understanding of randomisation, double-blinding and the use of placebo in the microbicide trial. The main aim was sub-divided into specific objectives.

4.2 SPECIFIC OBJECTIVES

The specific secondary objectives of the study were as follows:

Cluster 1

- To assess and describe the processes and methods that research staff engage in to explain double-blinding, randomisation and the use of a placebo in a microbicide trial.
- To explore the attitudes of research staff regarding full disclosure of information regarding double-blinding, randomisation and placebo to research participants.

Cluster 2:

- To understand whether research participants understand the trial procedures as well as the personal implications of these concepts on themselves.
- To assess research participants' attitudes towards randomisation, double-blinding and use of placebos.

Cluster 3:

If indicated by cluster 2 above,

- to develop and test an intervention for improving trial participants' understanding of the above three key concepts and their implications and, if it is successful, to recommend it to researchers for use in future as a way of promoting better informed consent processes.

4.3 RESEARCH QUESTIONS

The empirical study focused on two main areas; (1) how research staff and study information sheets explain the concepts of double-blinding, randomisation and the use of the placebo and what prominence they give them; and (2) research participants' understanding and attitudes towards the concepts and whether they considered these three key concepts in making decisions on participation in the microbicide trial.

The main research question for the study was therefore as follows:

- Are trial participants aware that they are participating in a trial which employs randomisation, double-blinding and placebo use and are they aware of the purposes and personal implications of these procedures?

In attempting to address the main research question, the main research question was broken down into various manageable sub-research questions as follows:

1. How do trial related documents explain the concepts of randomisation, double-blinding and placebo use?
2. How do study staff explain the concepts of randomisation, double-blinding and placebo use to prospective trial participants?

3. Are participants aware of the purpose of the study?
4. Are participants aware that they are participating in a trial to test a product whose efficacy is not known?
5. Are participants aware that they are still exposed to HIV infection while they are using the experimental product they have been issued with?
6. Are trial participants aware that randomisation, double-blinding and placebo use are part of the study?
7. Are trial participants aware of the reasons why randomisation, double-blinding and placebos are used in the study?
8. Are participants aware of the various study arms in the microbicide study?
9. Are participants aware that they have been randomised into different groups?
10. Are participants aware that they may be receiving a placebo?
11. Are participants aware that neither themselves nor the trial nurses and doctors (i.e., research personnel) are aware of the arms they are in?
12. Are trial participants aware of the personal implications of randomisation, double-blinding and placebo use?
13. Are participants aware of the implications of their participation, regarding protection from infection by the product under test?
14. What are the attitudes of the trial participants regarding randomisation, double-blinding and placebo use?
15. Can an intervention improve trial participants' understanding of research, randomisation, double-blinding and placebo use?

4.4 STUDY HYPOTHESES

The hypotheses for the current study were formulated on the basis of the aims, specific objectives and research questions that were generated for the study. Hypotheses were only generated for the most important research questions as follows:

A. Informed consent forms and materials provide adequate information on randomisation, double-blinding and placebo use. This hypothesis was tested using data from document review and indepth interview with study staff responsible for obtaining informed consent.

B. Research staff have a positive attitude regarding full disclosure of information on blinding, randomisation and placebos to research participants. This hypothesis was tested using data from structured interviews and focus group discussions with participants from the microbicide study.

C. Trial participants are aware that the procedures of double-blinding, randomisation and placebo use are being used in the trial. This hypothesis was tested using quantitative and qualitative data from the structured interviews and focus group discussions with selected microbicide trial participants.

D. Trial participants are aware of the purpose of double-blinding, randomisation and placebo use in research. This hypothesis was tested using quantitative and qualitative data from the structured interviews and focus group discussions with selected microbicide trial participants.

E. Trial participants understand the personal implications of the trial procedures under study. This hypothesis was tested using quantitative and qualitative data from the structured interviews and focus group discussions with selected microbicide trial participants.

F. Trial participants do not believe that they are completely protected from HIV infection by the microbicide under study. This hypothesis was tested using quantitative and qualitative data from the structured interviews and focus group discussions with selected microbicide trial participants.

G. Trial participants have a positive attitude towards double-blinding, randomisation, and use of placebos. This hypothesis was tested using quantitative and qualitative data from the structured interviews and focus group discussions with selected microbicide trial participants.

H. Research staff provide adequate information on double-blinding, randomisation and placebo use to trial participants. This hypothesis was tested using qualitative data from the indepth interviews with four study staff members responsible for obtaining informed consent. Data from the focus group discussions with selected microbicide trial participants was also used in considering whether to support or reject this hypothesis.

I. An intervention using common language and examples can assist in improving understanding about randomisation, double blinding and placebo use. Quantitative and qualitative data from the implementation phase of the current study was used in considering whether to accept or reject this hypothesis.

4.5 SCOPING THE BOUNDARIES OF THE STUDY

It is important to clearly demarcate the boundaries of this study in line with the main research question, sub-research questions, main aim, specific objectives and hypotheses of the study. In this section, the boundaries of the study are clearly laid out.

- The study which forms the subject of this thesis was conducted in Blantyre and Lilongwe in Malawi. The findings may therefore not be generalisable to participants from any other sites or clinical trials beside the two study sites.

- The study specifically sought to assess the understanding of trial procedures by participants from a specific microbicide trial (HPTN035).
- The study is not aimed at focusing on the making of decisions to participate in research broadly, but seeks to find out if participants had understood the procedures of randomisation, double-blinding and placebo use as these are important in making their decisions to participate.
- The study population for the study consisted of 780 women from 2 sites in Malawi who were on the 3 gel-arms of the 4-arm microbicide study, and study staff who were involved in obtaining informed consent for participation in HPTN035. The participants from the microbicide study formed the main units of analysis.
- The study attempted to interpret why trial participants understand or do not understand by focusing on the information that was provided to them (looking at trial documents and interviewing study staff) and by assessing a sample of the microbicide trial participants.
- The main purpose of the study was to assess understanding using a tool that was developed specifically for the study and thereafter to test an intervention that was also specifically designed for the study. The main purpose was not to test the usefulness of an existing test of understanding.
- The main aim of the study was not to improve informed consent. While the study is aimed at improving informed consent, the focus was on understanding of the three concepts under study. In this way the current study contributes in an indirect way towards the improvement of informed consent as informed consent is much broader than an understanding of the three concepts.

4.6 SUMMARY

The main aim of this chapter was to clearly lay down the main aim of the study, followed by the specific objectives, study questions, study hypothesis and boundaries of the study. The main aim of the study as the topic suggests was to assess microbicide trial participants' understanding of randomisation, double blinding and placebo use. Based on the review of literature and anecdotal evidence from the field, the researcher believed that research participants with low levels of understanding would be identified. This placed on the investigator an ethical obligation to offer a potential intervention should the study reveal low understanding. The intervention was to be based on the findings from the current study and on previous research identified in the literature review. The answers to the hypotheses and research questions are presented in Chapter 11.

CHAPTER 5
RESEARCH METHODOLOGY

5.0 INTRODUCTION

This chapter discusses the methods that were used in collecting data for this study. The chapter is aimed at giving a description of the methods used in conducting this study. The chapter begins with brief descriptions of the study design, study area and study context. This is followed by brief descriptions of the study population, sampling procedure, data collection tools including their reliability and validity. The last section focuses on the ethical issues related to the study and the measures that were taken to address the issues.

5.1 STUDY DESIGN

An exploratory descriptive design with research approaches from both qualitative and quantitative methodology was adopted. A descriptive design was selected for the study as the main aim of the study was simply to describe how study staff and study documents explain the concepts under study. The study was mainly aimed at describing the levels of understanding of the three concepts, the understanding of the implications of the three procedures, as well as the participants' attitudes to the three clinical trial procedures. The design was therefore guided by the research question. This would, in turn, determine the mixed-methods approach which was adopted for data collection. The current study specifically used a structured sequential design which was made up of two main phases and seven specific stages as reflected in Figure 5.1 below.

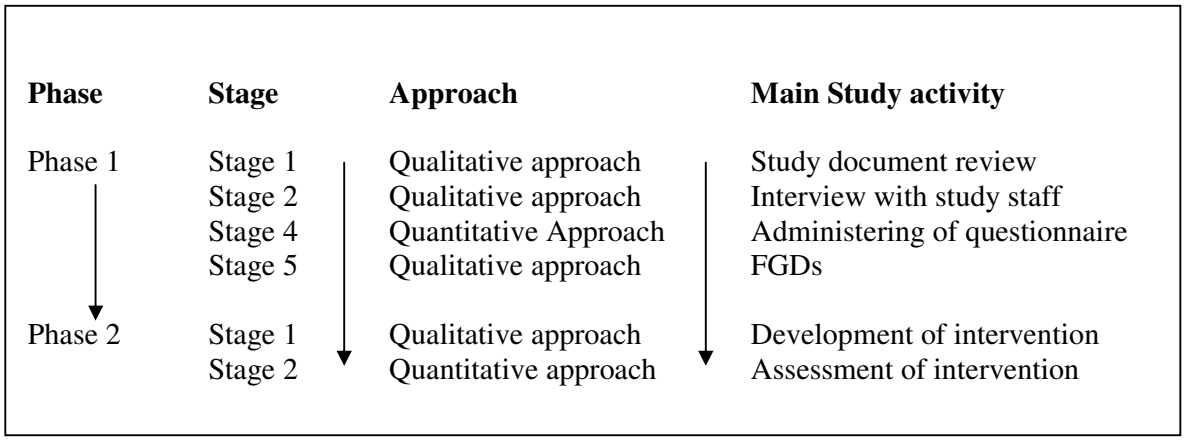


Figure 5.1 Sequential design showing various study components

The rationale or purpose of the study was, from a broad perspective, to assess trial participants' understanding of the clinical trial concepts under study. Thus, as a result of the nature of the subject under study, the first phase had four separate but interrelated methodological components because understanding of concepts needed to be viewed externally (objectively), based on assessments or measurements, and internally (subjectively), based on perceptions and feelings. All four components aimed at contributing towards understanding trial participants' understanding of the concepts under study. The various methods in Phase 1 are described in greater detail in Section 5.7.

A quantitative component, specifically the collection of data using structured interviews was included in the assessment of understanding because it meet typical scientific standards: the tests can be repeated under similar conditions and comparisons can be made. This was done against the background of an objectivist and positivist viewpoint which accepts the test scores as a reality: the scores stand for something, in this case they are taken to be a reflection of trial participants' understanding (Tashakkori & Creswell, 2007). The problem with test scores is that they may fail to truly reflect what they would have been set to reflect. On the other hand, the in-depth interviews and the focus group discussions employed in Phase 1 attempted to capture trial participants' perceptions and experiences of the microbicide trial procedures in the

context of the microbicide trial environment. Understanding is a unique and personal experience that is best studied using qualitative methods (Leedy & Ormrod, 2001; Moustakas, 1994). The study intentionally reflects on the system which produces levels of understanding among individuals. To the extent that the study does so, it is a systematic study (Silverman, 2004). Phase 2 similarly consisted of both qualitative and quantitative elements. In Phase 2, the design and development of the intervention which is described in this thesis was based more on qualitative approaches, whilst the evaluation of the intervention was based more on quantitative approaches. The methods used in Phase 2 are described in greater detail in Chapters 8 and 9. A cross-sectional study approach was determined to be the best method to answer the research question. A cross-sectional survey is often used in descriptive studies as it provides a picture or snap view of the phenomenon under study at a particular time in a particular place.

5.2 STUDY AREA

The study which forms the subject of this thesis was conducted in the cities of Blantyre and Lilongwe in Malawi. Malawi is a land locked country in South/Eastern Africa and shares borders with Mozambique, Zambia and Tanzania (see Figure 5.2). Malawi has an estimated total population of over 13 million people and life expectancy is around 41 years. Birth rate is on average 5.9 per woman, a rate which is high by modern standards. Literacy rate is just over 62 percent (National Statistical Office Malawi, 2004). The economy of Malawi is predominately agricultural, with about 90 percent of the population living in rural areas. Agriculture accounts for a significant proportion of both GDP and export revenues. The economy depends on substantial inflows of economic assistance from the IMF, the World Bank, and individual donor nations. The government faces strong challenges, including improving health and educational facilities and dealing with the rapidly growing problem of

HIV/AIDS. It is among the poorest countries worldwide, with a gross domestic product (GDP) of US$ 519 per capita (Record & Mohiddin, 2006). Malawi has a huge human resources problem, particularly in the health sector, and is ranked as one of the last countries on the WHO list of estimates of health personnel with 2 doctors per 100,000 people (Harries *et al*., 2004)

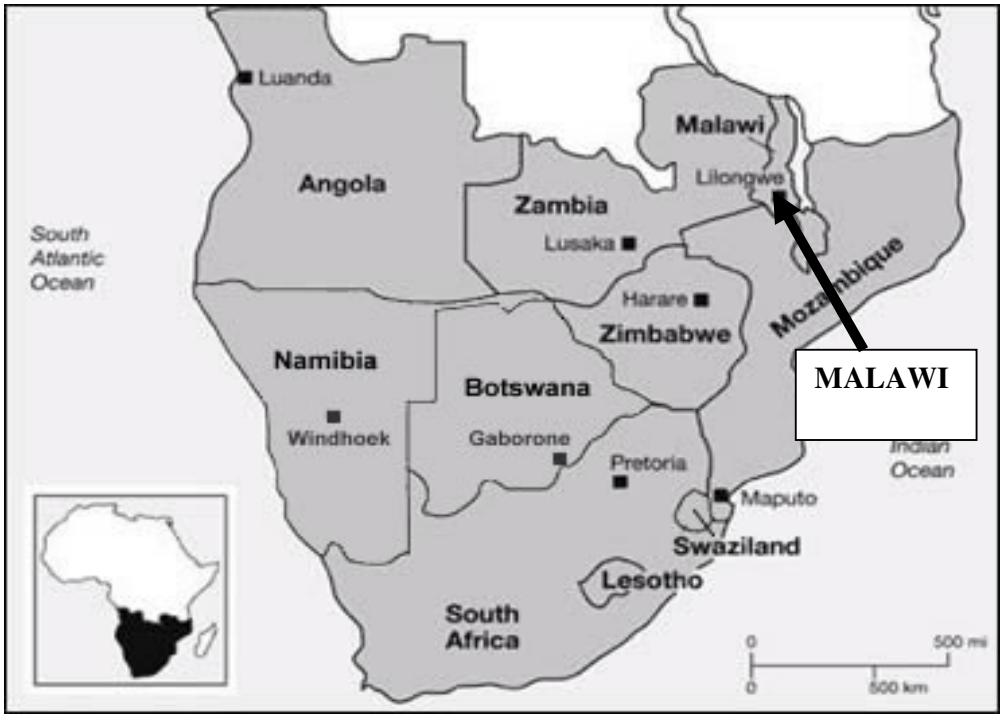


Figure 5.2 Map showing the position of Malawi in Southern Africa

Source:www.canoncollins.org.uk/about/index.php

The major languages in Malawi are ChiChewa 57.2 percent (official language), ChiNyanja 12.8 percent, ChiYao 10.1 percent, ChiTumbuka 9.5 percent, ChiSena 2.7 percent, ChiLomwe 2.4 percent, ChiTonga 1.7 percent, and other 3.6 percent. The ethnic groups consist of the Chewa, Nyanja, Tumbuka, Yao, Lomwe, Sena, Tonga, Ngoni, Ngonde, Asian, and European. In terms of religion, Christians make the majority of the population (79.9 percent), followed by Muslims (12.8 percent), other 3 percent, and none 4.3 percent (National Statistical Office Malawi, 2004).

Lilongwe and Blantyre are about 300 km apart and Lilongwe is the Administrative capital while Blantyre is the Commercial capital (see Figure 5.3).

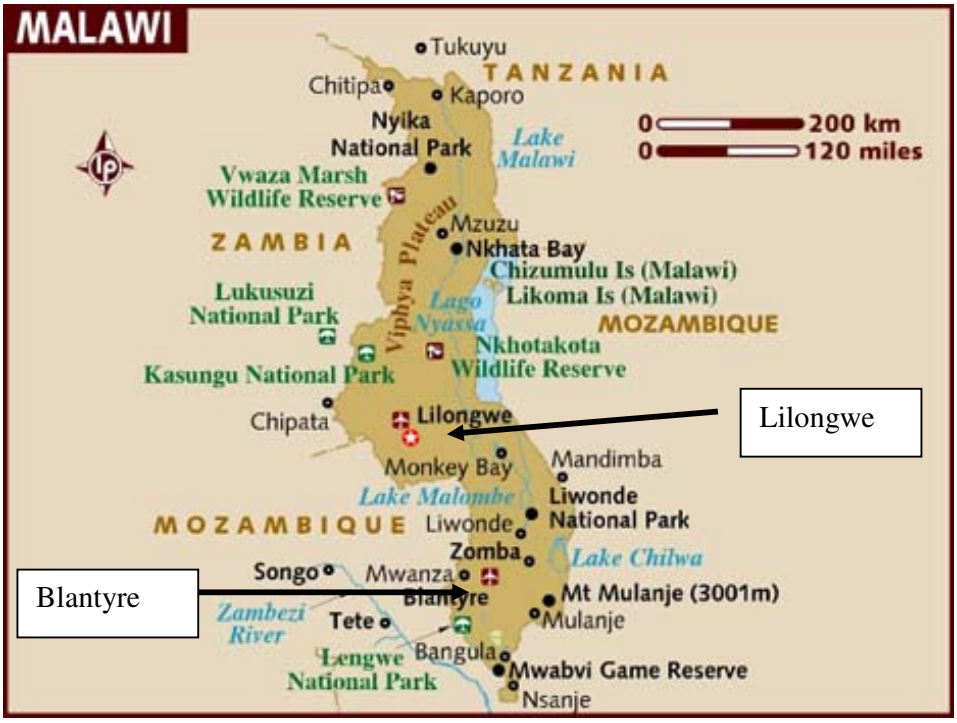


Figure 5.3 :Map of Malawi showing Lilongwe and Blantyre

Source: http://www.lonelyplanet.com/maps/africa/malawi/

5.3 STUDY SITES

The study which forms the subject of this dissertation was conducted at two sites, namely the University of North Carolina (UNC) Project in Lilongwe, and the Johns Hopkins Research Centre in Blantyre. These are described briefly below.

5.3.1 University of North Carolina (UNC) Project

University of North Carolina (UNC) Project is a collaborative research effort between the University of North Carolina in the USA and Malawi, and is based at Tidziwe Centre at Kamuzu Central Hospital. Kamuzu Central Hospital is one of two major referral government

hospitals in Malawi. "Tidziwe" is a ChiChewa word which means, "We should find out". The Tidziwe Centre is adjacent to the Kamuzu Central Hospital Sexually Transmitted Diseases (STD) Clinic and the Lighthouse HIV Patient Care Centre. The Centre is a two-story building that includes 14 clinic exam rooms for outpatient and research examinations, counselling rooms, a state of the art laboratory, medical library with satellite web connections supporting journal access, a lecture hall and classroom with teleconferencing capacity, a data management area with remote and local data entry capacity, secure data storage space, a pharmacy and dispensary, and offices for scientists, administrative staff and community liaison personnel (see Figure 5.4). The UNC Project employs more than 250 staff in Malawi, consisting of medical and clinical officers, nurses, laboratory and pharmacy technicians, data officers and administrative and logistical support staff. The UNC Project has a collaborative relationship with the Ministry of Health and the College of Medicine (COM) of the University of Malawi based in Blantyre, and also works in partnership with several international organizations. The UNC Project has satellite offices at the College of medicine in Blantyre.

Figure:5.4. Picture of the UNC Research Centre in Lilongwe, Malawi

Source: Photo by Paul Ndebele

The UNC Project provides staff to the Lighthouse HIV out-patient clinic at Kamuzu Central Hospital and also operates the Kamuzu Central Hospital STD clinic. The Clinic includes clinical and research areas including exam and counselling rooms and an auxiliary laboratory. Various research projects have been conducted at the UNC Project, including studies aimed at improving the treatment of STDs and reducing transmission of HIV from men to women and mother to child.

5.3.2 Johns Hopkins Research Centre

The Johns Hopkins Research Centre is based at Queen Elizabeth Central Hospital in Blantyre and is a collaborative effort between the Bloomberg School of Public Health at Johns Hopkins University in Maryland, USA and the College of Medicine of the University of Malawi. Queen Elizabeth Hospital is located in Central Blantyre and is one of the two main referral government hospitals in Malawi and is also used as the teaching hospital for the College of Medicine. Johns Hopkins is one of the leading research universities in the USA. The collaborative project was aimed at contributing to Malawi's national efforts to develop effective interventions against HIV/AIDS and to build capacity for high quality biomedical research in Malawi.

The Johns Hopkins Centre was established in 1989 and focuses exclusively on HIV/AIDS and reproductive health research. The project serves as a site for the AIDS Clinical Trials Group, Center for HIV/AIDS Vaccine Immunology, Microbicide Trials Network, the HIV Vaccine Trials Network and the International Maternal Pediatric Adolescent AIDS Clinical Trials. The Centre is based in a three-storey building which includes offices, laboratories, library and computer room. The Centre has also been provided with some space in the main hospital buildings (see Figure 5.5). This space comprises counselling rooms, examination rooms, specimen processing rooms, data storage rooms and office space for some operational research

staff. The Centre has a staff complement of more than 100 members including full-time clinicians, nurses and study coordinators, as well as other dedicated staff working in its research laboratory, pharmacy, and data management and community education departments. As a way of ensuring that the views of the Blantyre community are included in the shaping of their research programmes, the Johns Hopkins Centre has established a Community Advisory Board (CAB) called Friends of Johns Hopkins. The CAB includes community representatives and previous study participants and serves as a link between the Project and the community.

Figure 5.5: Picture of Johns Hopkins Research Centre in Blantyre, Malawi

Source: Photo by Paul Ndebele

5.4 STUDY POPULATION

The study which is reported in this thesis was conducted within the context of the HPTN035 microbicide trial which was formally titled ***"Phase II/IIb Safety and Effectiveness Study of the Vaginal Microbicides BufferGel and 0.5% PRO2000/5 Gel (P) for the Prevention of HIV Infection in Women"***. The population for the study therefore consisted of the following:

- 780 women from the three gel arms of the HPTN-035's four-arms who had been enroled for at least three months in both Lilongwe and Blantyre. The main reason for selecting those women who had been enroled for more than 3 months was that there would be at least a three month period between enrolment in the microbicide trial and contact for this study. It was assumed that women who would have been involved in the microbicide trial for a lengthy period would be more conversant with the trial as compared to those who would have joined the trial recently. All participants in the no-treatment arm were excluded since some of the procedures under study did not apply to them (double-blinding and placebo use). The microbicide trial had a total of 1040 participants in Malawi. Six hundred (600) of these participants were based at UNC in Lilongwe, and 440 were at the Johns Hopkins Centre in Blantyre. In Lilongwe, 450 were randomised into the three gel arms, while 330 were randomised into the three gel arms in Blantyre, to make a total of 780 participants who were eligible for this study.
- All study staff who were involved in obtaining informed consent for the microbicide trial at the two sites.

5.5 DESCRIPTION OF THE MICROBICIDE TRIAL (HPTN035 STUDY)

Information on the HPTN035 study was obtained with permission of the investigators of the two HPTN035 sites, from various documents including the study protocol, study information sheets (including informed consent documents) and the HPTN website

(http://www.hptn.org/research_studies/hptn035.asp). HPTN 035 was conducted by a team of African and U.S. researchers associated with the Microbicide Trials Network (MTN), an HIV/AIDS clinical trials network established and funded in 2006 by the National Institute of Allergy and Infectious Diseases (NIAID), with co-funding by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) and the National Institute of Mental Health (NIMH). HPTN035 was a multi-center clinical research study that was aimed at evaluating the safety and effectiveness of two candidate vaginal microbicides, BufferGel and 0.5% PRO 2000/5 Gel (P), for the prevention of HIV infection in women. The study was conducted between February 2005 and September 2008 through a partnership involving US and African researchers and was conducted in various countries including Malawi, South Africa, United States, Zambia and Zimbabwe. As mentioned previously, in Malawi the study was conducted at two sites namely UNC Lilongwe and Johns Hopkins Project in Blantyre.

The primary objectives of this study were as follows:

- To evaluate the safety of Buffergel and 0.5% PRO 2000/5 Gel (P) when applied intravaginally by women at risk for sexually-transmitted HIV infection.
- To estimate the effectiveness of Buffergel and 0.5% PRO 2000/5 Gel (P) in preventing HIV infection among at-risk women.

The secondary objectives included the following:

- Estimating the effectiveness of Buffergel and 0.5% PRO 2000/5 Gel (P) in preventing the following among women at risk for sexually-transmitted HIV infection: bacterial vaginosis, chlamydia infection, genital ulcer disease, gonorrhea infection, herpes simplex virus-2 infection, pregnancy, syphilis infection, trichomoniasis and

- Assessing the acceptability of Buffergel and 0.5% PRO 2000 Gel (P) for use as a vaginal microbicide.

HPTN 035 was as a combination Phase II/Phase IIb trial designed to determine whether either candidate microbicide had sufficient promise to be considered for testing in a larger Phase III trial. According to the WHO/UNAIDS/IAVI Expert Group (2007), design and implementation of phase IIB 'test of concept' trials (phase IIB-TOC), which are also referred to as 'proof of concept' trials, is important in efforts to accelerate HIV vaccine and microbicide development. Phase IIb trials provide a flexible approach to screen various AIDS vaccine candidates and to direct further vaccine development in a shorter timeframe. This accelerates the development of the most promising vaccine candidates or approaches, thereby ensuring optimal usage of the limited resources available for large efficacy trials (Excler, Rida, Priddy, Fast & Koff, 2007). It was hoped that by directing research efforts and accelerating the development of candidate vaccines or microbicides, the Phase IIb trials would lead to the saving of human lives by ensuring that effective products are licenced for marketing within the shortest possible period.

In the HPTN035 trial, the first primary objective of the microbicide study which was related to safety was the focus of the Phase II portion of the study. Taken together, the two primary objectives of the study relating to safety and effectiveness, formed the Phase IIb portion of the study. The Phase II portion of the study involved intensive safety evaluations among the first 799 women enroled. The Phase IIb portion involved the first 799 women and an additional 2,300 women.

The study was a four-arm, multi-site, randomised controlled trial comparing BufferGel and 0.5% PRO 2000/5 Gel (P) with a placebo gel and with no gel. The three study gel arms were double-blinded. HPTN 035 was not designed to compare the two gels, but rather to compare

each against a placebo gel with no active ingredient, and with no gel at all. Women took part in the study for 12 to 30 months (20 months on average) and completed monthly clinic visits throughout their participation. The population for the study consisted of sexually active HIV-uninfected women above 18 years from the following study sites: Blantyre, Malawi; Lilongwe, Malawi; Durban, South Africa; Hlabisa, South Africa; Lusaka, Zambia; Harare, Zimbabwe; Philadelphia, USA

In total 3,099 HIV-negative women were recruited at seven clinical research sites in Malawi, South Africa, Zambia, Zimbabwe and the United States. Participants were randomly assigned in approximately equal numbers to one of four study groups: BufferGel, PRO 2000 gel, placebo gel, and no gel. Women assigned to the three gel groups were instructed to apply gel up to one hour before sexual intercourse using pre-filled applicators. The three gels were similar in appearance and packaged in identical applicators so that neither researchers nor participants would know which women were using which gel during the study. Participants assigned to the three study gel groups were instructed to apply a single dose of their randomly assigned product – BufferGel, 0.5% PRO 2000/5 Gel (P), or placebo gel – intravaginally up to 60 minutes before each act of vaginal intercourse using single-use, pre-filled applicators. Participants in all four groups received ongoing HIV risk reduction counselling, condoms, and diagnosis and treatment of sexually transmitted diseases.

According to Microbicide Trials Network [MTN] (2009), BufferGel, developed by ReProtect, Inc., U.S.A., was developed as a vaginal defense enhancer designed to boost the natural acidity of the vagina in the presence of seminal fluid. Semen reduces the acidity of the vagina, making it more receptive for pathogens that cause sexually transmitted infections, such as HIV. PRO 2000, developed by Indevus Pharmaceuticals, Inc, in U.S.A., is an entry/fusion inhibitor designed to hamper HIV's ability to attach to and infect healthy cells (MTN, 2009). In

HPTN035, researchers tested the low dose 0.5 percent concentration of PRO 2000. Both candidate microbicides had undergone extensive laboratory study and, before HPTN 035, were tested in other early-phase human safety clinical studies involving women in both developed and developing countries. The pre-clinical laboratory research suggested that the gels may reduce the sexual transmission of HIV, while the early-phase clinical studies indicated the gels were well-tolerated and safe and could be considered for further testing in larger trials (MTN, 2009).

In terms of participant safety, a detailed informed consent process was put in place to ensure that participants understood the procedures, risks and benefits of the study, and that they were not obliged to participate and could leave the study, without consequence, at any time. The informed consent documents, while being site specific, were developed from a single template provided by the sponsor. At each site, researchers were responsible for ensuring that the informed consent forms were relevant for the specific site and community advisory boards (CABs) at each site were responsible for reviewing the forms and providing inputs. Participant safety was monitored by the researchers and clinical staff at each site. Designated researchers and staff comprised the study's Protocol Safety Review Team at each site. The team was expected to ensure that all adverse events were reported to the central data processing unit and that all serious adverse events were reported to the local ethics committees, drug regulatory authorities and also the study's central monitoring unit. The study also had a central independent Data and Safety Monitoring Board (DSMB) which was responsible for reviewing study data after every four months throughout the duration of the study. According to evidence available through the HPTN035 protocol, the research team members were expected to play an important role in reducing risky behaviours among participants by providing free condoms, risk reduction counselling, and testing and treatment for STIs. Nevertheless, some women were expected to become infected with HIV while participating in the study, and these women were

given the option to remain in the study if they wished. Women who acquired HIV during the study were counselled and referred by study staff to local medical care and support programmes offering psychosocial services and HIV care, including antiretroviral therapy (MTN, 2009).

Upon conclusion of the HPTN 035 trial in September 2008, it was established that 194 out of 3099 women in the study had become infected with HIV. Of these infections, 36 occurred in the PRO 2000 group, 54 in the BufferGel group, 51 in the placebo gel group, and 53 among those who did not use gel (MTN, 2009). Based on these data, PRO 2000 was 30 percent effective compared with no gel. BufferGel had no detectable effect on preventing HIV infection. Overall, the researchers concluded that the effect of the two test products was not statistically significant. Both microbicides were found to be well-tolerated and did not result in any significant adverse events. The study demonstrated for the first time the promise of a vaginal microbicide gel for preventing HIV infection in women. In the final analysis, although the volunteers in the PRO 2000 study arm had a 30 percent lower rate of HIV infection compared with the other three study groups, this finding was not statistically significant. Approximately 33 percent efficacy would have been considered statistically significant (MTN, 2009). The researchers therefore concluded that additional clinical evidence was necessary for them to more conclusively determine whether PRO 2000 prevents HIV infection in women. Of note was the fact that HPTN 035 had successfully retained a majority of its enrolees, with 94 percent completing their participation (MTN, 2009). Throughout the study, participants reported regular use of the investigational gels (81 percent of sex acts), and nearly all (99 percent) said they would use the products if approved for HIV prevention. Reported condom usage also was high throughout the course of the trial, with 74 percent of women reporting condom usage during most of their sexual encounters (MTN, 2009).

5.6 STUDY PERIOD

Data collection activities for the initial phase of the present study were conducted from September to November 2008. This was also the time that the HPTN 035 study was closing down after reaching its enrolment and follow-up targets. The second phase of the present study, which involved the implementation of a pilot intervention aimed at improving trial participants' understanding, was implemented in August 2009, nine months after the initial phase and four months after the termination of the HPTN035 study participant follow-up and debriefing activities. The study therefore did not impact on the microbicide study in any significant way in terms of recruitment or retention of participants. The intervention was focused on addressing the three dimensions of the Meerwein model namely information dimension, the emotional dimension and the interactional dimension (see Chapter 3). The design and development of the pilot intervention are described in detail in Chapters 8, 9 and 10.

5.7 SAMPLE SIZE AND SAMPLING PROCEDURE

The sample size of 199 microbicide trial participants was determined to be appropriate using Cochran's sample size formula for categorical data, and has been determined to be sufficiently large to enable detection of differences at $\alpha = .05$ and margin of error =.06. (Bartlett, Kotrlik & Higgins, 2001; Israel, 1992). While a total sample size of 199 had been calculated for the study, a total of 203 participants were recruited for the study. All the steps used in calculating sample size are listed below:

$$\text{Sample Size} = \frac{n}{1 + (n/\text{population})}$$

$$\text{In which } n = \frac{Z * Z\,[P\,(1-P)}{(D*D)]}$$

P = True proportion of factor in the population, or the expected frequency value
D = Maximum difference between the sample mean and the population mean,
Or Expected Frequency Value minus (-) Worst Acceptable Value
Z = Area under normal curve corresponding to the desired confidence level

Assumptions
1. The sample to be taken must be a simple random or otherwise representative sample.
2. The question being asked must have a "yes/no" or other two-choice answer, leading to a proportion of the population (the "yes's") as the final result.

Values necessary for calculating sample size were as follows:

- Population Value: 780
- Expected Frequency of good scores: 50 percent (This value is recommended for dichotomous variables as it results in the maximization of variance and produces the maximum sample size – Bartlett, Kotrlik & Higgins, 2001)
- Confidence Interval:6 percent
- Worst acceptable frequency 56 percent or 44 percent
- Confidence level 95 percent
- Value for Z at 95 percent confidence level = 1.960

The value of "n" was calculated first as follows:

P = Expected Frequency Value= 50 percent
D = (Expected Frequency - Worst Acceptable) = 56-50=6 percent, OR 50-44=6 percent
Z = 1.960 with Confidence Level of 95 percent

$$n = \frac{Z * Z [P (1-P)}{(D*D)]}$$

$$n = \frac{1.960 * 1.960 [0.50(1 - 0.50)}{(0.06 * 0.06)}$$

$$n = \frac{1.960 * 1.960 [0.50(0.50)}{(0.0036)}$$

n = 1.960 * 1.960 [.25 / .0036]

n = 1.960 * 1.960 [69.44]

n = 1.960 * 136.11

n = 266.78

***n*=267**

Since the value of "n" exceeds 5 percent of the population (780 X 0.05 =39), Cochran's (1977) correction formula was used to calculate the final sample size (Bartlett, Kotrlik & Higgins, 2001). Sample size (S) was therefore calculated for the given population of 780 microbicide participants as follows:

$$S = \frac{n}{1 + (n / \text{population})}$$

S = 267 / [1 + (266.78 / 780)]

S = 267 / [1 +. 342]

S = 267 / 1.342

S = 199

The sample size which was obtained using the above formulae, was confirmed using the Macorr sample size calculator, a web based sample size calculation tool. Figure 5.6 shows the sample size calculation that was obtained using Macorr calculator and using the confidence levels that were used in the manual calculation.

Determine Sample Size		
Confidence Level:	95%	
Confidence Interval:	6 (%)	
Population:	780	
Sample Size:	199	
Find Confidence Interval		
Confidence Level:	95%	
Sample Size:	199	
Population:	780	
Percentage:	50 (%)	
Confidence Interval:	6 (%)	

Figure 5.6: Confirmation of sample size using the Macorr Sample size calculator

(source: http://www.macorr.com/ss_calculator.htm)

In order to ensure that the sample was random and representative of the microbicide study population, women were invited to participate in this study as and when they came to the Microbicide Clinics for study follow-up activities. Confirmation was obtained from the study coordinators concerning the randomness of the follow-up schedule. The follow-up visits were based on the dates of enrolment. After obtaining permission from the heads of the two sites (Lilongwe and Blantyre), a total of 54 participants were enroled in Lilongwe and a total of 149 in Blantyre for structured interviews. A further 18 participants from the three gel arms were

randomly selected to participate in two focus group discussions (eight in Lilongwe and 10 in Blantyre). Inclusion criteria for this study included the following:

- Participation in the microbicide trial for a period of three months or more
- Aged 18 years and above
- Given informed consent to participate in this study
- Agreement to be contacted in future for follow-up activities related to this study should the need arise.

Exclusion criteria included:

- Non participation in the microbicide trial
- Less than three months participation in the microbicide study
- Refusal to participate
- Refusal to be contacted in the future for follow-up activities
- Inclusion in the non-intervention arm of the microbicide trial

All staff affiliated with the research project responsible for obtaining informed consent were eligible to be interviewed. Two staff members were interviewed at each site. The research assistant of the current study identified eligible staff with the assistance of the Principal Investigators (PI) and coordinators at the sites. The PIs facilitated the introduction of the research assistant to the coordinators and the eligible staff, either in person or through written or e-mail correspondence briefing them on the proposed study. Eligible staff were then invited to participate in the study and provided with a small slip to complete and return to the Research Assistant providing their name, contact information and time when they may be available for an interview. Inclusion criteria included the following:

- Working as research staff at the research site

- Involved in obtaining informed consent for the microbicide trial during past 3 months or more
- Available at the site during the data collection period
- Provided informed consent for the in-depth interview

5.8 RESEARCH QUESTIONS AND METHODS

This section is an attempt to link the study research questions with the methods that were employed in the study. All the methods are described in greater detail in a later section. This section is specifically aimed at providing clarity on the various methods that were used to answer the specific research questions.

The main research question for the study was as follows:

- Are trial participants aware that they are participating in a trial which employs randomisation, double-blinding and placebo use, and are they aware of the purposes and personal implications of these procedures?

In order to answer this research question, the empirical study mainly focused on two inter-related areas namely the information that was disclosed to research participants and the participants' understanding of the disclosed information.

5.8.1 Recruitment methods and sampling

As the present study depended on the microbicide study for recruitment, staff in the microbicide staff were informed of the present study and requested to inform and refer the microbicide trial participants as they were exiting from their routine study visits. The research assistant for the current study was based at the site exits to intercept and welcome any

microbicide trial participants as they were exiting the sites. Upon confirmation of their participation in the microbicide study as well as their microbicide study arm, the eligible women were then briefed about the present study. The study only recruited women from the 3 gel arms of the four arm study. Upon obtaining their verbal consent, the respondents for the present study were then selected using a random procedure. Each potential respondent was requested to pick up a small piece of paper from a box. In the box were small pieces of paper labeled either 1 or 2. All those who picked small pieces of paper labeled with figure 2, were invited to participate in the structured interviews or focus group discussion. In the box there were twice the number of papers labeled 2 as compared to those labeled 1. This was aimed at speeding up the recruitment drive in view of the limited study resources. Using this procedure, 54 women were recruited for structured interviews at the Lilongwe site and 149 at the Blantyre site. For the focus group discussions, women who picked up small papers labeled 2 were invited for the discussions on specified times at the two cites. Using the same procedure, 10 women were invited at each site for the focus group discussion. At the Blantyre site, 8 women responded to the invitation while 10 responded positively at the Lilongwe site. Those who picked up papers labeled number 1 were thanked for their patience, offered refreshments and excused. This procedure was aimed at ensuring the randomness of the samples for both structured interviews and focus group discussions.

5.8.2 Information Disclosure

The study focused on how research staff and study information sheets explained the concepts of double-blinding, randomisation and the use of placebo, and what prominence they gave them.. In order to answer the question about the information disclosure, the following sub-questions were asked:

a. How do trial related documents explain the concepts of randomisation, double-blinding and placebo use, and what level of prominence are the concepts given?

b. How do study staff explain the concepts of randomisation, double-blinding and placebo use to prospective trial participants, and what prominence are they given?

To answer these questions, trial documents were analysed for content and in-depth interviews were conducted with study staff who were involved in the processes of obtaining informed consent. The various methods used are described in greater detail in Section 5.9. In-depth interviews allowed for direct contact with the respondents and the opportunity to use probing questions to obtain pertinent data on the informed consent processes and the disclosure of information to trial participants. To triangulate and verify data on the disclosure of information, data was collected from various sources: programme documents, staff involved in informed consent, and trial participants. Using the data obtained in response to the above sub-questions, the following hypotheses were tested:

a. Research documents adequately explain the purpose, implementation and personal implications of randomisation, placebo use and double-blinding.
b. Research staff provide adequate information on double-blinding, randomisation and placebo use to trial participants.
c. Research staff have a positive attitude regarding full disclosure of information on double-blinding, randomisation and placebos to research participants

5.8.2 Research Participants' Understanding

The study focused on how the procedures of randomisation, double-blinding and placebo use were understood by the participants, as well as their attitudes to these procedures. The study also sought to understand whether the participants had considered these three key concepts in making decisions about participation in the microbicide trial. In attempting to

address the question about trial participants' understanding, the following sub-questions were asked:

a. Are participants aware of the purpose of the study?
b. Are participants aware that they are participating in a trial to test a product whose efficacy is not known?
c. Are participants aware that they are still exposed to HIV infection even as they are using the product that they have been issued with?
d. Are trial participants aware that randomisation, double-blinding and placebo use are part of the study?
e. Are trial participants aware of why randomisation, double-blinding and placebos are used in the study?
f. Are participants aware of the various study arms in the microbicide study?
g. Are participants aware that they have been randomised into different groups?
h. Are participants aware that they may be receiving a placebo?
i. Are participants aware that neither themselves nor the trial nurses and doctors (i.e., research personnel) are aware of the arms they are in?
j. Are trial participants aware of the personal implications of randomisation, double-blinding and placebo use?
k. Are participants aware of the implications of their participation, regarding protection from infection by the product under test?
l. What is the opinion of the trial participants regarding randomisation, double-blinding and placebo use?
m. In making the decision to join the microbicide study, did trial participants consider the fact that the study involves randomisation, double-blinding and placebo use?

To answer these questions, structured interviews and focus group discussions were held with a sample of the women participating in the microbicide trial. To triangulate and verify data on participants' understanding, data was collected using various methods. Some data from the review of study documents, in-depth interviews with study staff, and field notes were used to verify or support the findings from the structured interviews and focus group discussions. Using the data collected in response to the above sub-questions, the following hypotheses were tested:

A. Trial participants are aware that the procedures of double-blinding, randomisation and placebo use are being used in the trial.
B. Trial participants are aware of the purpose of double-blinding, randomisation and placebo use in research.
C. Trial participants understand the personal implications of the trial procedures under study.
D. Trial participants consider the three concepts when making a decision to agree or refuse to participate in the microbicide trial.
E. Trial participants do not believe that they are completely protected from HIV infection by the microbicide under study.
F. Trial participants have a positive opinion regarding double-blinding, randomisation, and use of placebos.

5.8.3 Intervention to Improve Understanding

In the event that some microbicide trial participants with low levels of understanding were identified, an intervention aimed at improving understanding was designed, developed, implemented and evaluated. From an ethical point of view, it would have been inappropriate not to take some action aimed at correcting a situation after a problem has been identified. The idea of an intervention was also stimulated by findings from previous

studies reviewed in Chapter 2 which had identified low levels of understanding among participants from various trials. Following on the findings from these studies, it had been postulated that the likelihood of identifying some participants with low levels of understanding would be high. Once the intervention had been implemented, the study would proceed to investigate the usefulness of the intervention in improving understanding regarding the procedures under study. The assessment would assist in determining whether the intervention can be recommended for use by other investigators. The following question was specifically developed for the pilot intervention:

a. Can the designed intervention improve trial participants' understanding of research, randomisation, double-blinding and placebo use?

The development and implementation of the intervention are reported in greater detail in Chapter 9.

5.9 DATA COLLECTION METHODS AND TOOLS

This section is devoted to a detailed description of the methods that were used for collecting data for this study. In this study, data was obtained through various methods, including document review, structured interviews with a random sample of trial participants, focus group discussions with two groups of women, in-depth interviews with staff members who were involved in obtaining consent for the microbicide study, and observations. The use of the various methods was aimed at providing for triangulation and verification of study findings. The various methods that were used are indicated below:

5.9.1 Document Review: Document review served as a very valuable source of information as it provided background information about the informed consent processes and procedures designed for the microbicide trial. Microbicide study documents such as study protocol, informed consent forms, information sheets, advertisements, standard operating procedures and

other study related documents made available to the principal investigator were reviewed for both process and content. For each document, the following questions were asked:

a. What kind of document is it?
b. What is the purpose of the document?
c. What terms does it use?
d. Who produced the document?
e. Is the document complete?
f. What gaps exists in the document, if any? The operational definition of understanding adopted for this study assisted in this assessment.

This information was then used to obtain background information on the disclosure of information in the study.

5.9.2 Structured Interviews: The structured questionnaire was identified as the most suitable instrument for collecting data on trial participants' understanding, given that the main aim of the study was to assess how the respondents understood the concepts under study and how they viewed or appreciated them (attitudes). Although the concepts under study are generally difficult to understand, questions were formulated to make them easy to understand. Both closed and open-ended questions were used. Open questions were used to invite the respondents to give their own opinions or views on trial procedures. The questionnaire consisted of three sections: personal data, questions about understanding of research, and their opinions and suggestions on research in general. It was administered to all participants by one trained research assistant (See Appendix 2 and 4 for English and ChiChewa versions of the structured questionnaire).

The questionnaire was administered to a total of 203 participants from the microbicide study. Seven women refused to participate citing constraints of time and fatigue. Four of the women

reported that they were taking advantage of the temporary absence of their partners to visit the clinics as they were participating in the microbicide trial without the approval of their partners. Such women had to ensure that they were at home before the times that their partners came back. Three women indicated that were not interested in responding to the questionnaire as they had already responded to too many questionnaires during the past months.

5.9.2.1 The Development of the Structured Questionnaire

The questionnaire consisted of 100 response items and each interview took approximately 40-45 minutes on average (see Appendices 2 and 4). For each of the three concepts under study, the questionnaire included some questions which covered understanding of procedures used in the study, the purpose of the procedure, and the implications of the procedure for each participant personally. The dependent variables were measured using numeric scores. The questionnaire included several questions on understanding related to each of the three concepts under study. For each participant, a score was obtained for each concept and a composite score obtained after adding scores from each of the concepts under study. The study relied on the scoring method used by Joffe *et al*. (2001). This scoring method has been found to be reliable and valid. No weights were assigned to concepts or questions, as each one was viewed as equally important in facilitating understanding. Questionnaires used in previous related studies were consulted during the development of the questionnaire for this study (Ellis, Butow, Tattersall, Dunn & Houssami, 2001; Joffe *et al*., 2001; Kass, Maman & Atkinson, 2005; Lindegger *et al*., 2006; Quieroz da Fonseca & Lie, 1995, 1999).

The questionnaire and the scoring system were reviewed by various experts including an epidemiologist, two biostatisticians, a seasoned immunologist and researcher, and three social scientists. All agreed that the results should be generalisable to the study population and the study should be replicable. The biostatisticians suggested some significant changes to the

layout of the questionnaire and recommended the use of tables to capture data on the concepts under study. They also assisted in the sample size calculation. One of the biostatisticians assisted by creating the database in SPSS and entering and cleaning all the data from the structured questionnaires. The social scientists provided useful insights into the use of words such as randomisation, placebo and double-blinding and the challenges that these may present. They assisted in generating alternative phrases and ways that could be used in bringing out these concepts. For example, regarding placebo, they suggested that one could find out what the respondents knew by asking them about the number of different gels that were being provided to the participants and to list them. The epidemiologist mainly assisted generally in determining the procedures for this study.

Several measures were taken to ensure the reliability of the questionnaire. A limited number of Yes/No questions were included in the questionnaire in order to avoid responses based on guesswork. True/false questions were also used minimally for generating some data on general knowledge on the three concepts (Peterson, 2000). There were a number of questions using different formats under each concept to counter the effects of guess work. Some of the questions were not aimed at recall – but the use of disclosed information in making sense of the personal implications of the study procedures.

The main questionnaire was aimed at coming up with baseline data which would determine the design and implementation of an intervention. The questionnaire was aimed at examining the knowledge of the women concerning a real study in real life and not a simulation of a study as compared to that investigating understanding within the context of a simulated trial (Pace & Emanuel, 2005). The questions also sought to assess actual understanding and not perceived understanding. English and ChiChewa versions of the structured questionnaire are included as Appendices 2 and 4. The English and ChiChewa versions of the informed consent forms which

were used are attached as Appendices 3 and 5 accordingly. After implementation of the intervention aimed at improving understanding, a shorter questionnaire with about 50 questions was administered to participants in both the intervention and non-intervention groups. The English and ChiChewa versions of the evaluation forms are attached as Appendices 12 and 14. The English and ChiChewa informed consent forms for the intervention phase are attached as Appendices 13 and 15.

5.9.3 In-depth Interviews: In-depth interviews were held with two study nurses at each site. The study nurses were responsible for obtaining informed consent. A copy of the in-depth interview guide is included in Appendix 6. In-depth interview is a technique designed to elicit a vivid picture of participants' perspectives on the research topic. It is conducted face to face between the participant and the researcher, and is also a tool that explores an individual's perception, practices, beliefs and experiences about a specific topic or event (Greenhalgh & Taylor, 1997; Polit & Beck, 2004). Because of its flexible nature, this tool has an added advantage that an *a priori* topic can be explored and new related topics that arise during the interview can also be discussed within the overall research topic (Green & Thorogood, 2004). In this regard, an in-depth interview guide containing a range of semi structured and open-ended questions was used to elicit individual's in-depth information pertaining to study objectives relating to the disclosure of information during informed consent process.

The staff questionnaire included questions relating to their experiences in explaining randomisation, double-blinding and use of placebo in the trial. The in-depth interview guide consisted of open-ended questions which allowed for a greater degree of communication and flexibility so that the staff could freely share their thoughts. Respondents were given time to elaborate on points of interest. The questions asked were aimed at obtaining data from the perspective of the trial staff and also from the perspective of the trial participants. The guide

also sought some demographic data on the staff themselves. Such data included sex, level of education, training, and experience with health research, as these were deemed to be relevant variables. A copy of the staff in-depth interview guide is also included as Appendix 6. The informed consent document for in-depth interviews with staff is included as appendix 7.

All the in-depth interviews were conducted in person by the researcher. The interviews were conducted in English, the official language of communication in which all respondents were fluent. The bias of the researcher was evident in the choice of research topic. The researcher had worked as a Trial Inspector/Trainer in Zimbabwe, hence the emphasis on improving consent. It is however important to note that in Malawi the researcher was not working as a Trial inspector/Trainer but was working in an academic Unit which worked closely with the two sites. The researcher was not in any way directly linked to the study nor to the two sites.

Care was taken during the interviews to avoid personal biases and intrusions about the topic of study by adopting a reductionist approach in which the researcher approached the participants without personal preconceived beliefs and opinions about the adequacy of information they disclosed to participants. A reductionist approach is achieved by bracketing the world and doing away with any presuppositions when conducting in-depth interviews. In social science oriented qualitative research interviews, bracketing is a process during which the researcher identifies personal biases about the phenomenon of interest to clarify how personal experience and beliefs may affect or distort what is heard and reported (Wood & Harber, 2002).

During the interviews, responses of the participants were carefully noted verbatim and the interview was voice recorded with consent to allow ease of transcribing and comparison of what had been written down verbatim and what had been transcribed for accuracy of the captured responses. In this regard, materials used included pen, data collection sheets of paper for recording verbatim responses, and a power chargeable voice recorder.

5.9.4 Focus Group Discussions (FGD): Two FGDs were held with a total of 18 microbicide trial participants who had not participated in the individual interviews. The FGDs were used to obtain opinion and attitude at group level. Groups create their own structure and meaning and a group interview provides access to their level of meaning, in addition to clarifying arguments and revealing diversity in views and opinions (Denzin & Lincoln, 1994). The FGDs were used as a source of validation for information obtained through the administration of a questionnaire with other research participants. The FGDs also provided an opportunity to clarify responses that remained unclear during the administration of the structured questionnaire. Each group consisted of a maximum of 10 participants in order to ensure that each and every participant had a fair chance of presenting their own opinions. The FGD guide consisted of 42 questions and the discussions took two hours on average (see Appendices 8 and 9). The FGD consent forms are also included as Appendices 9 and 11.

5.9.5 Observations: During the process of data collection, some unstructured observations of facility layout, interactions with trial participants and informed consent processes were made. Observations draw on the direct evidence of the eyes and ears to witness events first hand. They are based on the fact that, for certain purposes, it is best to observe what actually happened than to be informed about what happened (Denscombe, 1998). This method was used because it is best to observe and evaluate what actually happens at research sites. Field notes were made during the observations to record phenomena, behaviours of persons, and the processes followed during informed consent at the sites.

5.10 VALIDITY AND RELIABILITY IN DATA COLLECTION

This section outlines the steps taken to maximise validity and reliability in data collection. Validity is about ensuring that a tool measures what it claims to measure. In this case, the claim is made that the questionnaire administered to the trial participants was aimed at measuring their level of understanding on randomisation, double-blinding and placebo use within the context of the microbicide trial. Reliability is about whether the tool gives consistent measures over time and it allows for replicability of research over time and over groups (Hochhauser, 2008). The following measures were implemented to maximize validity and reliability of tools:

Design stage – Expert opinion was sought to ensure that the design and tools were appropriate. Experts consulted included biostatisticians and social scientists from both the University of KwaZulu-Natal and the University of Malawi. Appropriate tools for gathering the type of data necessary to answer the study questions were developed.

Triangulation - Methodological triangulation refers to the use of multiple methods to study a research problem, while data triangulation refers to the use of a variety of data sources in a study to verify or support findings (Denzin, 1994). In this study, three main tools were used to collect data; similar questions were repeated in the different instruments so that the responses of the various groups could be compared. This technique allowed for verification of data. Five different methods of data collection were used.

Translation of questionnaire – The structured questionnaire for the participants was translated separately by three persons in order to ensure that the questions had the same meaning. The three individuals comprised of an undergraduate student, a female non-scientist with limited

research experience, and a seasoned social science researcher. The use of three different persons led to various changes that related to how some questions especially relating to the concept of placebo and double-blinding were asked. It also led to the removal of some questions which were not clear and some which had been repeated.

Pilot-testing of tools – The questionnaire, in-depth interview guide and the FGD guide were pilot tested in Blantyre before the actual data collection. Testing was done to ensure that the wording, sequence of questions, and the types of questions used in the instruments were related to the research questions and to the study as a whole. The pilot testing led to the further refinement of the tools. Issues such as redundant questions and meaning were addressed at this stage. Any ambiguity in terms of instructions, terms and questions was accordingly addressed and leading questions omitted. It was also ensured that the language levels of the tools were appropriate and that instruments were not too long or too short. The administration procedures were also tested - for example the time it took to administer the instruments. This was done in order to facilitate planning. The piloting was done during an on-site visit to the site in Blantyre. The data collected during the piloting was not used in the study findings.

Recruitment of research assistants - A graduate research assistant was recruited for the first Phase. Two graduate research assistants were recruited for the assessment in Phase 2. The research assistants hired for both phases had extensive experience of research prior to this study.

Reliability - The reliability of the structured questionnaire was tested using the Cronbach's alpha. A report on the test is presented in Section 6.3.

Training – The research assistants were trained on how to administer the tools before implementation.

Supervision of research assistants: At each site, the assistants were supervised by an experienced researcher. The experienced supervisors were also responsible for checking questionnaires for content, completeness and consistency on a daily basis. The research assistants and supervisors also provided periodic reports on their work, including any unanticipated challenges.

Data analysis – During the data analysis stage, subjective interpretation of data was avoided and coding of open-ended questions was done carefully. In order to ensure some level of objectivity, coding of open-ended responses was done by two different individuals. The role of the second coder was to confirm the coding by the first one. Where there were inconsistencies, these were referred to the relevant research assistant for clarification. This was done in order to ensure consistency in the meaning captured out of the responses.

Data reporting – During the data reporting stage, selective and unrepresentative use of data was avoided. Only claims substantiated by data were made.

5.11 STUDY PROCEDURES

A structured questionnaire was administered to a random sample of 203 women participating in the HPTN035 microbicide trial who were selected using the procedure described in 5.8.2 above. The questionnaire for trial participants included some questions that were used to score their understanding on placebo use, randomisation and double-blinding (see Appendices 2 and 4). High scorers (G1) and low scorers were identified. High scorers included those who scored 75 percent and above, while low scorers included those who scored 74 percent and below. A pool of low scorers were randomly identified and randomised into two groups (G2 and G3). An intervention aimed at improving understanding was administered to G3 (n=18), while standard information was provided by study staff to G2 (n=18). The pre-intervention and post-

intervention scores for G2 and G3 were then compared to establish the effectiveness of the intervention. Figure 5.7 provides a diagrammatic representation of the study procedures.

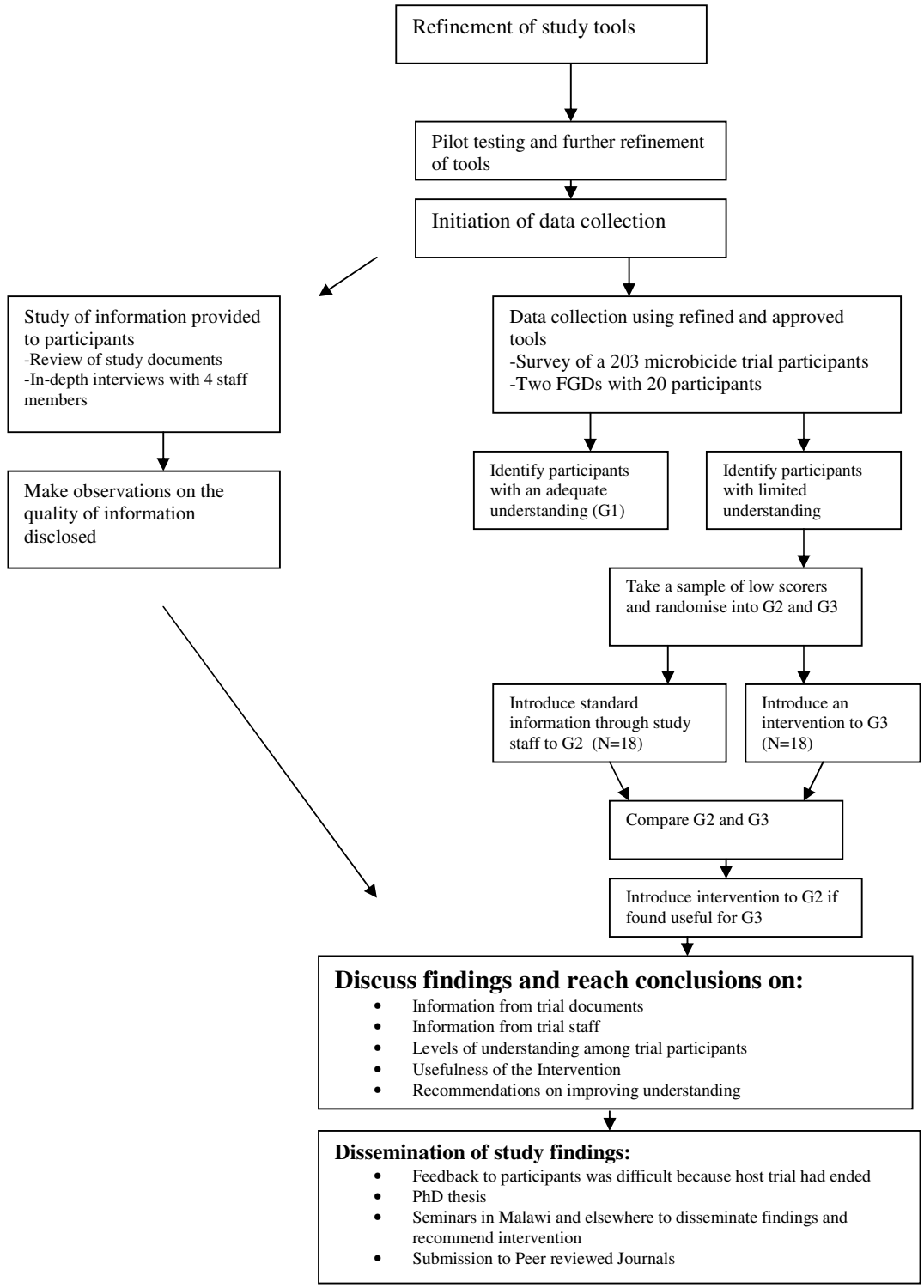


Figure 5.7: Diagrammatic representation of the study procedures

5.12 OPERATIONAL AND STATISTICAL DEFINITIONS

Words mean different things in different contexts. In this section, some general definitions, operational definitions, and statistical definitions of important concepts are presented. A glossary of the other important general terms that are used in this thesis is included as Appendix 1.

5.12.1 General Definition of "Understanding"

The term "understanding" is used in day-to-day life in various ways. Most researchers who have studied understanding or comprehension in clinical trials have not provided operational definitions, apparently assuming that it was what was measured by their comprehension tests (Hochhauser, 2005). The *Oxford Advanced Learner's Dictionary (2002)* defines understanding to mean knowledge that someone has about something; to know or realise why something happens and how it works or why it is important. Understanding is also defined elsewhere as the ability to apply broad knowledge to situations likely to be incurred, to recognise significant deviations, and to be able to reach reasonable decisions (Indiana University, 2004). These two definitions emphasise knowledge and its application. Awareness is about knowing that something exists and that it might be important (*Oxford learner's Dictionary, 2002*). The fact that awareness is about knowing that something exists therefore implies that awareness is a necessary condition for understanding. One cannot understand something without being aware of it.

Hochhauser (2005) highlights six levels of cognitive skills from Bloom's Taxonomy of Educational objectives that are relevant to informed consent. The lowest level is knowledge, which is the most concrete. This is confirmed by recalling specific information and is associated with verbs such as describing, recalling, listing and recollecting. The second level is

comprehension, which can be taken to be the lowest level of understanding. This level does not include appreciation of personal implications for oneself and is associated with such verbs as summarizing, interpreting and estimating. The third level is application, which is about using abstract ideas in specific situations and is associated with verbs such as examining, calculating and discovering. The fourth level is analysis, which is associated with breaking down information into components and ordering and classifying the information in a meaningful way. The fifth level is synthesis, which is about combining elements to come up with a whole picture. It is associated with verbs such as formulating, integrating and preparing. The highest level of cognitive skill is evaluation, which is the most abstract. It has to do with judging the value of material based on criteria. It is associated with making decisions, drawing conclusions and ranking various options. Understanding a concept involves encoding information, retaining information and processing the information, and this involves attention, memory and cognition. The terms commonly used include understanding, comprehension, knowledge and recall, with recall representing a low level which does not entail capability to process the information in a meaningful way (Dunn & Jeste, 2001)

Wirshing, Wirshing, Marder, Liberman and Mintz (1998) recommend the use of legal standards in assessing patients' understanding as a way of ensuring standardisation of procedures. According to these authors, capacity to understand exists if a person has the following abilities:

- To express choice – this is not conceptually the same as understanding. Rather it is about voluntariness or autonomy.
- To understand information relevant to the decision they are supposed to make
- To appreciate the significance of the information for their own situation
- To manipulate the information rationally in a manner that allows the individual to make comparisons and weigh outcomes.

This study borrowed from the above definitions and adapted a definition specific to this study. The definition developed for this study emphasises the disclosure of information in ways that make it understandable, disclosure of adequate information, understanding of disclosed information and ultimately use of the disclosed information in making an informed decision. In this thesis, understanding is defined as having knowledge of the nature, purpose and implications of research and the various research procedures being used in the study. Regarding microbicide trial participants, according to this thesis, "understanding" would cover the following elements:

1. Awareness that they are participating in a trial to test a product whose efficacy is not known
2. Awareness of the purpose of the research
3. Awareness of the implications of their participation, regarding protection from infection by the product under test
4. Awareness that they were going to be randomised into different groups
5. Awareness that they could have been receiving either a placebo or the test product
6. Awareness that they themselves as well as the trial nurses and doctors are not aware of the arms they are in or what products they are being provided with
7. Awareness of the purpose of each of the trial procedures under study
8. Awareness of the personal implications of randomisation, placebo use and double-blinding
9. Awareness that by choosing to participate in research, they still face the risk of HIV infection.

It is assumed that the presence of the above elements would lead to the making of an informed decision regarding research, which takes into consideration the three procedures of

randomisation, double-blinding and placebo use. The tools used for data collection in this study were designed to cover all the above elements.

5.12.2 Operational Definition of "Understanding"

In this study a person who has adequate understanding about the concept under study is classified as someone fulfilling the following:

- Awareness of what the procedure is and that it is being used in the study.
- Knowledge concerning the reason(s) why it is important for the procedure to be used in the trial or why the procedure is being used in the trial.
- Awareness of the personal implications of the procedure.

Figure 5.8 below highlights the components that are important elements of understanding a particular concept.

Concept	Description of the procedure	Reason why procedure is use the study	Personal implications of procedure
Randomisation	Is a method that is used for assigning individuals participating in a trial into treatment groups. It is an effective method for balancing confounding factors between treatment groups	It is used for creating similar groups for comparisons and avoidance of preference or bias in assigning individuals to group.	The participants cannot make a choice regarding which arm to join or which treatment to receive and neither can the study staff.
Placebo	In a clinical trial, a placebo is An inactive substance resembling a medication, given for psychological effect or as a control in evaluating a medicine believed to be active. It is usually a tablet, capsule or injection that contains a harmless substance but appears to be the same as the medicine being tested.	To make it easy to compare the test product against something inactive which looks like the test product makes comparison easy and findings much clearer.	It is possible that one may be on a placebo which does not have any active ingredient. If the participant has joined the study hoping to benefit from the test product, it is possible that they may actually receive a placebo.
Double-blinding	Term used to described the assignment of treatment in a study in such a way that both the investigator or the participant are blind to (unaware of) the nature of the treatment the participant is receiving.	Used for avoiding bias by staff caring for the participants and also avoid bias in terms of how participants may respond if they knew which product they would have received. Double-blind trials are aimed at producing objective results, since the expectations of the researcher and the participant about the experimental treatment such as a drug do not affect the outcome.	Assignment of treatment is not on the basis of your medical needs or health condition. It is based on chance alone. Even study staff are not aware what treatment the participant is receiving. Treatment being provided is not for the purpose of treating participant but for the purpose of testing the usefulness of the product under study

Figure 5.8: Components that constitute adequate understanding of concepts

5.12.3 Statistical Definition

A statistical definition is important for a study such as this as it seeks to answer the important questions (Agre *et al*., 2003). A statistical definition has to do with the measurability of a phenomenon. The important questions that relate to a statistical definition for this study include the following;

- How much should participants know for us to be satisfied that they have an adequate understanding?
- What should be the gold standard of understanding?
- What should we expect people to know? What would qualify as an adequate level of understanding in a test of understanding?

In terms of a statistical definition that was selected for this study, a person who has an adequate level of understanding about a particular concept is one who would have scored 75 percent and above for that particular concept. A composite score was obtained for each participant after adding the scores for each concept and converting this into a percentage. The same threshold of 75 percent and above was used for the composite score. The level of 75 percent was selected for various reasons:

- A score of 50 percent represents a halfway mark in terms of understanding. The 75-100 percent range is often taken in school and university examinations to represent a high level of understanding.
- The figure of 75 percent was also used in a study conducted by Minnies *et al*. (2008).
- To take a lower figure such as 50 percent would be to condone decisions that are possibly not based on adequate understanding of information.
- To take a higher level as the desired level is to emphasise the need for decisions that are based on full or adequate understanding of information.

The following assumptions were made regarding the test and the test score:

- that the test scores are the result of something the individuals did.
- that the test scores contain information about the individual, hidden as it were, inside the scores, especially in terms of patterns which are discernable.

- that the test scores fit into a body of knowledge about test scores, how they are derived and what they are meant to impart.
- that the test scores have predictability built in because the process of generating them is repeatable with the same or similar groups.
- the test scores act as verifiable evidence.

5.13 DATA MANAGEMENT

All questionnaires were checked by a supervisor for completeness and consistency. An SPSS database was created by a statistician with expertise in using SPSS. All open-ended questions in the structured questionnaire were coded before data was entered into SPSS using Version 10. Data from the structured questionnaires was entered into the computer and appropriately cleaned using the appropriate techniques including double checking. Answers to a few open-ended questions that were included in the structured questionnaire were analysed, grouped together in related themes and assigned numeric codes. Quantitative data was analysed using frequencies, percentages, means, standard deviations, cross tabulations and other statistical tests such as chi-square test. Figures, percentages, tables and graphs were used to summarise the data so that it is presented in a manner that is easy to interpret.

Bivariate analysis was done so as to assess the relationship between independent variables and selected dependent variables. Pearson's chi-square test or Fischer's exact test were used to check if there was a relationship between variables. The Chi-square test is a test of independence and confirms if there is a relationship between two variables. Fischer's exact test was used in cross-tabulations in which the Pearson's test was not appropriate. The Pearson's test assumes that the expected value for each cell is 5 or higher. Fischer's exact test was therefore used in cases where there was a value less than 5 in any of the cells. In such cases, the

variables had to be re-configured so they could yield a 2 by 2 table, as the Fischer's exact test only works with 2 by 2 tables.

With these two chi-square tests, a *p*-value of 0.05 or less, indicates that there is a statistically significant relationship between two variables. The effect of the intervention was assessed using Fischer's exact test by comparing the post intervention responses of women in the intervention arm with those women in the control group. Matched-pair analysis was also undertaken to compare respondents' knowledge before and after the intervention. A paired *t*-test was also done to check if the means of the respondents before the intervention and after the intervention differed from one another.

A voluminous amount of data was generated, especially using the other qualitative methods namely the document review, in-depth interviews with four staff members, two focus group discussions and observations during the fieldwork. Transcripts of the two FGDs are included as Appendices 24 and 25. Data analysis in qualitative research involves a search for general statements about relationships among categories of data, and is a process of bringing order, structure and meaning to the collected data (Speziale & Carpenter, 2003). Three forms of data were collected in this study, namely data collected through desk review of documents, data collected through in-depth interviews, and data collected through observations.

Descriptive data allows the researcher to meaningfully describe many pieces of data with a few indices (Gay & Airasian, 2003). The qualitative data was processed and analyzed according to the method proposed by Bernard (2000). The method involves the following steps;

- Producing the transcripts of interviews and reading through the text. Transcribed text of each of the interviews and responses that had been carefully written down verbatim

during each interview was read over and over again to find recurring words or statements of meanings that were each given a common code.

- Identifying potential analytical categories/themes that arise: Words or sentences or statements of meanings that were given a common code were then grouped together and aggregated into a common theme.
- As categories or themes emerge, pool all the data from the categories/themes together and compare them: Comparison of the pooled data was conducted to look for relationships among themes and for purposes of performing content analysis under each theme.
- Think how categories/themes are linked: Careful thought-processing about what links the themes together is done in order to confirm relationships among themes.
- Present the results of the analysis using exemplars, that is, quotes from interviews that illuminate the phenomenon: Direct quotes in participants' own words were isolated from transcripts and responses that had been written down verbatim during data collection. These quotes were used to illuminate the identified themes.

Some of the qualitative findings were used to verify or support some of the quantitative findings that were obtained through the structured interviews with 203 participants.

5.14 ETHICAL CONSIDERATIONS

In order to ensure that the study was conducted in accordance with the ethical principles of respect for persons, beneficence, nonmaleficence and justice, the following were undertaken:

Accessing the sites: Permission was sought in writing and granted by the Principal Investigators at the two sites. The Principal Investigators at the two sites gave permission as they thought that the study was aimed at strengthening ethical conduct at their sites. They

insisted that the researcher should share the findings with them so that they could use them for strengthening informed consent processes (See Appendices 20 and 21 for letters requesting for permission and Appendices 22 and 23 for letters granting permission).

Review and Ethical Approval: The study was reviewed and approved by Research Ethics Committees at the University of KwaZulu Natal and the College of Medicine, University of Malawi (see Appendices 18 and 19 for the approvals by the two Ethics Committees).

Informed consent: Written informed consent was sought from all the participants after explaining the study purpose and procedures fully (see Appendices 3 and 5 for the English and ChiChewa versions of the informed consent forms for structured interviews). Those who refused to participate in the study for whatever reason were excluded. Seven women refused to participate in the first phase while three refused to participate in the intervention phase. Four of the seven women who refused to participate in the first phase mentioned that they were afraid that their partners would discover that they were participating in the microbicide trial if they spent a long time away from home. Three indicated research fatigue as their reason. Two of the three women who refused to participate in the intervention phase indicated that they could not participate in the second phase due to other commitments. They indicated that they were supposed to pick up their children from school. The remaining woman indicated that she was afraid that her spouse would find out that she had visited the Research Centre if she was away from home for a long time. The same challenge was also encountered by Nyika, Wassenaar and Mamotte (2009). Informed consent was also sought from staff (see Appendix 7), for participation in focus group discussions (FGD) (see Appendices 9 and 11 for English and ChiChewa versions), as well as for participant in the intervention phase (see Appendices 13 and 15 for the English and ChiChewa versions of the informed consent forms).

Confidentiality and privacy: Efforts were made to ensure that all interviews were conducted in locations that made it difficult for others to listen to the conversations. At both sites, rooms were provided for use during data collection and the implementation of the intervention.

Participants were assured that their names would not be used in the reports of the study. No pictures of the participants were taken. All study materials were kept securely and could only be accessed by the researcher, statistician and other study related staff. Paper documents were kept in a locked steel cabinet and the informed consent forms were stored separately from the questionnaires so as to avoid linking the two documents. Electronic data did not contain any names of study participants and were kept in a computer which was protected by a password. The link-log which linked the questionnaires to the respondents was kept by the researcher in a separate lockable steel cabinet.

Reimbursements: The women who participated in both phases of the study were reimbursed for transport using the standard rate applicable at both sites. This reimbursement had not been budgeted for initially but had to be added after it was realised that the majority of respondents expected some reimbursement after an encounter with researchers.

5.15 SUMMARY

This chapter has outlined the methodology used for this study. The chapter has presented a brief description of the research area, including the microbicide study (HPTN035) in which the study was nested as a sub-study A mixed-methods design was utilised in order to provide a rich representation of the phenomenon under study. More specifically, the study employed a sequential design which involved the systematic sequencing of methods. The chapter also provided information with regard to the various stages of the research process such as sampling, data collection and data analysis. Data on trial participants' understanding was mainly obtained through the administration of a structured questionnaire to a sample of 203 of the 780 microbicide trial participants who were eligible for selection. This data collection strategy was determined to be suitable for the research question. The next chapter provides the

results of the findings obtained using the qualitative and quantitative methods used in the first phase of the study.

CHAPTER 6

FINDINGS FROM THE MAIN PHASE OF THE STUDY

6.0 INTRODUCTION

In this chapter, findings from the main phase of the study are presented. The main phase of the study was aimed at assessing participants' understanding of the study procedures of randomisation, double-blinding and placebo use as well as the participants' attitudes to these procedures. This phase was followed by the development and implementation of an intervention aimed at improving understanding. The development and implementation of the intervention is reported in the Chapter 8.0.

This chapter is divided into two main sections. The first section presents findings related to the disclosure of information to the trial participants. Data for this section was mainly derived from document review and in-depth interviews with study staff involved in obtaining informed consent at the two sites. The second section deals with findings on participants' levels of understanding. The second section is divided into sub-sections which include: general issues about the study, findings on understanding of randomisation, double-blinding and placebo use, and findings on understanding of personal implications of participation. For each of the three concepts under study, basic frequencies are presented. These are followed by cross-tabulations with some independent variables such as study site, age and level of education of the respondents.

6.1 FINDINGS FROM DOCUMENT REVIEW

The following documents were reviewed at each site after obtaining permission from the site investigators:

- Study Protocol
- Informed consent forms
- Enrolment Informed Consent assessment Checklist
- Ongoing informed consent assessment checklist
- Informed consent Booklet

In the following sections, the review of each of the documents is provided. Each document was reviewed for purpose, area of strength and areas of inadequacy as related to the subject under study.

6.1.1 Study Protocol

The microbicide study protocol stated that written informed consent was to be obtained from each study participant prior to both screening and enrolment. Written informed consent was also to be obtained for long term specimen storage and possible future testing; however, consent for specimen storage was not required for study participation. Study staff were required to document the informed consent process in accordance with the Standard Operating Procedure (SOP) for Source Documentation. Participants were required to be provided with copies of the informed consent forms if they were willing to receive them. Each study site was responsible for translating template forms into local languages based on the templates that were provided by the study sponsor. Each site was also required to verify the accuracy of the translation by performing an independent back-translation. At both sites, therefore, there were informed consent documents in both English and ChiChewa, and study participants were free to choose which they preferred.

The informed consent form for enrolment was supposed to describe the purpose of the study, the procedures to be followed, and the risks and benefits of participation, in accordance with US regulations 45 CFR 46 (US Department of Health and Human Services, 2009) since the study fell under the jurisdiction of the Food and Drugs Administration (FDA). In addition to the informed consent forms, local investigators were required to work with study staff and community representatives to develop locally-appropriate information materials about the study and a standardised approach to the informed consent process to be implemented at the study site. The process and materials were required to be pilot tested prior to study start-up to ensure cultural appropriateness at each site.

6.1.2 Informed Consent Forms

The informed consent document for both screening and enrolment covered all elements of informed consent required by US regulations according to 45 CFR 46 (US Department of Health and Human Services, 2009), including the following topics that were deemed to be important to this study:

- The unknown safety and unproven efficacy of the study products.
- The need to practice safer sex behaviours regardless of study treatment group.
- The importance of participants in all four study groups to the success of the study.
- The importance of adherence to the study visit and procedures schedule.
- The potential medical risks of study participation (and what do if such risks are experienced).
- The potential social harms associated with study participation (and what do if such harms are experienced).
- The real, yet limited, benefits of study participation.
- The distinction between research and clinical care.

• The right to withdraw from the study at any time.

The informed consent forms also included the following statements, some of which included some important parts that were emphasised **in bold**:

About benefits the informed consent forms stated:

> *You may get no direct benefit from being in this study.* ***We do not know if BufferGel or PRO 2000 Gel work to protect against HIV.***

About double-blinding, the informed consent forms stated:

> *You may be placed in a group that gets Buffergel, or PRO 2000 Gel or placebo gel. If you are placed in one of the gel groups, you will not know which gel you are getting. Because of this, study staff will remind you of the importance of using condoms to protect against HIV.*

About alternatives to participation, the forms stated:

> *There are no gels known to protect against HIV during sex.* ***The only known way to protect against HIV during sex is to use a condom every time you have sex.***

About risks of the study gels the form stated:

> *If you are in one of the study groups that will be using a gel, the gel could cause some bad effects. We do not yet know all the effects of the gels, but some women who used the gels in other studies have had:*
>
> - *redness, itching, burning, dryness, or other irritation of the genital area and vagina*
> - *genital soreness or pain*
> - *genital blisters or sores*
> - *genital bleeding*
> - *increased vaginal fluids or discharge*
> - *difficulty or pain when urinating*
> - *abdominal pain*
> - *nausea or feeling sick to your stomach*
> - *diarrhea*
>
> *You could have these effects or other effects that we do not know about. It is unlikely that the study gels will be absorbed from your vagina into your blood. If this happens, we do not know if it might cause bad effects.*
> *If the study gels cause genital sores, this could increase your risk of getting HIV and other infections passed during sex. Because of this, study staff will remind you of the importance of using condoms to protect against HIV.*

About avoidance of risky behaviour, the forms stated:

> *No matter what study group you are in, you must remember that we do not know if any of the study gels work to protect women from getting HIV. The only known way to protect against getting HIV during sex is to use a condom every time you have sex.*

About randomisation, the informed consent documents stated:

- *If you decide to take part in the study, you will be placed in 1 of 4 study groups. Women in 3 of the groups will get a study gel to insert in the vagina before sex. One group will get BufferGel. One group will get PRO 2000 Gel. One group will get a placebo gel. The placebo gel is a gel that looks and feels like BufferGel and PRO 2000 Gel, but it does not have the ingredients from BufferGel and PRO 2000 Gel that may protect against HIV. The fourth group will not get a gel. The study group that you will be in will be chosen "by lot" [or other equivalent local term, for example, like flipping a coin or throwing dice]. You cannot choose your group, and the study staff cannot choose your group for you. You have an equal chance of being placed in each group.*
- *All four groups are very important to this study. Women in all groups will have the same study visits. All women will get condoms and counseling on how to avoid HIV and other infections passed during sex.*

About the use of placebo, the form stated:

> *The placebo gel is a gel that looks and feels like BufferGel and PRO 2000 Gel, but it does not have the ingredients from BufferGel and PRO 2000 Gel that may protect against HIV.*

It is important to note that the last part of the above sentence "that may protect against HIV" may create some false confidence in the trial participants as it presents a message of hope. An alternative may be something which may read "that are being tested in this study to find out if they can protect against HIV".

The informed consent form was accompanied by a coversheet on which the staff could write notes on issues such as name of staff member conducting the informed consent process, whether the participant had reached legal age of majority, language used, whether the participant can read, whether the participant comprehended all information provided, whether the participant was given adequate time to ask questions, and whether the participant agreed to take a copy of the informed consent sheet home. The review of the informed consent forms

showed that the investigators in the microbicide study had tried as much as possible to provide information regarding the possibility of becoming infected with HIV while one was participating in the study. However, the informed consent document did not provide justification for randomisation, double-blinding and placebo use in the microbicide study. The informed consent document did not provide information on personal implications in a systematic way that would link the implications to the study procedures of randomisation, double-blinding and placebo use. Some information on implications was, however, provided, and some of the information was written in bold so as to emphasise its importance.

6.1.3 Assessment of Participants' Comprehension by Microbicide Trial Staff

The informed consent process included an assessment of each potential participant's comprehension prior to screening and enrolment decision making. Participants who were not able to demonstrate adequate understanding of key concepts after exhaustive educational efforts were not enroled in the study. Participants were also assessed on an on-going basis during the study visits using the Ongoing Informed Consent Checklist. For quality assurance purposes, similar assessments of participant understanding were undertaken among a randomly selected sub-sample of participants during follow-up. The results from these quality assurance assessments were used to provide feedback and recommendations to the relevant study site staff to optimize the informed consent process.

6.1.3.1 Enrolment Informed Consent Comprehension Checklist

The Enrolment checklist included the following eight (8) questions which were aimed at meeting the requirements of US regulations according to 45 CFR 46 (US Department of Health and Human Services, 2009):

- *Please describe your understanding of the purpose of the study.*
- *What do you understand that you are being asked to do in this study?*
- *What do you understand about possible risks that might happen as a result of being in the study?*
- *What will happen if you do not join the study?*
- *Please tell me about the different groups of women in the study.*
- *How will the information about you be protected?*
- *What are the benefits to you of participating in this study?*
- *What should you do if you have any questions about what is happening in the study?*

It is obvious from the above questions that participants were only expected to be aware that they would be randomised to different groups. The elements of double-blinding and placebo use were excluded. Participants were, however, expected to be aware of risks associated with the study, such as the possibility of becoming infected with HIV while participating in the study.

6.1.3.2 Ongoing Informed Consent Checklist

The ongoing informed consent checklist was administered during the scheduled visits to the sites. The checklist included seven questions, which were as follows:

- *Please describe your understanding of the purpose of the study.*
- *Please tell me about the different groups of women in the study.*
- *If a woman always uses study gel, but does not use condoms, can she get HIV?*
- *What do you understand about the possible risks of participating in this study?*
- *What are the benefits of participating in this study?*
- *What should women do if they have a question about the study or a problem related to being in the study?*
- *Are women who join the study allowed to leave the study?*

From this list it is evident that the women were not expected to know about double-blinding or the reasons why the three procedures under study were being used in the study. Importantly, there was one question which addressed the possibility of being infected with HIV while participating in the study. The checklist was accompanied by a cover sheet on which the staff could write details such as such as name of staff member doing the assessment, date of assessment, language of assessment, and whether participant was able to demonstrate comprehension on all checklist items. Staff were also free to write some notes on the test.

6.1.4 Informed Consent Booklet

A booklet was available at all sites which provided more information about the study in simple language. The booklet was written in both English and ChiChewa and included some pictures which were aimed at making the study information meaningful to the participants. Notably, the booklet was focused on providing information on the study procedures in terms of what the participants were expected to do during the course of participating in the study. The booklet did not provide justification for the adoption of randomisation, double-blinding and placebo use, nor a clear discussion of the personal implications of these procedures.

6.2 FINDINGS FROM IN-DEPTH INTERVIEWS WITH STAFF

At each site, two staff members involved in obtaining informed consent for the microbicide study were interviewed using an open-ended discussion guide (See Appendices 6 and 7 for the guide and the informed consent document). All four staff members interviewed were female nurses who had a minimum of a Diploma in Nursing. They had on average eight years of experience each as a practicing nurse, four of which were in a research environment. The nurses were involved in obtaining informed consent from potential trial participamts, collecting specimens, HIV counselling and conducting other examinations of patients. In the recruitment

of participants, they were specifically involved in obtaining informed consent from participants, motivation talks, and follow-up of participants.

The nurses reported that the informed consent process for the study was structured into two phases. The first phase involved the dissemination of information on the study to groups of women either at the site or in their communities. During this phase, the study staff described the study and the products to be used, and answered all questions by the participants. They would then invite those individuals who were interested in joining the study to visit the study site for further discussions on a one-on-one basis. During these one-on-one discussions, they would further explain the study and study procedures to the women and answer any questions that the women might have. They would then administer a comprehension checklist before screening or enroling the individual woman into the study. If the women failed any of the questions on the checklist, staff would then provide them with more information related to that particular aspect. The staff would then re-administer the specific questions for which the women would have given wrong answers. They would only enrol an individual woman after she had succeeded in answering all the questions on the enrolment comprehension checklist. The nurses also administered the ongoing comprehension checklist to the women who were selected at random during the routine study visits.

The nurses indicated that they were aware that some participants join research because of the money that is offered to them as reimbursements, while others join research in order to access good quality care at the research sites. They reported that participants were seen by doctors at the sites during most of the study visits, while in the government hospitals they are only attended to by nurses. They also opined that some women joined the study so that they could have their health problems addressed while some joined because they were interested in research outcomes.

The study nurses reported that they had some challenges in explaining the study purpose and procedures to potential participants as some of them found it difficult to understand them. They opined that this was probably due to the low levels of education. They indicated that it was very rare for participants to refuse to join studies when invited to join due to trust. The element of trust also came out during focus group discussions with some participants, who indicated that they trusted the site as well as the staff. The majority of those who had refused to participate had done so due to fears of blood specimen collection, rumours, and fear that they could get into trouble with their partners if they found out that they were using microbicide.

The study nurses indicated that participants frequently asked questions on blood draws and duration of study, while very few asked about randomisation, double-blinding and placebo use. They indicated that they used enrolment and visit checklists at all times to assess comprehension and took steps to improve comprehension whenever they came across a participant who could not g*et al*l the questions right. All the nurses adequately described to the researcher how randomisation, double-blinding and placebo were being used in the study. The nurses also adequately explained the justifications for these procedures to the researcher. They were, however, taken by surprise when they were asked by the researcher to explain the personal implications of these procedures. They indicated that while they knew the justification of the procedures, they were not required to explain them to the participants and in most cases participants did not ask any questions relating to purpose and implications as they would have been satisfied by the information disclosed.

When asked about the respondents' attitudes to the study procedures, the nurses agreed that most participants did not appreciate placebos and randomisation as they wanted to ensure that they were on the active product arms. One of the nurses reported that some women came to her

to find out which arm of the study they were on, and the nurse informed them that she was not aware. The nurses also reported that during talks with them, mentioned that they were hoping that they were on the active product arms.

The study nurses were in agreement that there was a possibility that some women could have engaged in risky behaviours if they did not understand that they were participating in a study to test the effectiveness of the microbicides. The nurses indicated, however, that they had not come across any woman who had refused to participate or had withdrawn because of concerns around randomisation, double-blinding and placebo use. The study nurses also indicated that comprehension of the study procedures was a major problem in obtaining informed consent. They also cited the time factor as a challenge since they were expected to meet some accrual targets as individuals and as a site. The nurses reported that some illiterate persons understood the study better than some literate ones after they had explained the study to them. The nurses indicated that study gels had been collected from all the study participants at the end of the study and the results from the microbicide study had been disseminated to the participants in February 2009. They reported that when the women were getting the results on a one-on-one basis, most of the women felt relieved after being told about the study arm that they were on during the study. The debriefing of participants in the microbicide study was noteworthy as some studies do not debrief participants when they are over. The debriefing of participants is commendable as it ensures that former trial participants at least benefit from the new knowledge generated by the study they would have participated in.

During the collection of this data, it became clear by watching the staff interacting with the participants, that there was a relationship of trust. The staff knew the names of most of the women who were visiting the sites and the women could talk freely with the study nurses, an indication that the environment which was maintained at the two sites was one of friendliness

and trust. The trust and friendliness was also evident during the implementation of the intervention at the Blantyre site. Before and after the implementation of the intervention activities, some of the women could be seen visiting the study nurses in their offices to greet them or to bid them farewell.

6.3 FINDINGS RELATING TO THE RELIABILITY OF THE MAIN DATA COLLECTION TOOL

The reliability of the structured questionnaire, which was the main data collection tool for the first phase of the study, was determined using Cronbach's alpha. Cronbach's alpha is a test which determines the internal consistency or average correlation of items in a survey instrument to determine its reliability. Alpha coefficients range in value from 0–1 , and the higher the score, the more reliable the scale is. Alpha coefficients of 0.7 indicate an acceptable reliability but lower thresholds have been used in some literature (Nunnaly, 1978). Using SPSS, an alpha coefficient of 0.7028 was obtained using the three-category scale (0-49%, 50-74% and 75-100%) for the five items included in the "understanding" construct (see Table 6.1). This alpha coefficient which is above 0.7 confirms the acceptability of the reliability of the scale used and hence the questionnaire itself. The item-total correlation coefficients, which are all greater than .3, confirm that the reliability for all items is very high and that they are all contributing towards measurement of the same construct.

Table 6.1:
Cronbach's Alpha analysis for the five items included in the "Understanding" Construct using the three-category scale of understanding

Item-total Statistics

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Alpha if Item Deleted
Composite score category (Q100C)	9.5271	3.1218	.0.8009	0.5300
Implications Category (Q97C)	9.8522	3.1464	0.3781	0.7098
Double Blinding category (Q96C)	9.8670	3.1159	0.4520	0.6637
Placebo-use category (Q95C)	9.1970	3.7630	0.4315	0.6669
Randomisation category (Q94C)	9.0640	4.0404	0.3754	0.6877

Reliability Coefficients

N of Cases = 203.0 n of Items = 5

Alpha = 0.7028

Analysis using 10 items which includes the dichotomous and the three-category scales for each of the five items used in Table 6.2 below, yielded a higher alpha coefficient of 0.8501, confirming that all 10 items are contributing towards the measuring of the same construct. The item-total correlation coefficients for all ten items are greater than .3 confirming that the reliability for all 10 items is high and that all items are contributing significantly towards the measurement of the construct under study.

Table 6.2:
Cronbach's Alpha analysis for ten items included in the "Understanding" Construct using the dichotomous and 3-category scales

Item-total Statistics

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Alpha if Item Deleted
Randomisation Category (2 cat)Q94D	17.6749	12.3789	0.4558	0.8452
Placebo use category (2-cat)Q95D	17.8030	11.8125	0.5303	0.8388
Blinding category (2 cat) Q96D	18.2118	11.7024	0.5420	0.8377
Implications Category (2 cat) Q97D	18.1576	11.5889	0.5535	0.8365
Composite category (2 cat)Q101	18.1379	10.8522	0.7936	0.8174
Composite score category (3 cat)Q100C	17.1773	10.3248	0.8454	0.8092
Implications category (3 cat) Q97C	17.5025	10.1819	0.5083	0.8500
Blinding category (3 cat)Q96C	17.5172	10.1915	0.5615	0.8400
Placebo-use cat (3-cat)Q95C	16.8473	11.3776	0.5239	0.8384
Randomisation cat (3-cat)Q94C	16.7143	11.9675	0.4341	0.8455

Reliability Coefficients

N of Cases = 203.0 n of Items = 10

Alpha = 0.8501

6.4 FINDINGS RELATING TO THE MICROBICIDE STUDY PARTICIPANTS

All of the 203 respondents to the structured questionnaire, which was the main data collection tool, were women who were participating in the HPTN035 trial in Blantyre and Lilongwe. The Lilongwe site (HPTN035-631) contributed 26,6 percent (n=54) of the total number of respondents while 73.4 percent (n=149) were from the Blantyre site (HPTN035-630). This imbalance was a result of logistical factors beyond the control of the researcher. The researcher and the research assistant were both stationed in Blantyre and had to stay in

Lilongwe during the process of data collection. Accrual was very slow as most of the participants in the microbicide study were only coming to the clinic for their last follow-up visits. Table 6.3 below shows the distribution of respondents by site.

Table 6.3:
Distribution of respondents by site

Study Site	Frequency	Percent	Valid Percent	Cumulative Percent
Blantyre HPTN035-630	149	73.4	73.4	73.4
Lilongwe HPTN035-631	54	26.6	26.6	100.0
Total		100.0	100.0	

6.5 DEMOGRAPHIC CHARACTERISTICS OF RESPONDENTS

The microbicide study recruited participants who were aged 18 and above, and who were sexually active. The current study adopted the inclusion criteria of the microbicide trial. About 73.4percent (n=149) of participants recruited for the current study were aged between 20-30 years. The youngest respondent, the only one below 20 years of age, was aged 19 years. Only two women aged 41 years and above were recruited for this study. Table 6.4 shows the age distribution for the 203 respondents.

Table 6.4:
Age Distribution of Respondents

Age Group	Frequency	Percent	Valid Percent	Cumulative Percent
Below 20	1	.5	.5	.5
20-25	79	38.9	38.9	39.4
26-30	70	34.5	34.5	73.9
31-35	41	20.2	20.2	94.1
36-40	10	4.9	4.9	99.0
41+	2	1.0	1.0	100.0
Total	203	100.0	100.0	

About 96 percent (n=195) of the respondents reported that they were in some form of conjugal union inclusive of marriage and co-habitation, while 4 percent (n=8) indicated that they were not involved in any kind of conjugal union (including the single, divorced and separated). This finding is not surprising in view of the inclusion criteria of the microbicide study. The microbicide study only recruited women aged 18 and above who were sexually active. The majority of respondents had five to eight years of primary education (46.6 percent; n=95) followed by 32.5 percent (n=66) who had one to four years of secondary education. Interestingly, none of the 203 women had tertiary education. This distribution is also reflective of the educational demographics for Malawi (National Statistical Office Malawi, 2004). Table 6.5 below shows distribution of respondents by level of formal education attained.

Table 6.5:
Educational levels of respondents

Education level	Frequency	Percent	Valid Percent	Cumulative Percent
No formal education	16	7.9	7.9	7.9
Standard 1-4	26	12.8	12.8	20.7
Standards 5-8	95	46.8	46.8	67.5
Forms 1-4	66	32.5	32.5	100.0
Total	203	100.0	100.0	

The majority of respondents were from the Chewa tribal group (90.6 percent; *n*=184), followed by the Lomwe (3.4 percent; *n*=7) and others (5.9 percent; *n*=12). This finding was reflective of the national distribution of tribes in Malawi (National Statistical Office Malawi, 2004). The Chewa tribal group is generally dominant in the Southern and Central Regions of the country that cover the cities of Blantyre and Lilongwe. The interviews and focus group discussions with respondents were held in ChiChewa. The majority of people from the other tribes generally communicate fluently in ChiChewa. The majority of participants were from areas classified as urban areas (58.6 percent; *n*=118), while the remainder were from either rural or peri-urban areas (41.4 percent; *n*=84). The areas that were classified as urban were those that fell within the boundaries of municipalities and included low density areas and townships.

In terms of economic activities, 55.7 percent (113) were engaged in informal employment, mainly trading, 7.9 percent (*n*=16) were engaged in formal employment, and 34 percent (69) reported that they were housewives. Table 6.6 below presents the distribution of respondents by economic activity.

Table 6.6:
Distribution of respondents by economic activity

Economic Activity	Frequency	Percent	Valid percent	Cumulative Percent
Student	1	.5	.5	.5
Housewife	69	34.0	34.0	34.5
Formal employment	16	7.9	7.9	42.4
Informal employment	113	55.7	55.7	98.0
Not engaged in any economic activity	4	2.0	2.0	100.0

About 68percent (*n*=138) stayed in their own houses while 27.1percent (*n*=55) were tenants. The remaining 4.9percent (*n*=10) stayed with either family, relatives, friends, or employer. It is important to note that, in Malawi, ownership of a house is not necessarily a reliable economic status indicator as family members often sub-divide plots into small sub-plots and build some structures of different standards.

Regarding to access to health care, the majority of respondents (70.9percent; *n*=144) relied on care provided by government for free in government medical institutions, while 24.6percent (*n*=50) reported that they paid for the medical services they used. For the remaining 4.5percent (*n*=9), medical care is provided through either medical insurance or through other means. This is not surprising in view of the economic situation in Malawi. Table 6.7 below presents findings on the sources of support for medical care.

Table 6.7:
Sources of support for medical care

Source of health care support	Frequency	Percent	Valid Percent	Cumulative Percent
Pay for myself	50	24.6	24.6	24.6
Medical aid scheme	5	2.5	2.5	27.1
Someone pays for me	4	2.0	2.0	29.1
Free care provided by Govt	144	70.9	70.9	100.0
Total	203	100.0	100.0	

6.6 FINDINGS ON UNDERSTANDING OF RESEARCH

Several questions aimed at eliciting information about the respondents' understanding of the microbicide trial itself were included in the questionnaire as well as the FGDs. These ranged from understanding of purpose, difference between research and routine care, and others. In this section, findings on understanding of research obtained through the structured questionnaire as well as the FGDs are presented. Findings obtained using the two methods are presented simultaneously since FGDs were specifically used to complement findings from the structured interview.

6.6.1 Purpose of the Microbicide Study

Women were asked about the purpose of the study that they were participating in. The majority of women (88.7 percent; n=180) correctly pointed out that the study was aimed at testing a new microbicide, while 10.8 percent (n=22) believed that the study was aimed at protecting women against HIV infection. The belief that the study was aimed at protecting women against HIV infection can be interpreted in two ways. It may mean that some of the

women thought that the microbicide trial was a programme specifically aimed at protecting them against HIV infection in the literal sense. It may also be interpreted to mean that some of these women believed that the trial was aimed at testing a way to protect women against HIV infection. The following quotations from the focus group discussions confirm the finding that some of the women who were participating in the microbicide trial were aware of the main aim of the microbicide study:

> ***LLP6:*** *It is a study that is testing some gels to find out if they can prevent the spread of HIV/AIDS.*
>
> ***LLP4:*** *I think what she has said is true, but I just want to add that the researchers would also like to find out if the use of the gels can cause some side effects to the woman or her partner. They are also interested in finding out if husbands enjoy sex when a woman is using the gels (**OTHERS:** Laugh)*
>
> ***LLP2:*** *We were told that in this study they are trying to find out the usefulness of different types of gels in preventing HIV transmission from a man to a woman.*
>
> ***LLP5:*** *Apart from the effectiveness of the gels, they were also trying to find out if the gels are safe to be used in the vagina, whether they would cause any irritation or itching when applied to the vagina.*
>
> ***LLP7:*** *The main objective is to find out if the different gels can protect women from contracting HIV from a man, that's all!*
>
> ***BTP7:*** *It is a study about the use of a special gel to find out if the gel is effective in preventing transmission of HIV/AIDS.*
>
> ***BTP5:*** *Yah in the study, they are also trying to find out if men can accept the use of the gel by their wives. You know there are some men who do not want to see anything in the vagina when they are having intercourse (OTHERS: Laugh). Yes, this is true. So, the researchers want to know if men can allow their women to use the gel.*
>
> ***BTP3:*** *Anyway, when we were asked to take part in the Microbicide Trial, we did not know what the trial was all about until the researchers explained to us what the research was all about (F: Hmm). What they said was that in the research they were trying to investigate into the effectiveness of using the gel in the prevention of HIV/AIDS. One of the requirements was that one had to be tested for HIV/Aids if one accepted it. So, this is what we were told during the research.*

***BTP6**: It is to find out if the gel can help prevent transmission of the virus from a man to a woman.*

***BTP2**: I think the main aim is to prevent the spread of HIV/AIDS. If the gel is effective, it means it will help in the prevention of the spread of HIV/AIDS.*

***BTP6:** Yah but the objective you have given is not different from mine because I said the aim of the trial is to help prevent HIV transmission from a man to a woman.*

***BTP2:** Of course, it is not very different but I have stressed the fact that it is the main aim of the trial.*

During the focus group discussions, some women who were not quite sure about the purpose of the trial mentioned the following:

***LLP8:** Since you have said a study can have different objectives, then one of the objectives of this study could be to encourage people to use condoms as one way of fighting HIV/AIDS. Yes, it was because we were being encouraged to use condoms to prevent the spread of HIV/AIDS.*

***LLP3:** We were told that the gels had the potential to kill the virus in the vagina, in this case, if one sleeps with a man who is HIV positive and the virus is deposited into the vagina during intercourse, the gel could kill the virus before it circulates into the blood system.*

***LLP7:** For those who received a placebo, they were advised to use condoms whenever they had intercourse.*

***LLP7:** They wanted to compare whether the use of condoms and the use of gels could prevent the spread of HIV/AIDS.*

***LLP2:** We were advised to apply the gels in the vagina some minutes before sexual intercourse and have sexual intercourse while the vagina was awash with the gels. In this way, we would be protected from becoming infected with the virus.*

***BTP10**: Another objective is to provide counselling, HIV testing and support to those who test positive.*

***BTP4:** I think another objective is to know the number of people with HIV/AIDS.*

***BTP8:** No, they didn't say they wanted to find out the number of people with HIV/AIDS. However, from the HIV tests, they were able to know the number of people with HIV/AIDS from our group. And it's possible that one of the objectives of the study was to find out the prevalence of HIV/AIDS among women.*

6.6.2 Difference Between Research and Routine Care

When asked through the questionnaire about the difference between research and routine care 71.4 percent (n=145) reported that research was aimed at testing new interventions, while 18.7 percent (n=38) reported that they did not know the difference, and 9.9 percent (n=20) believed that there was no difference. This also came out clearly during the FGDs. Some women clearly demonstrated that they were aware of the difference and mentioned the following:

> ***LLP4:*** *Research is about finding out what one does not know.*
>
> ***LLP4:*** *Yes, for example, if you hear that there is a new drug which can cure TB, you try to find out what that drug is and you come to know it.*
>
> ***LLP4:*** *Yes, that is a research because you are trying to find out what you don't know and you eventually know it.*
>
> ***LLP8:*** *Research can also mean looking around for something so that you know what problems are there in the area; therefore, the word research stands for looking around here and there in order to find out what goes on in a village or community.*
>
> ***LLP5:*** *Thank you. My understanding is that a research involves investigation into a disease; to find out how and why the disease has come about, how to prevent it incase it has no cure as well as how to find a cure for the disease. So, in the course of their investigation, people say they (the researchers) are conducting a research. For instance, there is cancer as a disease (F: Hmm). And they conduct a research on cancer to find out its causes and how to combat it.*
>
> ***LLP1:*** *For me I think is it one aspect of trying to find out the origins of some issues concerning our health, like diseases; they can do a research to find out what caused the disease.*

Those who were not clear about the difference between research and routine care mentioned the following:

> ***LLP4:*** *The difference is that at the hospital they can diagnose us with malaria or diarrhea and give us medicine. While in clinical research, they take blood samples and screen them and eventually inform us about the disease we are*

suffering from before giving us medicine. For example, in this study, our blood samples were taken and tested for HIV but we did not receive any medication.

LLP5: *Yes to some extent there is treatment in both cases. But as my friend has said, researchers approach you to participate in research – you don't go to them. And if they screen you and find that you are sick, they may treat you before you enrol in their research or even in the course of your participation in the research.*

LLP4: *And in clinical research, they give you better drugs than at the hospital!*

LLF: *Hmm, I would like you to clarify. Do you mean that at the hospital they don't give you good medicine unlike in research?*

LLP4: *Well, the medicine can be helpful. I can give an example. When you are sick at the hospital they can screen you and if they see that you are coughing, they may give you medicine for a cough while it is TB. While in clinical research, they take your blood, screen it and find the TB quite quickly. They then tell you that you have TB and give you the right medicine. The difference is not necessarily that they may give you drugs that are not powerful. Rather, the difference is in the screening process. In research, they screen in a way that they find the results quickly and rightly, yes.*

LLP7*: Let me answer like my friend. It is true; you may go to the hospital and tell them you are suffering from headache or you have fever. They just prescribe the medicine for you for fever. They do not screen you. While when you go into a health research, they screen you first to find out exactly what the problem is. Soon after the diagnosis, you are given medicine.*

LLP8*: In research, they may tell you to have your urine or stool screened. They find the diseases fast. While at the hospital they just tell you that you are suffering from this and prescribe medication without proper diagnosis.*

LLP7: *Yes, they understand the difference as she has said. We all know that we go to the hospital to receive treatment when we are sick while we are normally asked by health workers to participate in research.*

BTP4: *The difference is that in clinical research we visit villages to see how people live and their health (F: Hmm) while we go to the clinic to get medical attention when we are sick (F: ok) yes.*

BTP5: *The other difference is that when we go to the clinic, we explain our problem and receive treatment (F: Hmm) while in clinical research, they investigate into the problem before they give you treatment - they investigate the problem and from the investigations they are able to find the best treatment for the disease.*

BTP7: *We go to the clinic to receive treatment for ailments while in research we go to visit sick people in the village, those suffering from malaria or TB. After visiting them, we inform the doctors at the clinic about the people suffering. So this is different from the health care we get from the clinic everyday.*

***BTP1**: Yes, there is a difference between the two because when you are sick you rush to the clinic to get medical attention. In clinical research, they advise us to go to the clinic when we are sick and to rush any seriously sick person to the hospital. I don't know if I am right.*

***BTP3**: At the hospital we get treatment when we are sick while research can be conducted even if one is not sick (F: hmm) hmm.*
***BTP4**: The difference is that we get medical treatment when sick whereas in research you are given all sorts of assistance even if you are not sick*

***BTP9:** Health personnel most of the times help us in form of food while at the hospital we get assistance in form of medicine.*

***BTP2**: The difference is that you go to the hospital when you are not feeling well while in research you can enrol even if you are ok, depending on the type of research whether they are trying to find out if you have certain diseases.*

***BTP9:** I also think that many people understand the difference because normally people are asked to participate in research while people go to the hospital to receive treatment on their own when they don't feel well.*

***BTP7:** Well, I agree with those who have said that many people understand the difference between clinical research and clinical care. In clinical research, people are always asked to give their permission before they participate and in most cases nurses are the ones who ask people to participate in research. If one does not want to participate he/she is free to refuse. Those who participate are the ones who are willing and give their permission.*

***LLP2**: Clinical research means trying to find out how people are taking care of themselves healthwise. If they get health care when sick, how they travel to the hospital; how far it is to the hospital and how are they taken care of at the hospital.*

***LLP3**: They do research on a person with the aim of examining his/her body to see how it is functioning; if he/she has malaria, they will know and the person will be informed and given treatment.*

***LLP6**: It is like when we are pregnant and go to the hospital, they take your blood to test and see if you are alright and they tell you the results e.g. if you have malaria, they pick you by car to your home.*

***LLP5**: When they say research they mean when they want to assist on a specific part of our welfare such as wells to see if there is enough hygiene i.e. how we are*
taking care of them……. That is what I can say, anybody can continue if there are other views.

***LLP2**: The views that I have are that research is where we hear a lot about the diseases that attack us and do not seem to get treated. The main thing is to have our blood tested in order to see how things are and what can be done about it.*

***LLP6**: Research also aims at finding out how people are behaving like if they are following the advice given by health workers in terms of sanitation in the households. They look at things like availability of toilets, bathrooms and the like; and if they are not available, they make sure that they visit those households to ensure that the facility is constructed in order to reduce the burden of diseases.*

***BTP9:** They (researchers) conduct a research in order to find out if a person is HIV positive or not. Sometimes they also conduct it to investigate into other diseases such as Candidiasis (mauka), gonorrhea (chizonono) or even malaria. [F: Hmm] yes.*

***BTP1**: In most research, they take blood from the arm in the ward and test it for sexually transmitted infections.*

***BTP1**: Yes, for example, HIV/AIDS, gonorrhea [chizonono] (F: Ok) and they give medication every month if you test positive.*

***BTP8:** In research (F: Hmm) they investigate into the health of people, whether diseases such as HIV/Aids affect them or not. If you are HIV positive (F: Hmm), they give you antiretroviral drugs to boost your immune system.*

***BTP3**: Research means investigation into people's everyday lives (F: Hmm). For example, in the research I am participating, they are investigating into the health of women and how they can prevent the transmission of HIV/AIDS. So, if you ask me the meaning of the term research, in short, it means investigating into a person's health. This is done if the person has accepted to be investigated.*

From the above quotes, it is evident that there were individual differences in terms of knowledge concerning the distinction between research and routine care. The several quotes from women who were not aware of the difference between the two, are cause for concern as they suggest some gaps in the trial participants' knowledge about research. The findings from the FGDs illuminate the findings from the structured interview as they provide some rich text that in turn provides a clear picture of the respondents' knowledge. The various views as expressed in the above quotes, suggest that people may be describing research and routine care using by a whole range of factors that they see (not necessarily confusing the two). For example they are associating research with someone

who is sick, or not, whether there are other benefits, and where the activities are done (homes or villages).

6.6.3 Pre-enrolment sources of information about the microbicide study

The majority of women 58.1 percent (n=118) indicated that they were informed about the study by their relatives and friends; 26.6 percent (n=54) had been informed about the research study during a visit by study staff; 15.3 percent (n=31) had heard about the study from other sources. The distribution of respondents by pre-enrolment source of information is shown in Table 6.8. The finding that most of the participants heard about the study through social networks, was also confirmed by study staff in Blantyre. As a result, study participants were concentrated in certain areas as compared to others.

Table 6.8:
Pre-enrolment source of information about the microbicide study

Source of information	Frequency	Percent	Valid Percent	Cumulative Percent
Visited at home by study staff	54	26.6	26.6	26.6
Referred by relative or friend	118	58.1	58.1	84.7
Heard about program from other sources	31	15.3	15.3	100.0
Total	203	100.0	100.0	

The use of "the grapevine" in spreading information about the study in some cases led to the surfacing of rumours that could have skewed the recruitment exercise for the microbicide trial.

During FGDs, some respondents highlighted the following rumours that had been circulating in the communities through social networks:

> ***LLP2:*** *There were stories that people who used the gels would become HIV infected.*
>
> ***LLP5****: Some were also saying that people who use the gels become infertile.*
>
> ***LLP2:*** *She said they were lies and that the gels were meant to prevent the transmission of HIV/AIDS from a man to a woman.*
>
> ***LLP6:*** *Yes, we were satisfied because the study staff know better than our fellow friends who tell such lies (LL**P7:** chips in and says; some have never come to Tidziwe and know nothing about the gels. They just spread these rumors without facts).*
>
> ***BTP8:*** *Yes some refused to take part because there were rumors that people who use the gels would become barren.*
>
> ***BTP4:*** *A neighbor of mine discouraged me from participating but I told her that it is my right to participate or not.*
>
> ***BTP4:*** *Yes, the sister (Nurse) asked her to participate but she refused because of the rumors people were circulating about the gels.*
>
> ***BTP4:*** *The rumors that people who use the gels can not bear children and that one can become infected with the virus.*
> ***BTP5:*** *Yes, there were rumors that people who used the gels would become HIV positive because the researchers had put the virus in the gels to see if people who used the gels would contract it (P2 chips in and says; but those were just false rumors!).*

Almost all of the respondents (99 percent; *n*=201) reported that they were satisfied with the amount of information that had been provided, as well as by the responses given by study staff in response to their questions. This was also evident during the focus group discussions. Some of the quotes illustrate that the participants really wanted the researchers to know how hard the study staff tried to explain the work and perhaps did not want the researchers to find fault with the staff. What is also interesting is whether they saw the current study as a test of whether the microbicide study staff had developed good relations with their 'friend'. There was emphasis on friendship, appreciation and protection.

***BTP5**: The nurse who consented me explained that there was a possibility that the gel could reduce the male to female transmission of HIV. However, she insisted that they were only testing the gels and that they have not yet found them to be effective in preventing the transmission of HIV/AIDS from a man to a woman. I think this is what she also explained to the others.*

***BTP8**: She also said that if the gel worked, we would not become infected by the virus from an infected person.*

"Facilitator: *Hmm, what about those who cannot read and the information sheet had to be read for them by others, did you understand what the study was all about by listening to the information on the sheet?*
***LLP1:** Their message on the leaflets was enough. They wrote in simple ChiChewa and we could understand it.*
Facilitator: *Allright, what about the explanation that was given to you by the study staff, was it enough for you to understand what the study was all about?*
***LLP6:** The nurse who consented me explained what the study was all about in her own words and after explaining she asked me some questions about the study and after that she asked me if I had some questions or I needed any clarification on the study."*

The fact that they felt they were able to say no when they wanted to and did not want to be told otherwise by anyone is interesting.

***BTP4:** Yes, the information was enough, that's why we were able to say yes or no. If it was not enough, we would not have accepted to participate in the trial.*

***BTP8**: I think the information was very enough. In fact, the nurse who approached us explained the study to us and again when we came to the Clinic, they also explained to us clearly and requested us to ask questions where we didn't understand. We also had leaflets given to us so that we could read at home. So, we can't blame the researchers about information about the study (P5 chips in and says)*

***BTP5**: Their message was very clear and it was up to us to decide. Nobody can cheat you that the researchers did not explain the study to us.*

***LLP3:** In my view, the information was readable and clear. I think for all of us who can read, we understood what the study was all about.*

The majority of discussants in the focus group discussions reported that they benefited more from the verbal information provided by staff as compared to the information that was availed through study documents. They also said that they learned more about the microbicide trial

from discussions that they had among themselves as participants during the site visits, on the way home or within their communities.

> ***LLP7:*** *The oral information was the best because we could ask questions where we didn't understand and it was interactive.*
>
> ***BTP8:*** *Both were clear. However, the oral information was the best because we could ask questions where we didn't understand.*

About 53.2 percent (*n*=108) of respondents indicated that they had asked some questions while the rest (46.8 percent; *n*=95) did not ask any questions as they felt that the information that had been provided was adequate. Some of the questions related to the study procedures, some related to the microbicide, while some related to other issues. None had asked questions related to the use of placebo, randomisation or double-blinding. All respondents who indicated that they had asked some questions, indicated that they had been satisfied by the responses they received to their questions. When asked what was the one thing that they wanted to know most about, the majority of respondents (84.2 percent; *n*=171) indicated that they were more interested in learning more about the microbicide, 1.5 percent (*n*=3), about trial procedures, and 1.0 percent (*n*=2) about other issues. About 13.3 percent (*n*=27) were indifferent. When asked whether the study involved anything new or special, 14.8 percent (*n*=30) said yes, while 85.2 percent (*n*=173) did not think that there was anything new being studied. About 89.7 percent (*n*=26) of the 30 respondents who indicated that the study involved something new, indicated the microbicide as the new element.

6.6.4 Time taken to make a decision to join trial

About 18.7 percent (*n*=38) of the respondents reported that they decided to join the study on the first day they were invited, while 34.5 percent (*n*=70) joined after about one week. The rest of the participants took longer to consult others and to think about the invitation, with 21.2

percent (*n*=43) indicating that they took more than four weeks to make a decision. Table 6.9 below presents the time taken by the respondents in making decisions on participation.

Table 6.9:
Time taken to make decisions to participate in microbicide trial

Time taken to make Decision	Frequency	Percent	Valid Percen	Cumulative Percent
Decided on first day	38	18.7	18.7	18.7
After 1 week	70	34.5	34.5	53.2
2-4 weeks	51	25.1	25.1	78.3
More than 4 weeks	43	21.2	21.2	99.5
Do not know /forgotten	1	.5	.5	100.0
Total	203	100.0	100.0	

The above shows that the majority of respondents took some time to think about the study. A significant proportion however made their decision on the first day. It is possible that some of these based their decisions on trust, or other benefits that they were expecting from the study.

6.6.5 Reasons for joining the microbicide study

When asked about the reasons for joining the microbicide study, 80.8 percent (*n*=164) indicated that they joined the study so they could know about their HIV sero-status, 16.7 percent (*n*=34) to benefit mankind, and 2.5 percent (*n*=5) to access the free medical care that was offered at the study sites. Table 6.10 below presents a distribution of the reasons for joining the microbicide trial.

Table 6.10:
Reasons for joining the microbicide study

Reason for joining microbicide study	Frequency	%	Valid Percen	Cumulative Percent
To know my HIV status	164	80.8	80.8	80.8
To access free medical care	5	2.5	2.5	83.3
To benefit mankind	34	16.7	16.7	100.0
Total	203	100.0	100.0	

During the FGD, various responses were received regarding the reasons why the women decided to join the microbicide study:

LLP6*: I think most of us were just convinced by what the nurse explained.*

LLP6: *The fact that the gels could prevent the transmission of HIV from a man to a woman.*

LLP3: *Some of us are used to taking part here at Tidziwe. So, when the nurse approached us, we couldn't refuse.*

LLP8: *In my case, I just wanted to see for myself what the gels look like and how they work because I heard a lot about them from people. So, when the nurse asked me to participate, I had to accept.*

BTP6: *I was asked by the nurse to take part in this study and since I have been participating in other studies conducted by the Johns Hopkins, I decided to take part in this study as well.*

BTP6*: I was just interested in taking part in this study.*

BTP3: *I wanted to know my status because we were told that they would test us for HIV.*

BTP7*: Anyway, when we were asked to take part in the research, we were told that the researchers would provide us with treatment whenever we fell sick (F: Hmm).*

They would also test us for HIV at each and every visit and prescribe drugs for the cure of any diseases one was suffering from. So, how could I refuse such a free service?

***BTP1**: No, we don't pay for the services but sometimes we are told that there are no drugs at the hospital pharmacy and they ask us to buy drugs at private pharmacies which we can't afford.*

***BTP8**: and sometimes they just give us the very same drugs like panadol… (Speaks faintly)*

I said they give us panadol all the time (F: Hmm) [kids noise] so when we heard that they were providing drugs free of charge, we decided to join [P8: continues speaking but cannot be heard because of kids' noise]

***BTP10:** In my case, I just wanted to know what was happening in the research since they*
were looking for people to participate in the research (F: Hmm). Yes.

Specifically, the issue of accessing better quality care came out clearly during focus group discussions:

***BTP10:** One of the benefits is that whenever we are sick and come to the hospital, we will be treated faster than our friends – we were told that whenever we become sick we should always come to the clinic for treatment.*

***BTP10:** Yes, because we are given this special treatment due to the fact that we are participating in this study.*

***BTP2:** As we have already explained, people who participate in clinical research are given better treatment than other people. This is why people do not refuse to participate in research.*

***LL- P7:** Let me answer like my friend. It is true; you may go to the hospital and tell them you are suffering from headache or you have fever. They just prescribe the medicine for you for fever. They do not screen you. While when you go into a health research, they screen you first to find out exactly what the problem is. Soon after the diagnosis, you are given medicine.*

***BTP7:** Anyway, when we were asked to take part in the research, we were told that the researchers would provide us with treatment whenever we fell sick (**F:** Hmm).*

***BTP1**: No, we don't pay for the services but sometimes we are told that there are no drugs at the hospital pharmacy and they ask us to buy drugs at private pharmacies which we can't afford.*

***BTP8**: and sometimes they just give us the very same drugs like panadol… (Speaks faintly)*

BTP8: *I said they give us panadol all the time (F: Hmm) [kids noise] so when we heard that they were providing drugs free of charge, we decided to join [P8: continues speaking but cannot be heard because of kids' noise]*

LLP8: *The problem we have in our hospitals is that they don't have sufficient drugs and every time we go to the hospital, they provide the same drugs. While in research they have enough drugs and they provide drugs that cure the disease you are suffering from.*

LLP8: *Another benefit is that we are allowed to come for treatment here at Tidziwe whenever we fall sick – this is for us and our families.*
BTP10: *One of the benefits is that whenever we are sick and come to the hospital, we will be treated faster than our friends – we were told that whenever we become sick we should always come to the clinic for treatment.*

BTP10: *Yes, because we are given this special treatment due to the fact that we are participating in this study.*

BTP2: *As we have already explained, people who participate in clinical research are given better treatment than other people. This is why people do not refuse to participate in research.*

The majority of respondents (72.9 percent; n=148) indicated that they thought that, in general, individuals should join research so as to benefit mankind, and 23 percent thought that individuals should participate in research so that they can enjoy the direct benefits that are associated with participation.

The majority of respondents (93.1 percent; n=189) indicated that they found it easy to make a decision to join the study, and a total of 56.2 percent (n=114) of the respondents had consulted others in making the decision to participate. The majority of those 114 who consulted others, consulted their partners (74.6 percent; n=85). Table 6.11 below presents a distribution of the persons consulted by the respondents before joining the study. About 39.9 percent (n=81) of all respondents indicated that they joined the microbicide study because they themselves thought that it was a good idea to join, while 60.1 percent (n=122) joined as they had been persuaded by others who thought that it would be a good idea for them to join. The majority

of respondents (84.2 percent: *n*=171), indicated that they were very keen to learn more about the microbicide whilst only 1.5 percent (n=3) indicated that they were keen to know more about the study procedures.

Table 6.11:
Individuals consulted before agreeing to join the study

Individuals consulted	Frequency	Percent	Valid Percent	Cumulative Percent
Partner	85	41.9	74.6	74.6
Parents	4	2.0	3.5	78.1
Friend	18	8.9	15.8	93.9
Other	7	3.4	6.1	100.0
Total	114	56.2	100.0	
Did not consult	89	43.8		
Total	203	100.0		

6.6.6 Risks associated with participation in the microbicide study

During the focus group discussions, some of the discussants mentioned some of the risks that were associated with participation in the trial. Risks mentioned included unintentional exposure to stigma as a result of the inclusion and exclusion criteria, time inconvenience and some side effects caused by the gels such as itching. They stated that one's HIV status would be revealed to the public once they were not recruited into the microbicide study:

> ***BTP9:*** *We would know if one was tested and did not join us.*
>
> ***BTP8:*** *After some days, you would see her going to the ART Clinic and we would say "sorry" for our friend.*
>
> ***BTP2****: It is not a secret at all when one tests positive because we know each other.*
>
> **Facilitator:** *Hmm, does this mean there is no confidentiality on the part of those people who test positive?*
> ***BTP6:*** *Confidentiality is there because each one is told privately. However, when one goes for counselling and testing and does not join us in the study, we automatically know that that person has not met the requirements (eligibility*

criteria), one of which is her HIV status. So, it's very easy for us to know that one is HIV positive and if one attempts to join the trial.

BTP1: *One disadvantage is that we take long when we come to the clinic for the study. Some of us come early in the morning and we go back home very late in the afternoon.*

BTP8: *Another disadvantage is that when one applies the gel on the vagina, it itches and it is discomforting to some people.*

Overall, the respondents indicated that they were generally happy with their participation and were even prepared to encourage others to join the study. One respondent summed up her gratitude as follows:

LLP3: *We also appreciate what the researchers at Tidziwe are doing. A lot of us are benefiting from their work. Please, encourage them to continue conducting these studies.*

6.7 FINDINGS RELATED TO UNDERSTANDING OF RANDOMISATION

Respondents were asked whether they knew that, in the microbicide study, participants were randomly allocated to different groups. The majority of respondents (99 percent; n=201) reported that they were aware of this fact. An additional question was included in the questionnaire to confirm their awareness. The majority of respondents (89.2 percent; n=181) indicated that they were definitely aware that individuals in the trial were randomly assigned to different groups. When they were asked to list all the different groups, only 49.8 percent (n=101) listed all four arms of the trial. About 7.4 percent (n=15) were not aware of the role of chance in the assignment of study arm. The low percentage of those who were not aware of the role of chance in assignment of study arm was not surprising in view of the fact that the majority of respondents got high scores on understanding of randomisation. Table 6.12 below shows the distribution of respondents by awareness of the four arms of the trial. About 50.2% of all respondents could not list the four correct arms of the microbicide trial.

Table 6.12:
Awareness of the various arms of the trial

Awareness of study arms	Frequency	Percent	Valid Percent	Cumulative Percent
1 arm / do not know	5	2.5	2.5	2.5
2 arms (gel + placebo)	3	1.5	1.5	3.9
3 arms (2 gels + placebo)	94	46.3	46.3	50.2
4 correct arms	101	49.8	49.8	100.0
Total		100.0	100.0	

The respondents were asked to describe how participants were randomised into the various study arms. About 92.6 percent (n=188) of the respondents correctly described the process. More than half of respondents (53.7 percent; n=109) were not aware of the reasons why individuals are assigned to the various groups, while 50.2 percent (n=102) were not aware of the personal implications of randomisation. The 22 respondents specifically did not indicate the fact that randomisation means that they do not have a choice regarding the trial arm or product they want to receive.

A score was assigned for the questions relating to randomisation. Overall, 85.2 percent (n=173) of respondents scored 75 percent and above (Refer to Table 6:13 below).

Table 6.13:
Scores on understanding of randomisation on a dichotomous scale

Scores	Frequency	Percent	Valid Percent	Cumulative Percent
Low score 0-74%	30	14.8	14.8	14.8
High Score 75%+	173	85.2	85.2	100.0
Total	203	100.0	100.0	

When the scores were further broken down into a three point scale, it was still evident that the majority of respondents had shown some high levels of understanding. A very small proportion of the respondents (3.9 percent; *n*=8) scored below 50 percent and 10.8 percent (*n*=22) scored between 50-74 percent. Table 6:14 presents the distribution of scores on a three-category scale.

Table 6:14:
Scores on understanding of randomisation on a three-category scale

Scores	Frequency	Percent	Valid Percent	Cumulative Percent
0% - 49%	8	3.9	3.9	3.9
50% - 74%	22	10.8	10.8	14.8
75%+	173	85.2	85.2	100.0
Total	203	100.0	100.0	

The following quotes from the focus group discussions, confirm that some of the participants were conversant with the process of randomisation:

> ***BTP1:*** *During the consent process, we were told that we would randomly be assigned to four groups. In the groups, some would receive gels and others would receive nothing.*
>
> ***BTP7:*** *We were also told that we would not know the arms to which we would be assigned. However, in my case I was in a group in which we received gels.*
>
> ***BTP8:*** *We don't know how we were assigned to the groups.*
>
> ***BTP3:*** *We were given numbers and each one chose the gel which corresponded to her number.*
>
> ***BTP10:*** *Yes, they explained clearly. As my colleagues have stated, the nurses explained that it was the computer which assigned us to the different groups and that the nurses would not know to which group each one belonged. We understood that the nurses were not assigning us to the groups.*
>
> ***LLP7:*** *The nurse explained that randomisation is the process of putting people in different groups.*
>
> ***LLP7:*** *Another thing she said about randomisation is that it is like a game of chance whereby you do not know who will get this or that – it is by chance that some people received the real gels and others did not get any gel.*
>
> ***LLP6:*** *She said it was done by a computer.*
>
> ***LLP3:*** *We don't know how the computer does it. We were just told that we were assigned those numbers by a computer and not anybody.*

6.7.1 Study Site and Understanding of Randomisation

Cross tabulations of sites and levels of understanding about randomisation, revealed that site had an effect on understanding of randomisation. About 91.3 percent (n=136) of the 149 respondents from the Blantyre site got scores above 75 percent, compared to only 68.5 percent (n=37) of the 54 respondents from Lilongwe (See Table 6.15). Using the Fischer's exact test, a value of p=.000 was obtained. This p-value represents a statistically significant relationship between study site and understanding of randomisation. Participants at the Blantyre site were

more likely to score highly or to have a better understanding of randomisation as compared to participants from the Lilongwe site.

Table 6.15:
Cross tabulation of site by understanding of randomisation

Study site	**Low scorers 0-49%**	**High scorers 75%+**	**TOTAL**
Blantyre HPTN035-630	8.72% (13)	91.28% (136)	100% (149)
Lilongwe HPTN035-631	31.48% (17)	68.52% (37)	100% (54)
TOTAL	14.78% (30)	85.22% (173)	100% (203)
			P=0.000

6.7.2 Age and Understanding of Randomisation

There was no statistically significant relationship between age and understanding of randomisation. A value of p=.406 was obtained using the chi-square test. The distribution of scores by age is presented in Table 6.16 below.

Table 6.16:
Cross tabulation of Age by understanding of randomisation

Age groups	Low Scorers 0-74%	High Scores 75%+	TOTAL
18-25	11.25% (9)	88.75% (71)	100% (80)
26-30	15.71% (11)	84.29% (59)	100% (70)
31-35	21.95% (9)	78.05% (32)	100% (41)
36-45	8.33% (1)	91.67% (11)	100% (12)
TOTAL	14.78% (30)	85.22% (173)	100% (203)

P=0.406

6.7.3 Level of Education and Randomisation

There was a statistically significant relationship between education level and understanding of randomisation. A *p*-value of .043 was obtained using Pearson's chi-square test. Those with 5 or more years of schooling were more likely to score highly than those with less than 5 years of schooling (see Table 6.17).

Table 6.17:
Cross tabulation of education and understanding of randomisation

	Low Scores 0-74%	High Scores 75%+	TOTAL
No formal education	31.25% (5)	68.75% (11)	100% (16)
Standard 1-4	19.23% (5)	80.77% (21)	100% (26)
Standards 5-8	16.84% (16)	83.16% (79)	100% (95)
Forms 1-4	6.06% (4)	93.94% (62)	100% (66)
TOTAL	14.78% (30)	85.22% (173)	100% (203)

P=0.043

6.7.4 Attitudes Towards Randomisation

Participants generally had a negative attitude towards randomisation. About 72.9 percent (n=148) indicated that they were of the opinion that research participants should be allowed to make their own choice regarding the group they wanted to belong to. About 36 percent (n= 73) were of the opinion that the active product should be given to only those with high risk behaviours and 39.4 percent (n= 80) thought that it should be given to those with low risk behaviours. About 25.6 percent (n=52) thought that they were receiving the active products (Buffergel and Pro2000). About 3 percent (n=6) of respondents indicated that they had concluded that they were on the active product arm since they had found out that the product was working well for them.

When asked which group they would want to be assigned to if offered the chance to be re-assigned, 40.9 percent (n=83) of respondents indicated that they would choose to be re-assigned to the Buffergel and Pro2000 arms. About 62.0 percent (n=52) of those 83 respondents who indicated that they would want to be re-assigned to the active arm gave the reason that they wanted to find out if the product really works and 3.4 percent (n=3) indicated that they would be assured of protection from HIV. During interviews with the study nurses and also during focus group discussions with some of the microbicide trial participants, there were anecdotal reports from both the nurses and participants of women who had swapped their assigned products as they wanted to have a feel of the different products. It was reported that some trial participants had "found out" that they were on placebo. These participants are said to have swapped their placebos with either Pro2000 or Buffergel so they could also be protected by the two products.

6.8 FINDINGS ON UNDERSTANDING OF DOUBLE-BLINDING

Respondents were asked if they knew whether the doctors and study nurses knew which product they had assigned to them. About 33.5 percent (n=68) of the respondents indicated that they believed that study staff were aware. About 57.6 percent (n=117) of respondents indicated that they were not aware of the reason why double-blinding was used in the study, and 78.8 percent (n=160) were not aware of any personal implications of double-blinding. Only 31.5 percent (n=64) of respondents scored 75 percent and above, with 30.5 percent (n=62) scoring between 0-49 percent, and 37.9 percent (n=77) scoring between 50-74 percent. The following statement by one respondent during the FGDs confirms that some of the participants were aware of double-blinding and what it meant:

> **BTP4:** *During the consent process, they stated that they would not know what each one would receive.*

During the focus group discussions, those respondents were not quite sure about the reasons why there was double-blinding in the study mentioned the following:

> **BTP9:** *They were afraid that if one knew that she was receiving a placebo gel, she would withdraw from the study.*
> **BTP9:** *They would not be able to recruit a good number of people because some would have dropped out.*
>
> **BTP5:** *Of course the nurse explained what they mean but it does not matter to us.*

6.8.1. Study Site by Understanding of Double-blinding

Participants from the Lilongwe site were more likely than those from the Blantyre site to show a better understanding about double-blinding (see Table 6.18). The Fischer's exact test gave a p-value of .002. This value is confirmation of the existence of a statistically significant relationship between understanding of double-blinding by site.

Table 6.18:
Cross tabulation of study site by understanding of double-blinding

Study site	**Low scorers 0-74%**	**High scorers 75%+**	**Total**
Blantyre HPTN035-630	62.42% (93)	37.58% (56)	100% (149)
Lilongwe HPTN035-631	85.19% (46)	14.81% (8)	100% (54)
TOTAL	68.47% (139)	31.53% (64)	100% (203)

P=0.002

6.8.2 Age by Understanding of Double-blinding

There was no statistically significant relationship between age and understanding of double-blinding (see Table 6.19). A *p*-value of 0.945 was found using Pearson's chi-square test. This finding indicates that age was not an important predictor of understanding of double-blinding.

Table 6.19:
Cross tabulation of age and understanding of double-blinding

AGE	**Low Scorers 0-74%**	**High Scorers 75%+**	**TOTAL**
18-25	68.75% (55)	31.25% (25)	100% (80)
26-30	68.57% (48)	31.43% (22)	100% (70)
31-35	65.85% (27)	34.15% (14)	100% (41)
36-45	75.00% (9)	25.00% (3)	100% (12)
TOTAL	68.47% (139)	31.53% (64)	100% (203)

P=0.945

6.8.3 Education and Understanding of Double-blinding.

A statistically significant relationship was observed between level of education and understanding about of blinding. A *p*-value of 0.002 was obtained using Pearson's chi-square test. Secondary education was found to be an important predictor of understanding of double-blinding. Participants with lower levels of education were less likely to understand double-blinding (See Table 6.20).

Table 6.20:
Cross tabulation of education and understanding of double-blinding

Level of Education	**Low Scorers 0-74%**	**High Scorers 75%+**	**TOTAL**
No formal education	81.25% (13)	18.75% (3)	100% (16)
Standard 1-4	84.62% (22)	15.38% (4)	100% (26)
Standards 5-8	73.68% (70)	26.32% (25)	100% (95)
Forms 1-4	51.52% (34)	48.48% (32)	100% (66)
TOTAL	68.47% (139)	31.53% (64)	100% (203)
			*p=0.*002

6.8.4 Attitudes Towards Double-Blinding

Respondents were asked various questions on their opinions of double-blinding. About 15.8 percent (*n*=32) found it to be acceptable and 42.9 percent (*n*=87) found it to be unacceptable while 41.4 percent (*n*=84) were indifferent. About 57.1 percent (*n*=116) thought that it was very bad practice for doctors not to be aware of what they were giving them, 32.5 percent (*n*=66) were indifferent and 10.3 percent (*n*=21) found no problem with this reality. Respondents were asked if they thought that researchers should advise participants whether they were on placebo or active product. About 78.3 percent (*n*=159) thought that researchers

should inform them. About 84.2 percent (n=171) felt strongly that doctors and nurses should be aware at all times what each participant was receiving. This was evidence that some respondents did not remember or chose not to remember what they had consented to at the time when they enroled into the study.

6.9 FINDINGS ON UNDERSTANDING OF PLACEBO USE

In order to assess out the awareness of respondents about placebo use in the study, respondents were asked to list the various products that were being used in the study. About 89.7 percent (n=182) correctly indicated that the study was using 3 gels consisting of 2 test products and one placebo (See Table 6.21). A different question specifically sought to find out if the women were aware that some women were being given a product which looked like the test product and yet did not contain the active chemical properties of the products being tested (Buffergel and Pro2000). In response to the question 84.7 percent (n=172) of respondents responded that they were aware. These findings confirm that some of the women (15.3 percent, were not very knowledgeable about the use of a placebo in the microbicide study. The following statements which came out during the FGDs confirm that some of the women were fully aware of what a placebo is and why it was being used in a study:

> ***BTP1:*** *It is a kind of medication which does not function like the actual medicine.*
>
> ***BTP3:*** *I think what she wants to say is that it is something which looks like the gel but it is not the actual that is being tested.*
>
> ***BTP3:*** *Yes, the nurse explained that some people would receive a placebo, something which looks like the gel but it is not the actual gel and others would receive totally nothing.*
>
> **Facilitator***: Ok, why do you think they are using a placebo in this study?*
> ***BTP9****: The nurse said they wanted to compare the different groups at the end of the study.*
>
> ***BTP5:*** *What she said was that the researchers wanted to find out if the gels were effective in preventing HIV transmission. In this case, with the use of the placebo*

gels, they would be able to know whether the gels were more effective than the placebo gels.

The above suggests that the reasons for using placebo in the study had been explained to the trial participants either through the study documents or during the informed consent procedures by the study staff. It is not clear whether the justification was provided only to those who asked questions or to everyone as part of the disclosure of information.

Table 6.21:
Responses on the different gels being used in the study

Gels being used in study	Freq	Percent	Valid Percent	Cumulative Percent
Microbicide only	1	.5	.5	.5
Microbicide + placebo	20	9.9	9.9	10.3
2 microbicide gels + 1 placebo	182	89.7	89.7	100.0
Total	203	100.0	100.0	

Close to half of the respondents (49.3 percent; *n*=100) were not aware of the reasons why a placebo was being used in the study. About 90.6 percent (*n*=184) of the women indicated that they were not sure which product they were receiving. The remainder (9.4 percent; *n*=19) indicated that they were aware that they were receiving either Pro2000 or Buffergel. About half (49.8 percent; *n*=101) were aware of the personal implications of placebo use in a study. Overall, 72.4 percent (*n*=147) of all respondents scored highly (75 percent+) on the understanding of placebo use. About 23.2 percent (*n*=47) scored between 50-74 percent and 4.4 percent (*n*=9) scored below 50 percent (See Table 6.22).

The following statements from the FGDs demonstrate inadequate knowledge about the use of a placebo in the microbicide trial:

LLP1: *They are trying three different types of gels (**P2** chips in and says; no, there are two gels they are testing).*

LLP8: *What I can remember is that they informed us that we would be allocated to different groups and in one group they would receive one type of gel, in the second group they would receive a different type and in the third group, they would also get a different type of gel. So, basically, there should be three different types of gels.*

LLP5: *My understanding was that there were testing two gels and other two groups would not receive anything. However, the names of the gels are difficult to say.*

BTP3: *The fact is that the nurse did not explain clearly why some people were receiving placebo gels, am I not right? [Others say eeh to show agreement] .*

Facilitator: *Ok, why are the researchers using a placebo in this Microbicide study?*

LLP8: *It was part of the design of the study*

LLP6: *The researchers themselves know.*

Facilitator: *Of course they may know but I would like you to tell me what you think about it; why you think they used the placebo gels!*

LLP8: *That is a difficult question because we were not there when the researchers thought of including placebo gels in this study.*

BTP6: *In my case, I am happy that I am in this group. Of course, I know some people are not happy that they are in a group in which they are not receiving anything.*

Table 6.22:
Distribution of scores on understanding of placebo use

Scores	Frequency	Percent	Valid Percer	Cumulative Percent
Low Scores 0-74%	56	27.6	27.6	27.6
High Scores 75%+	147	72.4	72.4	100.0
Total	203	100.0	100.0	

6.9.1 Site by Understanding of Placebo Use

Participants from the Blantyre site were more likely to have a better understanding of placebo use as compared to those from the Lilongwe site (Refer to Table 6.23). A *p*-value of *p=0.0001* was obtained using Fischer's exact test. This value was indicative of a statistically significant relationship.

Table 6.23:
Cross tabulation of site by understanding of placebo use

Study Site	**Lows Scorer 0-74%**	**High Scorers 75%+**	**TOTAL**
BLANTYRE HPTN035-630	20.13% (30)	79.87% (119)	100% (149)
LILONGWE HPTN035-631	48.15% (26)	51.85% (28)	100% (54)
TOTAL	27.59% (56)	72.41% (147)	100% (203)
			P=0.0001

6.9.2 Age by Understanding of Placebo Use

The relationship between age and understanding of placebo use was not found to be statistically significant (See Table 6.24). A *p*-value of 0.542 was obtained using Pearson's Chi-Square test.

Table 6.24:
Cross tabulation of age and understanding of placebo use

Age	Low Scorers 0-74%	High Scorers 75%+	TOTAL
18-25	22.50% (18)	77.50% (62)	100% (80)
26-30	28.57% (20)	71.43% (50)	100% (70)
31-35	34.15% (14)	65.85% (27)	100% (41)
36-45	33.33% (4)	66.67% (8)	100% (12)
TOTAL	27.59% (56)	72.41% (147)	100% (203)

p=.542

6.9.3 Level of Education and Understanding of Placebo Use

Women with secondary education were more likely to score highly than those with lower levels of education on understanding of placebo use than those with primary education (see Table 6.25). A p-value of .003 was obtained using Pearson's Chi-square test. This finding indicates that women who had gone through secondary school were more likely to grasp the informed consent messages around placebo-use than those with primary education or no schooling.

Table 6.25:
Cross tabulation of Education and Understanding of placebo use

Level of Education	Low Scorers 0-74%	High Scorers 75%+	Total
None	50.00% (8)	50.00% (8)	100% (16)
Standard 1-4	30.77% (8)	69.23% (18)	100% (26)
Standards 5-8	33.68% (32)	66.32% (63)	100% (95)
Forms 1-4	12.12% (8)	87.88% (58)	100% (66)
	27.59% (56)	72.41% (147)	100% (203)

p=0.003

6.9.4 Attitudes Towards Placebo Use

About 72.4percent (n=147) of respondents indicated that they found placebo use to be unacceptable, and 11.8percent (n=24) specifically categorized it as a very bad procedure. About 53.2percent (n=108) of respondents indicated that they would feel cheated or betrayed if they were informed that they were on the placebo arm at the end of the study. All 108 respondents indicated that they would feel that way as they were thinking during the study that they were on the active product arm which they were convinced, would provide some protection against HIV infection. About 15.3percent (n=31) of respondents indicated that they would be upset with the researchers if they were informed that the microbicide was found useful and that they were on the placebo arm However about 81.8percent (n=166) indicated that they would not be upset if the product was found to be ineffective and they were told they were on the placebo. The significant differences in opinion on the two questions was dependent on the results establishing that the test products were effective in preventing HIV infection. During the focus group discussion, participants were asked how they would feel if they were told at the end of the study that they were on placebo. The following statements reflect mixed positions on this question:

> **BTP8:** It would be ok because it was part of the arrangement of this study and we were all contributing to the success of the study.
>
> **BTP10:** *Aah it would be discouraging to some of us because we all felt we were receiving the actual gel.*
>
> **BTP2:** *I would also feel bad because I thought the gel I was receiving was protecting me from HIV.*
>
> **LLP4:** *Ooh, I did not like the part which talked about giving placebos to us. I would have loved it if they were giving gels to all of us so that we would benefit.*
>
> **LLP6:** *It's difficult to accept something which is not what you are looking for.*

During Focus Group discussions, the following question was asked**:** What if you had known in advance that you were receiving a placebo gel, would you have accepted it? Some interesting answers were obtained which confirmed that some participants had negative attitudes towards placebo us in the microbicide trial. The following statements clearly confirmed the fact that some participants had a negative attitudes towards placebo use in the microbicide trial:

> **BT10:** *I would not tell people that some will be receiving placebo gels or nothing for this would discourage some people and it would be as good as not taking part in the study.*
>
> **BTP10:** *It is not good to tell people because if one knows that she is not using the actual gel or that she is not receiving anything, next time, she will not be willing to participate in research.*
>
> **BTP3:** *I would have loved it we knew what we were given whether we received PRO-Gel, Buffer-Gel or Placebo-Gel.*
>
> **LLP4:** *Ooh, I did not like the part which talked about giving placebos to us. I would have loved it if they were giving gels to all of us so that we would benefit.*
>
> **LLP6:** *It's difficult to accept something which is not what you are looking for.*

6.10 FINDINGS ON AWARENESS OF PERSONAL IMPLICATIONS

A specific section on personal implications associated with the test product or participation in the microbicide study was included in the questionnaire (Questions 071-084). It was felt that personal implications and risks are very important and need to be taken into consideration when one is making a decision to participate in research. Most questions in this section required a True/False response, while some required a Yes/No response. About 67 percent (n=136) of the respondents indicated wrongly that it was true that the microbicide being tested would protect them against HIV infection. About 77.3 percent (n=157) indicated wrongly that everyone participating in the trial would receive the microbicide under study. Ninety nine percent (99 percent; n=201) of respondents agreed correctly that microbicide participants should use condoms to protect themselves against HIV infection. About half of participants

(49.8 percent; *n*=101) indicated wrongly that participants in the microbicide study would never have to worry about HIV infection no matter what they do.

About 57.6 percent (*n*=117) indicated wrongly that the microbicide being tested was 100 percent effective in preventing HIV infection. About 47.3 percent (*n*=96) indicated wrongly that it was impossible for one to become infected with HIV while participating in the study. About 98.5 percent (*n*=200) indicated correctly that participants in the microbicide trial still needed to continue taking precautionary measures. It is possible that the fact that all women were being given condoms came to mind, hence the high proportion of women who indicated the need for continuation of precautionary measures. About 36.9 percent (*n*=75) of all respondents scored highly (75 percent +) on the questions on personal implications, 28.6 percent (*n*=58) scored between 50-74 percent, while 34.5 percent (*n*=70) got low scores of below 49 percent. During focus group discussions, it was evident that some participants were conversant with some of the risks associated with the microbicide trial, as well as the implications of their participation:

> **BTP3:** *If one becomes HIV positive because of her careless behaviour, then it is her own fault but if she becomes HIV infected because of using the gels, which I doubt, then it would be unfair – she would have to claim for compensation and ask the researchers to provide treatment for her.*
>
> **BTP7:** *In my view, one can not become infected because of using the gels. If she becomes infected, it would be because of not following the instructions from the nurses or being careless about her life just like the other people who are getting infected with the virus.*

However, some discussants indicated that they believed that they did not view themselves as having higher chances of infection. Some were confident that they were being protected from HIV infection by the gels that had been provided as part of the microbicide study.

LLP1: *I don't think there are any risks in taking part in this study because every time we come for a visit, we are screened and if there is any problem we are advised what to do.*

LLP8: *You know it was difficult to know that one was getting a placebo gel. We all thought we were getting the real gels.*

BTP6: *We were only worried with the placebo gels and those who didn't receive anything.*

BTP2: *One of the benefits is that we might be protected from being infected by the virus. The nurse told us that there is a possibility that one can be prevented from becoming infected.*

BTP3: *The nurse said that the gel could prevent one from becoming infected after testing it first (**P5:** chips in and says; this is what they are trying to find out and it does not mean that the gels work)*

BTP10: *Aah it would be discouraging to some of us because we all felt we were receiving the actual gel.*

BTP2: *I would also feel bad because I thought the gel I was receiving was protecting me from HIV.*

LLP4: *Ooh, I did not like the part which talked about giving placebos to us. I would have loved it if they were giving gels to all of us so that we would benefit.*

LLP6*: It's difficult to accept something which is not what you are looking for.*

6.10.1 Site by Understanding of Implications

The Fischer's exact test was used to establish if there was a statistically significant relationship between trial site and understanding of personal implications. The test yielded a *p*-value of 0.070. This result indicated that there was no statistically significant relationship between trial site and understanding of personal implications. The findings on understanding of implications by site are presented in Table 6.26 below.

Table 6.26:
Cross tabulation of site by understanding of personal implications

Site	Low Scorer 0-74%	High Scorers 75%+	Total
Blantyre HPTN035-630	59.73% (89)	40.27% (60)	100% (149)
Lilongwe HPTN035-631	72.22% (39)	27.78% (15)	100% (54)
Total	63.05% (128)	36.95% (75)	100% (203)

p=0.070

6.10.2 Age by Understanding of Personal Implications

In order to establish if there was a relationship between age and understanding of personal implications, the Pearson's chi-square test was used. The test yielded a p-value of 0.*610,* which showed that there was no statistically significant relationship between age of respondent and understanding of personal implications. The findings are presented in Table 6.27 below.

Table 6.27:
Cross tabulation of age by understanding of personal implications

Age	Low scorers 0-74%	High Scorers 75%+	Total
18-25	57.50% (46)	42.50% (34)	100% (80)
26-30	65.71% (46)	34.29% (24)	100% (70)
31-35	68.29% (28)	31.71% (13)	100% (41)
36-45	66.67% (8)	33.33% (4)	100% (12)
Total	63.05% (128)	36.95% (75)	100% (203)

p=0.610

6.10.3 Education Level and Understanding of Personal Implications

Pearson's chi square test was used to find out if there was a statistically significant relationship between level of education and understanding of personal implications. The test yielded a *p*-value of 0.001. This result indicated that there was a statistically significant relationship between education level and understanding of personal implications. Those who completed standard 5 upwards were more likely to score highly than those with four or fewer years of schooling, and those with no schooling at all (Refer to Table 6.28).

Table 6.28:
Cross-tabulation of education by understanding of personal implications

Level of Education	**Low scorers 0-74%**	**High Scorers 75%+**	**TOTAL**
No education	75.00% (12)	25.00% (4)	100% (16)
Standard 1-4	84.62% (22)	15.38% (4)	100% (26)
Standards 5-8	68.42% (65)	31.58% (30)	100% (95)
Forms 1-4	43.94% (29)	56.06% (37)	100% (66)
	63.05% (128)	36.95% (75)	100% (203)

P=0.001

6.11 COMPOSITE SCORE FOR UNDERSTANDING

Overall, only 38.9 percent (*n*=79) obtained high scores (score of 75 percent and above) on questions relating to the four focus areas (randomisation, double-blinding, placebo use and personal implications). The remaining 61.1 percent scored less than 75 percent. A list of the low scorers is attached as Appendix 26 for the Blantyre site and Appendix 27 for the Lilongwe site. About 85.2 percent (*n*=173) of respondents scored 75percent and above for questions related to randomisation, 72.4percent (*n*=147) for questions relating to placebo use, 31.5percent (*n*=64) for questions related to double-blinding and 36.9percent (*n*=75) for

questions related to personal implications. From these figures it is obvious that participants demonstrated higher levels of understanding of randomisation and placebo use. The majority of respondents demonstrated limited understanding of issues around double-blinding and personal implications of randomisation, double-blinding and placebo use. The low levels of understanding of double blinding and personal implications led to the lower number of those who scored above 75 percent on the overall score. Table 6.29 below shows the distribution of the scores for the four areas under study (randomisation, double-blinding, placebo use and personal implications).

Table 6.29:
Summary of scores and measures of central tendency

Procedure	**Percentage of High Scorers**	**Percentage of Low Scorer**	**Mean score**	**Median**	**St Dev**	**Var**
Randomisation	85.2	14.8	78.0	75	12.78	163.37
Placebo use	72.4	27.6	74.9	78	17.83	318.07
Double-blinding	31.5	68.5	56.11	60	21.28	453.02
Personal implications	36.9	63.1	42.92	44	13.44	180.54
Composite score	38.9	61.1	60.53	60	8.5	72.20

The above table indicates that a majority of respondents appreciated and understood information surrounding randomisation and placebo use. Both mean and median scores for the two concepts were high (mean scores: 78 percent and 74. 9percent and median scores;75 percent and 78 percent respectively) compared to the scores for double blinding and personal implications (56.11 percent and 42.92 percent). The mean scores on randomisation and placebo suggest that overall, participants had adequate to high awareness and understanding of these two concepts. Participants clearly had much poorer awareness and understanding of double-

blinding and the personal implications of all three trial dimensions. It is evident from the above, that the mean composite score (60.53 percent) was affected by the low mean scores on double- blinding and personal implications.

6.11.1 Study Site by Composite score

Participants from the Lilongwe site were more likely to obtain lower scores than participants from the Blantyre site. A *p*-value of .000 was obtained using Fischer's test. This value, which represents a statistically significant relationship, confirms that trial site was an important predictor of composite score (Refer to Table 6.30 below).

Table 6.30:
Cross-tabulation of site by composite scores

Study Site		**Low Scorers 0-74%**	**High Scorers 75%+**	**Total**
Blantyre HPTN035-630	Count	77	72	149
	% within Site code	51.7%	48.3%	100.0%
Lilongwe HPTN035-631	Count	47	7	54
	% within Site code	87.0%	13.0%	100.0%
TOTAL	Count	124	79	203
		61.1%	38.9%	100.0%
				P=0.000

6.11.2 Age and overall score

The Pearson's chi-square test was used to establish if there was a statistically significant relationship between age and overall score. The test yielded a *p*-value of .914. This *p*-value confirms that the relationship between age and overall score was not statistically significant. Table 6.31 presents the findings on age and overall score.

Table 6.31:
Cross-tabulation of age and composite scores

Age	**Low Scorers 0-74%**	**High Scorers 75%+**	**Total**
18-25	58.75% (47)	41.25% (33)	100% (80)
26-30	64.29% (45)	35.71% (25)	100% (70)
31-35	60.98% (25)	39.02% (16)	100% (41)
36-45	58.33% (7)	41.67% (5)	100% (12)
TOTAL	61.08% (124)	38.92% (79)	100% (203)
			*p=0.*914

6.11.3 Education and overall score

The relationship between level of education and overall score was tested using Pearson's chi-square test. The test yielded a *p*-value of 0.000. This value confirmed a statistically significant relationship between level of education and overall score. From the Table 6.32 below, it is evident that those with 5 or more years of schooling were more likely to obtain higher overall scores than those with fewer years of schooling.

Table 6.32:
Cross tabulation of education level and composite score

Education level		Low scorers 0-74%	High Scorers 75%+	Total
No formal education	Count	11	5	16
	% within Q13	68.8%	31.3%	100.0%
Standard 1-4	Count	24	2	26
	% within Q13	92.3%	7.7%	100.0%
Standards 5-8	Count	61	34	95
	% within Q13	64.2%	35.8%	100.0%
Forms 1-4	Count	28	38	66
	% within Q13	42.4%	57.6%	100.0%
TOTAL		124	79	203
		61.1%	38.9%	100.0%

P=.000

6.12 SUMMARY

The assessment of information disclosure indicated that information which is generally considered to be important was provided through either study documents or through discussions with study staff during the informed consent process. It was evident, however, that information covering issues such as the purposes of randomisation, double-blinding and placebo use, and the personal implications of these procedures to the participants, were not included. Participants were clearly advised of the possibility of becoming infected with HIV during the course of the trial but this was not clearly linked to study participation nor the study procedures. An assessment of study participants' understanding revealed that there were some respondents who had low levels of understanding of all concepts under study. Overall, the majority of respondents obtained high scores on questions relating to randomisation and placebo use (85.2 percent and 72.4 percent respectively), while a greater proportion of the same

respondents obtained low scores on questions related to double-blinding and personal implications of the study procedures (68.5 percent and 63,1 percent respectively). The median and mean scores for double blinding and personal implications were found to be lower (mean: 56,11 percent and 42.92 percent respectively; median: 60 percent and 44 percent respectively) than those for randomisation and placebo use (mean:78 percent and 74.9 percent respectively; median:75 percent and 78 percent respectively).

Overall, the majority of respondents (61.1 percent; n=124) obtained low composite scores (scores lower than 75 percent). A list of the low scorers is included in Appendices 26 and 27. A significant proportion of respondents had some misgivings about the usage of randomisation, double blinding and placebo in general, and specifically within the microbicide trial. In the next chapter, these findings are discussed. There were differences in scores that were observed according to study site and education level. Participants from the Blantyre site were more likely to obtain high scores compared to participants from Lilongwe. Participants with secondary education were more likely to obtain higher scores compared to participants with primary education and those with no formal education. There were no significant differences by age.

CHAPTER 7

DISCUSSION OF FINDINGS FROM THE MAIN STUDY PHASE

7.0 INTRODUCTION

In this chapter, the findings that were reported in chapter 6 are discussed. The discussion is an attempt to critically understand the results reported in the previous chapter. The chapter is divided into various sections. In the first section, a summary of the main findings is presented. In the latter sections, the findings are discussed under each of the four main premises underlying the study. The findings are specifically used to answer the research questions that were introduced in the first chapter.

7.1 OVERVIEW OF THE FINDINGS

The study established that during the informed consent process, adequate information on the concepts of randomisation, double-blinding and placebo use. Study documents simply mentioned the use of these procedures in the study but did not explain their justification. This finding supports findings by Bhutta (2004) and Stead *et al*. (2004) who observed that information on justification and personal implications of procedures was often missing from informed consent documents. The informed consent documents addressed some of the personal implications related to participation in the study but did not in any way relate these to the three procedures. Related to the personal implications of the test products, the informed consent documents emphasised the possibility of becoming infected with HIV during the course of participation in the study. The finding also suggests that staff did not adequately address the concepts of randomisation, double-blinding and placebo, or their personal implications. All study documents relating to informed consent did not specifically require

them to provide information on reasons for adoption of the procedures as well as their personal implications.

The findings of the study also suggest that the majority of participants (61.1 percent) did not have adequate understanding of the concepts of randomisation, double-blinding and placebo use, which supports evidence from previous studies (Agre & Rapkin, 2003; Featherstone & Donovan, 1998; Kerr *et al*., 2006; Pace *et al*., 2005; Pucci *et al*., 1999; Stead *et al*., 2004; Yuval *et al*., 2000). Generally, the majority of participants in this study were found to have negative attitudes towards randomisation, double-blinding and placebo use. This finding was consistent with findings by Khalil *et al*. (2007). The findings suggest the important role that trust plays in the recruitment of trial participants and supports findings by Geissler, Kelley, Imoukhuede and Pool (2008). For the majority of participants, understanding was lacking in terms of the justification of the study procedures as well as the personal implications of those procedures. Based on these findings, it was evident that an intervention was necessary to try and improve the levels of understanding among those individuals identified as having obtained low scores.

7.1.1 Premise 1 – Information in the Study Documents

In this section, the findings relating to Premise 1 are discussed. Premise 1 asserts that the quality of information that is disclosed through the study informed consent documents determines whether participants understand the clinical trial procedures of randomisation, double-blinding and placebo use as well as their personal implications to the participants. The findings relating to this premise relate to the following research sub-question:

> How do trial related documents explain the concepts of randomisation, double-blinding and placebo use?

The following findings emerged relating to informed consent documents that were used in the microbicide trial:

- The informed consent form for enrolment that was used in the study provided information about randomisation, double-blinding and placebo use, but did not explain the purpose and personal implications of randomisation, double -blinding and placebo–use. The process of randomisation itself was well explained in terms of how it would be achieved.
- Regarding placebo use, the informed consent document mentioned that a product which looks like the test products would be used in the study. The document mentioned the possibility of becoming infected during the trial because the effectiveness of the products being tested was unknown. The informed consent documents hence emphasised the need for the microbicide trial participants to take measures aimed at ensuring that they protected themselves from HIV infection at all times.
- The informed consent booklet which served as complementary informed consent material mentioned the use of randomisation, double-blinding and placebo use, but did not adequately explain the purpose and personal implications of randomisation, double-blinding and placebo use. The document mentioned the possibility of becoming infected during the trial due to the fact that the effectiveness of the products being tested was unknown.
- The study protocol and informed consent Standard Operating Procedure (SOP) did not require study staff to give special attention to the justification and personal implications of randomisation, double-blinding and placebo use. The protocol and SOP required staff to emphasise the possibility of becoming infected during the study as a way of discouraging disinhibition of safe sex behaviours.

- The informed consent documents emphasised the possibility of becoming infected during the study and the need for individuals to take protective measures such as use of condoms.

The above findings confirm all of the three assumptions underlying this premise, namely that:

- Informed consent forms did not explain the purpose and personal implications of randomisation, double-blinding and placebo use.
- Complementary informed consent materials did not adequately explain the purpose and personal implications of randomisation, double-blinding and placebo use.
- Study documents did not require study staff to give special attention to the justification and personal implications of randomisation, double-blinding and placebo use.

The above findings confirm the work of Siminoff (2003) who found that informed consent documents mainly seek to explain study procedures without explaining their justification as well as personal implications. The findings on the information disclosed by study documents relate to the important aspect of information disclosure in the conceptual framework adopted for this study. The findings are not surprising, considering the elements of informed consent that are emphasised in literature on informed consent. The eight elements are also emphasised in the US Code of Federal Regulations 45 CFR 46 relating to informed consent (Dawson & Kass, 2005; Kripalani *et al*., 2008). The findings from this study confirm that viewing informed consent as a process which covers the eight elements is a limited way of looking at informed consent which seeks to fulfill US legal requirements. Informed consent which is truly based on moral grounds needs to go beyond the eight elements. The focus should be on ensuring that the individual is fully aware that they are participating in a clinical trial, as well as the personal implications associated with participation in that study, including implications associated with

the study procedures adopted for that particular study. It is assumed that it is enough just to ensure that the individuals are aware that the procedures are part of the study. This assumption goes against the foundations of informed consent – decisions based on adequate information. This assumption is based on paternalistic grounds as researchers make decisions regarding what they think an ordinary individual might want to know about. The assumption that those who need more information will ask questions might not be useful in some settings where people join research for various reasons, including trust of the researchers, access to good quality health care facilities and others (Pace *et al*., 2000; Yuval *et al*., 2000).

7.1.2 Premise 2 – The Disclosure of Information by Trial Staff

This premise relates to the process of disclosure of information and also covers a very important part of the informing process that is covered in the conceptual framework which was adopted for the present study. The quality of information that is disclosed by research staff as well as the way it is disclosed, determine whether participants understand the clinical trial procedures of randomisation, double-blinding and placebo use, as well as their implications to the participants. In order to examine this premise which was based on the review of literature in Chapter 2, the following assumptions were made:

- Trial staff do not spend adequate time explaining to participants about the purpose and personal implications of randomisation, double-blinding and placebo use
- There is a conflict between the messages that reach the participants from the study staff and study documents versus the contextual message that comes from the activities and the environment at the research site. When research participants look around at the activities involved in the trial and consider the attention they are receiving, and the medical trappings of the researchers, it is easy for them to infer that they are important and that some kind of medical care is being extended to them.

The above premise and assumptions were related to the following research sub-question:

How do study staff explain the concepts of randomisation, double-blinding and placebo use to prospective trial participants?

Interviews with staff and some respondents yielded the following findings relating to the role of research staff in the informing process:

- Study staff did mention the use of randomisation, double-blinding and placebo in the study but did not explain their justification or personal implications.
- Study staff emphasised and explained the possibility of becoming infected with HIV during participation as a result of the fact that the effectiveness of the test products was unknown.
- Staff were constantly engaged in counselling participants so that they would not engage in risky behaviours. This was part of the study procedures.
- Staff were very conversant with the justification of randomisation, double-blinding and placebo use and they clearly explained these to the researcher. It was evident that they could explain them to the trial participants if asked to do so by the participants.
- While staff demonstrated knowledge of the procedures, they had difficulty explaining the personal implications of the procedures to the researcher..
- Staff reported time constraints as they were supposed to assist in meeting site accrual targets. This meant that they could not spend as much time as they would have wanted to spend in the disclosure of information.

The study found that staff were adequately trained and experienced in research and informed consent issues. Staff were also complying with study documents such as the informed consent SOPs, informed consent form and informed consent booklet regarding the information they

were providing to research participants. In terms of the environment in which the information was disclosed, the participants gave very positive comments regarding how the staff treated them and also how they provided the information. This contributed to the very good relations that were observed between staff and research participants during the data collection phase of this study. Staff played an important role in assessing comprehension by administering the comprehension checklists and ensuring that they addressed areas in which the participants had given wrong answers. Staff also reported that it was difficult to explain the concepts of randomisation, double-blinding and placebo use to the participants due to their relatively low literacy levels.

During discussions with the study staff responsible for obtaining consent, when asked to explain the procedures to the researcher, some staff members found it difficult to explain the personal implications. Difficulties in explaining study procedures have been identified in previous studies (Featherstone & Donovan, 1998; Kerr *et al*., 2006; Pace *et al*., 2005; Pucci *et al*., 1999; Stead *et al.*, 2004; Yuval *et al*., 2000). As a result of these difficulties, it is generally accepted that lay people who normally participate in research would not understand these procedures.

The study found that staff who engaged in obtaining informed consent were also the ones who were engaged in providing counselling and assessment of comprehension. The same staff members would also be working under pressure in this international collaborative study as they were expected to assist in meeting the site accrual targets. In an ideal situation, the process of informed consent needs to be done by an individual who is mainly interested in the rights and welfare of research participants and is independent of accrual target pressures. The findings concerning the dual-role of staff in the informed consent process suggest the need to re-examine the roles of project staff so that conflicting roles are avoided. This however requires

due caution as there is need to allow good relations that are key to these trials. All these findings confirm the important role that principal investigators and study protocols play in determining the information that is disclosed and how research staff disclose the information.

7.1.3 Premise 3 – Participants' Understanding

Premise number 3 was related to an important part of the conceptual framework which relates to the understanding of the information provided during the informed consent process. This information is supposed to be used in the making of an informed decision to participate. The third premise stated that some trial participants have low levels of understanding of randomisation, double-blinding, placebo use and the personal implications of these procedures. Based on the review of literature, the following assumptions were made:

- Some research participants agree to participate in double blinded, randomised placebo controlled clinical trials without understanding the concepts of randomisation, double-blinding, and the use of placebos in research.
- Some research participants do not understand the implications for themselves as individuals.
- Some research participants have a negative attitude towards randomisation, double-blinding and placebo use.

In order to examine this premise, the following research sub-questions were put forward:

- Are participants aware of the purpose of the study?
- Are participants aware that they are participating in a trial to test a product whose efficacy is not known?
- Are participants aware that they are still exposed to HIV infection even as they are using the product they have been issued with?

- Are trial participants aware that randomisation, double-blinding and placebo use are part of the study?
- Are trial participants aware of the reasons why randomisation, double-blinding and placebos are used in the study?
- Are participants aware of the various study arms in the microbicide study?
- Are participants aware that they have been randomised into different groups?
- Are participants aware that they may be receiving a placebo?
- Are participants aware that neither themselves nor the trial nurses and doctors (i.e., research personnel) are aware of the arms they are in?
- Are trial participants aware of the personal implications of randomisation, double-blinding and placebo use?
- Are participants aware of the implications of their participation, regarding protection from infection by the product under test?
- What is the opinion of the trial participants regarding randomisation, double-blinding and placebo use?
- In making the decision to join the microbicide study, did trial participants consider the fact that the study involves randomisation, double-blinding and placebo use?

From the above sub-questions relating to this premise, it becomes obvious that this was the main premise for the study. From the findings provided in Chapter 5, it was evident that the majority of the participants in this study were aware of the purpose of the study (88.7 percent). However, some were not aware that they were participating in a study whose main aim was to test products whose efficacy was not known (11.30 percent). The majority of participants (87.2%: n=177) were aware that they were still exposed to the risk of HIV infection while they were using the products they had been issued with. It was interesting to note, however, that

some women (10.8 percent) were of the opinion that they were participating in a programme aimed at protecting them from HIV infection.

The relationship between education and understanding of the 3 procedures under study was found to be statistically significant (p=0.000). Women with secondary education were significantly more likely to understand the three concepts than those with primary education or no formal education. This finding confirms the finding by Kilmarx *et al.* (2001) who also found level of education to have an impact on understanding. Nyika, Wassenaar and Mamotte (2009) also found similar findings in a study they conducted among women in Zimbabwe. Interestingly, the majority of participants reported that they found the information disclosed to be adequate, and yet the assessments that were conducted as part of this study identified low levels of understanding among some respondents. Lynoë *et al.* (1991) report similar findings. These findings clearly confirm that perceived understanding is not a clear indication of actual understanding. Researchers need to assess real understanding by asking questions that seek to find out what the respondents really understand and not what they perceive to understand (Hochhauser, 2008).

7.2 UNDERSTANDING OF RANDOMISATION

Almost all participants (99 percent) were aware that they were being randomised to various arms. The procedures that were used for randomizing were clear as the nurses just assigned an envelope to the women following a sequential order and the number was determined by the assignment which was stated on a small paper which was inside the envelope. A large proportion of the trial participants (53.7 percent) were not aware, however, of the justification for randomisation nor the personal implications. This finding is consistent with findings by Featherstone and Donovan (1998) and Stead *et al*. (2004) who also found that the majority of

their respondents were aware that they were being randomised, yet did not know the justification for randomisation. The main reason could have been the fact that the reasons were not explained to them and the women did not ask any questions as they just trusted the staff members. In the Malawian context, people are generally familiar with the lottery scheme which is associated with luck and winning prizes that are useful. The lottery is not associated with processes that lead to a negative outcome. In the lottery, either one wins or gets nothing. It appears that trust of healthcare professionals and placebo use in low resource settings, are in some way irreconcilable. One may conclude that it maybe difficult to for one to appreciate that the person that they trust to assist them may give them some inert or fake products. This may be equated to a mother who gives a stone to a child who is asking for food.

The majority of research participants (99 percent) were aware that there were various arms and yet some of them (46.3 percent) failed to list all the study arms correctly. The idea of having study arms could have been made easier to understand by the mere fact that there was one arm that was only given condoms (without the gels). The women knew some of their peers or acquaintances who were in this arm. Such knowledge would keep them reminded about the different study arms.

While the majority of women were aware that randomisation was part of the trial, they were not aware of the justification for randomisation in the study. The majority of women were also not aware of the personal implications of randomisation. This could have resulted from the fact that the informed consent documents as well as the research staff involved in informed consent did not provide that information during the informed consent process. It would be unfair to expect the participants to deduce the justification and personal implications by themselves if these had not been provided through the informed consent documents and processes. Dunn, Palmer and

Keehan (2006) point out that failure to understand justification for the procedure leads to failure to understand the personal implications of the procedures.

The majority of participants were found to have a negative attitude towards randomisation as they did not find it meaningful to them. This finding is consistent with the finding from a qualitative study conducted by Robinson *et al*. (2004). The participants expected the staff to be taking care of them and advancing programmes that are aimed at promoting their health. Randomisation would not make much sense in a setting which is full of such expectations. The relationship of trust between the research staff and the participants could also have assisted in blurring the realities of the trial. A study by Khalil *et al*. (2007) also identified negative attitude towards randomisation.

7.3 UNDERSTANDING OF DOUBLE-BLINDING

A significant proportion of the women (33.5 percent) were not aware that double-blinding was a part of the study. About 57.6 percent of respondents were not aware of the justification for double-blinding. A large proportion of respondents (78.8 percent) were not aware of the personal implications of double-blinding. These low levels may have resulted from the fact that the justifications and the personal implications were not included during the process of disclosure of information. A majority of participants (78.1 percent) had a negative attitude towards double-blinding and indicated that they were of the opinion that doctors should truthfully inform trial participants about the arms they were on.

The low levels of understanding of double-blinding may be a result of the fact that it is not a part of the routine provision of care. It would thus be difficult for the women to fully appreciate the implications of double blinding on themselves as individuals (Rothman & Michels, 1994).

These findings confirm reports by Robinson *et al*. (2004) and Khalil *et al*. (2007) who found very low levels of understanding and negative attitudes towards double-blinding.

7.4 UNDERSTANDING OF PLACEBO USE

The study found that a significant majority of the women (84.7 percent) were aware of the fact that a placebo was being used as part of the study. Surprisingly, while a significant majority were aware of the use of a placebo in the study, 50.7 percent and 49.8 percent respectively indicated that they were not aware of the justification for this, as well as the personal implications. This could have been a result of the fact that the justification as well as the personal implications were not covered during the process of disclosing information nor in the informed consent documents. The study identified that the majority of respondents had negative attitudes towards placebo use.

Placebo use is incongruent with the therapeutic relationship as it implies that medical personnel are deliberately taking steps to give a client or patient something which has no active ingredients (Rothman & Michels, 1994). Medicines have active ingredients and yet in this case the medical staff gave some individuals something which did not contain the active ingredients. The findings on understanding of placebo use are consistent with reports by Quieroz da Fonseca and Lie (1995, 1999); Kilmarx *et al*. (2001) and Robinson *et al*. (2004).

7.5 AWARENESS OF PERSONAL IMPLICATIONS

It was obvious from the study findings that the majority of participants were also not aware of the personal implications associated with participation (61.1 percent). Some women even mentioned during the FGDs that the nurses had informed them that the products they had been given would protect them against HIV infection, while others just appeared to believe that the

trial products would protect them from HIV infection. During the first phase, the majority of women indicated that they were hoping that they were on the active product arm. This is a sign of therapeutic misconception as a person who had joined the study based on adequate information would respond that they could be on any arm if they fully understood the concept of randomisation. A person who is fully aware of the personal implications would not have the idea that the active product arm is protective as they would know that the product is being tested. It is possible that such a person may hope, though, that the active product will work as presumably do the researchers who invest in the trial. A person who is fully aware may join the trial so that they can contribute to the answering of the research question on the effectiveness of the test product or to gain other benefits that may be associated with the trial. Findings on awareness of personal implications were consistent with findings by Wazaify *et al.* (2008) who found some evidence of therapeutic misconception which was associated with failure to fully appreciate that one was participating in a study to test a product whose efficacy was unknown. The findings are also consistent with findings by Manafa *et al*. (2007), Hill *et al*. (2008) and Ramjee *et al*. (2000) who found that some of their respondents thought that they were receiving treatment, yet they were participating in a clinical trial. The findings also support assertions by Braham (1988) and Kilmarx *et al*. (2001) that failure to understand the scientific justification leads participants not to appreciate the risks involved in the study.

7.6 ATTITUDES TOWARDS THE THREE PROCEDURES

Overall, the findings from this study confirm the findings by various authors that found some evidence of negative attitudes towards the trial procedures under study (Ellis & Butow, 1998; Ellis *et al*., 1999; Glogowska *et al*., 2001; Heitenan *et al*, 2000; Llewellyn-Thomas *et al*., 1991; McQuellon *et al*.,1995; Slevin *et al*., 1995; Snowdon, Garcia & Elborne, 1998). The findings suggest that the majority of the respondents had negative attitudes towards

randomisation (72.9 percent) double blinding (57.1 percent) and placebo use (72.4 percent),. It is possible that the respondents found all these procedures to be unacceptable as they went against the expectation of care. Previous studies suggest that participants find it unacceptable for a doctor to suggest letting chance decide when they were uncertain of the best treatment (Ellis & Butow 1998; Robinson et al., 2005). In reality, when individuals come to the hospital for care, they expect the doctors to provide solutions which are tailored for them (Robinson *et al*., 2005).

7.7 MAKING DECISIONS REGARDING ENROLMENT

From the responses by the respondents, it was obvious that the majority of participants did not consider the procedures of randomisation, double-blinding and placebo use in the making of their decisions. For the majority, their decisions to join the microbicide study appeared to be based more on knowing their HIV status (80.8 percent) than on contributing to knowledge (16.7 percent). Other participants joined the microbicide study so they could enjoy the various benefits associated with the study, including good quality care (2.5 percent). This supports findings by Tindana *et al,* (2006), Oduro *et al*. (2008) and Tomamichel (2000), who found that a significant proportion of their respondents were enroling in research as a way of accessing good quality care.

7.8 SUMMARY

In summary, the findings from the first phase of the study have revealed that some participants have limited understanding of randomisation, double-blinding, and placebo use, as well as their personal implications. The findings suggest that the justifications for these procedures as well as their personal implications are not covered in a clear manner during the informed consent process. The findings from this study have confirmed some of the premises of the study. The findings on low levels of understanding among a significant proportion of the respondents

illustrated the need for the development and implementation of an intervention aimed at improving understanding. The next chapter describes the design and implementation of an intervention and the findings thereof.

CHAPTER 8

DESIGN AND DEVELOPMENT OF A PILOT INTERVENTION

8.0 INTRODUCTION

In this chapter, the implementation of the intervention which was developed to improve understanding is described. The intervention reported in this chapter was developed in response to the findings from the earlier phase of the study which had identified some respondents who were displaying signs of limited understanding. The intervention had been anticipated even before initiating the study due to the various studies conducted elsewhere which found low levels of understanding among study participants (Featherstone & Donovan, 1998; Kerr *et al*., 2006; Pace *et al*., 2005; Pucci *et al*., 1999; Stead *et al*., 2004; Yuval *et al*., 2000). It would have been unethical to ignore a problem after identifying it empirically. The researcher was also convinced by available literature suggesting the usefulness of well thought out interventions (Barnett *et al*., 2005 Butow *et al*., 2007; Eder *et al*., 2007; Kass *et al*., 2009; Kripalani *et al*., 2008). Before the initiation of the current study, the principal investigators at the two sites had also indicated that there were some efforts within the HPTN to identify some ways of improving understanding.

The chapter is divided into various sections covering different aspects of the intervention. In the first section, justification for the intervention is provided, together with a brief description of the important aspects of the intervention itself. A detailed description of the intervention is then provided, followed by a detailed description of how the intervention was implemented. The final section presents findings on the implementation and usefulness of the intervention. The intervention which was developed was based on Premise 4 of the thesis. Premise number 4 related to the development of an intervention that could be used in improving understanding.

According to Premise 4, if properly explained in lay terms, trial participants can improve their understanding of the nature, purpose and personal implications of trial procedures under study. Based on the literature review, two assumptions were developed as a way of addressing this premise:

- Some of the interventions that are developed to improve understanding are poorly thought out and are merely a repetition of the information from informed consent documents using different media (Flory & Emanuel, 2004).
- Trial participants can understand trial procedures and their implications if the explanations they are given about the procedures include details on how the procedure will be implemented, the justification for, and the personal implications of those procedures.

The following sub-question was specifically put forward in order to examine this premise:

- Can an intervention improve trial participants' understanding of research, randomisation, double blinding and placebo use?

8.1 ASSUMPTIONS IN SOME EXISTING INTERVENTIONS

The researcher reviewed various interventions aimed at improving understanding, including those reported in the literature review section of this thesis (for example Agre & Rapkin, 2003; Coletti *et al*., 2003; Davis *et al*., 1998; Dunn *et al*., 2002; Ellis, Butow & Tattersall, 2002; Fureman *et al*., 1997; Jimison *et al*., 1998; Ryan *et al*., 2008; Simes *et al*., 1986; Wray *et al*., 2005). The review identified several interventions found to be ineffective in improving understanding (Agre *et al*., 2003; Agre & Rapkin, 2003; Davis *et al*., 1998; Ellis Butow & Tattersall, 2002; Kripalani *et al*., 2008; Ryan *et al*., 2008; Wray *et al*., 2005). The review of previous interventions revealed the following weaknesses in some of the interventions:

- Some interventions assume people know what research is (for example Agre & Rapkin, 2003).
- Some interventions assume that people are familiar with clinical trial procedures (for example Coletti *et al*., 2003)
- Some interventions do not assist in making people aware of the trial procedures and their purposes (for example Wray *et al*., 2005).
- Some interventions reviewed do not deal at great depth with the personal implications of research participation and the trial procedures (for example Ryan *et al*., 2008)

8.2 THE INTERVENTION DEVELOPED FOR THE CURRENT STUDY

The intervention designed as part of this study was based on the nature of data that was yielded by the first data collection phase of the study (see Chapter 6 and 7 for findings from first phase). The following applies to the current intervention:

- It was aimed at improving understanding of research using everyday language.
- It sought to empower individuals to make informed decisions about participating in research.
- It sought to make people aware that research may fail.
- It used everyday examples in explaining clinical trial procedures and their implications. African cultures are generally well known for story telling as a way of educating individuals (Abrahams, 1983; Gecau, 1970). Stories with some meaning are often told as a way of ensuring that individuals understand a particular issue.
- It did not make any assumptions about pre-existing knowledge.
- It was based on the review of existing interventions and studies aimed at testing some related interventions. (see for example Agre & Rapkin, 2003; Coletti et al., 2003; Davis

et al., 1998; Dunn et al., 2002; Ellis, Butow and Tattersall, 2002; Fureman et al.,1997; Jimison et al., 1998; Ryan et al., 2008; Simes et al., 1986; Wray et al., 2005).

The intervention, which was aimed at improving understanding, was mainly based on a psychosocial schema, which views informed consent as being made up of three sequential behavioural steps: (a) reception, (b) comprehension and (c) utilisation of the comprehended information in reaching a decision whether or not to participate in a study (Faden & Beauchamp, 1980). The schema postulates that for consent to be informed, a prospective trial participant has to go through the three steps (Faden & Beauchamp, 1980). The intervention also borrowed from the Meerwein model of information processing. Meerwein's model defines three main dimensions of the informing process, namely (a) the information itself, (b) the emotional dimension concerned with rapport between the researcher and the participant, and (c) the interactional dimension which is concerned with the capacity and willingness of the research staff to perceive and discuss emotional needs, concerns and complaints of trial participants and to deal with these (Tomamichel *et al.*,1995). The model was described in greater detail in Chapter 3, which described the conceptual framework adopted for the present study. The main components of the intervention consisted of a PowerPoint presentation (see Appendices 16 and 17 for the English and ChiChewa versions) which included a mix of the following approaches:

- A hierarchic and modular approach to providing information (Jimison *et al.*, 1998). This entails providing information in some manageable chunks. The information becomes complex as one proceeds.
- Use of vignettes in explaining the trial concepts and research (Verheggen and Van Wijmen, 1996).

- Colourful pictures were included in the presentation to supplement written information and the discussions about microbicides and the study (Colletti *et al*., 2003; Fureman *et al,* 1997).
- Inclusion of purpose, justification and implications of research participation and trial procedures (Kerr *et al*., 2004).

The intervention also relied on the following;

- Asking patients to repeat in their own words or explain to others (Verheggen & Van Wijmen, 1996).
- Use of other appropriate ways of ensuring personal understanding, including inviting research participants to discuss with other participants (Lindegger *et al*., 2000, 2006).
- Use of a neutral team of disclosure staff distinct from the research team in group and individual discussions with trial participants. These were persons who had been trained to teach potential participants about the key methodologic aspects of research and who had experience in research (Hellman & Hellman, 1991).

8.3 DESCRIPTION OF THE INTERVENTION

In this section, a summary of the intervention that was designed and implemented is provided. The PowerPoint slides which were used in implementing the intervention are included in Appendices 16 and 17 followed by a narrative which was provided to the individual who gave the PowerPoint presentation. The intervention was based on a story about a company which intended to test a new fertilizer. Using the fertilizer story, the concepts of research, randomisation double blinding and placebo use are illustrated including the reasons why research is necessary and why these procedures were employed as well as the personal implications of these procedures to the farmers. Whilst the aim of the intervention was to

improve understanding, the intervention covered the application of the procedures as well as the interpretation of the findings from the study. This was aimed at ensuring that the intervention promoted a fuller understanding of research and trial procedures. It is important to emphasise that the intervention was not aimed at improving informed consent in the overall sense, but was aimed at improving understanding of the three concepts under study. After narrating the story, the presenter then related the potato research narrative and the procedures of the clinical trial, including the trial concepts under study (as well as their justification and personal implications).

8.4 SUMMARY

This chapter has presented a description of the intervention that was developed as part of the current study. The researcher reasoned that it would be unethical not to take action after identifying participants with low levels of understanding. The development of the intervention was guided by review of literature on the testing of related interventions. The intervention was based on a story which was narrated to the participants. The story covered all the concepts under study including their justifications and personal implications using simple everyday language and examples that are not alien to Malawian Communities. The next chapter describes in detail the implementation of the intervention, including findings on the impact of the intervention on understanding.

CHAPTER 9

FINDINGS ON THE IMPLEMENTATION AND EFFECTIVENESS OF THE PILOT INTERVENTION

9.0 INTRODUCTION

This chapter presents findings on the implementation and usefulness of the pilot intervention aimed at improving understanding of randomisation, double blinding and placebo use and their personal implications. The first section presents information on the implementation of the intervention. The second section describes the demographic characteristics of the respondents who participated in the intervention phase. This is followed by a third section in which findings on the effectiveness of the intervention are presented. The chapter ends with a summary on the findings. The findings which are described in this chapter are discussed in more detail in Chapter 10.

9.1 IMPLEMENTATION OF THE INTERVENTION

The intervention was implemented on 20th August 2009 at the Blantyre site only due to logistical and budgetary reasons. All follow-up activities of the HPTN035 had already come to an end and participants had been informed about the findings from the microbicide study in March 2009. This therefore meant that the intervention did not in any way impact on the microbicide study since the microbicide study activities had already come to an end. The microbicide study had established that the two products which were being tested, namely Buffergel and Pro2000, were not effective in protecting women against HIV infection (MTN, 2009). The intervention was approved by the principal investigator after being briefed about the findings from the previous phase. The principal investigator then informed the study team members about the impending interventions and requested them to support the intervention by providing space and logistical support.

A list of the low scorers from the Blantyre site was provided to the microbicide study staff so that they could assist with the follow-up of the women who had participated in the current study (see Appendices 26 and 27 for a list of the identifying codes for low scorers from the Blantyre and Lilongwe sites respectively). From a list of 77 participants who obtained low scores at the Blantyre site, current contact details could only be found for 63 participants who were still based in Blantyre. It was noted that 56 of the 63 participants who were identified were based in Manyowe and Manase areas. A decision was therefore made to follow-up only the 56 participants from Manyowe and Manase areas. Staff who were employed as field tracers at the microbicide trial site were requested to visit the homes of all 56 participants. It is important to note that after the initial interviews the women had given permission to be recontacted for the purpose of continuing with the current study. The researcher in the current study offered transport as well as other logistical support to the field tracers. The field tracers found 38 women at their homes and invited them to visit the study site for the continuation of the current study. For the remaining 18 who were not available, the field tracers left messages inviting them to visit the study site at 8:00am on Thursday August 20, 2009.

On Thursday 20th August 2009, by 8:30am there were 39 women present and a decision was made to proceed with the study activities. All 39 women had scored less than 75 percent during the initial assessment. Informed consent was sought from all 39 women after disclosure of information by a study team member. The information which was provided included reminding them about the microbicide study, the first phase of the current study, and then requesting their consent for the intervention phase of the study. Three women indicated that they could not spend more than one hour at the site as they were supposed to collect their children from school. The three were accordingly excluded from the study activities. The remaining 36 women indicated verbally that they were consenting to continue with their participation in the

current study and were prepared to go through all the remaining activities of the current study (Note that at this time, the microbicide study had already been terminated). The 36 women were accordingly randomised into two groups using small papers numbered from 1-36. All those who picked odd numbers were assigned to the intervention arm and those who picked even numbers were assigned to the non-intervention arm which was going to receive the microbicide trial informed consent information in addition to a session on cervical cancer prevention.

One trial nurse responsible for obtaining consent, was requested to present standard informed consent information on the microbicide study to the 18 women and to allow them to ask questions. The cervical cancer session was added to the non-intervention session for two reasons; the non-intervention session was going to be shorter than the intervention one since it took 30-40 minutes on average for the trial nurses to go through the information with individual potential participants. The addition of the cervical cancer session would also ensure that the women would get an additional benefit in the form of education since it was hoped that the women in the intervention arm would benefit through the intervention. Three women arrived more than 25 minutes after the two sessions had already begun. The three were not invited to join as they would have affected the flow of activities. They were, however, offered some refreshments and reimbursement for transport, and were given the opportunity to meet the microbicide study nurses for any issues that they might want to discuss with them.

The two sessions began at the same time and ended almost at the same time. The women were then invited for individual structured interviews on a one to one basis using the order of the numbers they had picked. The two groups were kept in separate rooms and there was one study team member who coordinated the movement to the separate rooms that had been assigned for the interviews. Each interview took on average ten minutes. All participants were

reimbursed for their transport and all those who were interviewed during or after lunch hour, were provided with refreshments.

The following measures were taken to remove bias:

- Interviewers were blinded regarding the group from which the individuals they were interviewing had participated in. The 36 women were randomly assigned to the two interviewers.
- Scoring was done by a different individual before unblinding of groups.
- The individuals involved in presenting the intervention and also the placebo programme did not participate in the assessment or in the scoring.
- The intervention and second assessment were done about eight months after the main study and first assessment. This could have assisted in eliminating the effects of history and maturation of instrument.

9.2 DEMOGRAPHIC CHARACTERISTICS OF RESPONDENTS WHO PARTICIPATED IN THE PILOT INTERVENTION.

There were 18 women in both the intervention and non intervention arms of the intervention study who had been randomly assigned. The following tables reflect the demographic characteristics of the total sample. There were 11 participants in each of the lower age categories and four participants in the upper age category (36-40 years). This distribution was roughly reflective of the distribution in the total study sample. The 36 women were also evenly distributed across the age strata. Table 9.1 shows the age distribution of the intervention sample.

Table 9.1:
Distribution of intervention phase participants by age and by group

Age	Frequency	Percent	Non Intervention	Intervention	Cumulative Percent
20-25	11	30.6	33.3% (6)	27.8% (5)	30.6
26-30	11	30.6	33.3% (6)	27.8% (5)	61.1
31-35	11	30.6	27.8% (5)	33.3% (6)	91.7
36-40	3	8.3	5.6% (1)	11.1% (2)	100.0
Total	36	100.0	100% (18)	100% (18)	

The majority of women (24) had 5-8 years of schooling, followed by those who had 1-4 years of secondary education (10). The distribution of the women by years of schooling was evenly balanced across the two groups and consistent with the main study, showing the effectiveness of the random sampling method that was adopted. Table 9.2 shows the distribution of the intervention sample by years of schooling across the two groups.

Table 9.2:
Distribution of intervention phase participants by Educational level and by group

Education	Freq	Percent	Non Intervention	Intervention	Cumulative Percent
Standard 1-4	2	5.6	5.6% (1)	5.6% (1)	5.6
Standard 5-8	24	66.7	72.2 (13)	61.1% (11)	72.2
Form 1-4	10	27.8	22.2% (4)	33.3% (6)	100.0
Total	36	100.0	100% (18)	100% 18	

Twenty three (23) of the women who participated in the intervention phase were on the two active product arms of the study, while 13 were on the placebo arm (See Table 9.3). By the time of implementing the intervention, women had already been informed about the

microbicide study arm they were in during the time they were informed about the study findings. This distribution shows that the random sampling strategy that was used in selecting participants for the intervention phase led to a balanced sample. The intervention sample included at least one third from each of the three gel arms of the microbicide study.

Table 9.3:
Distribution of intervention participants by study arms by group

Microbicide study arm	**Freq**	**Percent**	**Non Inter vention**	**Inter vention**	**Cumulative Percent**
Active product arms (Buffergel and Pro2000)	23	63.9	77.8% (14)	50% (9)	63.9
Placebo	13	36.1	22.2% (4)	50% (9)	100.0
Total	36	100.0	100% (18)	100% (8)	

Eight (8) of the 13 who were on placebo indicated that they felt cheated or betrayed when they were informed about the arm they were on during the study. This finding presented some evidence of false confidence among the participants. It also showed that participants did not appreciate the real possibility of being on placebo as well as the unproven nature of the test product. All eight (8) women reported that they felt betrayed as they thought that they were using the active product which would have protected them (Refer to Table 9.4).

Table 9.4:
How women on placebo felt when revealed by Group

How women felt after unblinding	Freq	Percent	Non Intervention	Intervention	Cumulative Percent
Cheated/betrayed	8	22.2	0	44.4% (8)	22.2
Indifferent/nothing	7	19.4	27.8% (5)	11.1% (2)	41.7
No problem because it was part of study	14	38.9	38.9% (7)	38.9% (7)	80.6
Other	7	19.4	33.3% (6)	5.6% (1)	100.0
Total	36	100.0	100%(18)	100% (18)	

9.3 FINDINGS ON THE EFFECTIVENESS OF THE INTERVENTION

In order to assess the effectiveness of the intervention, the average scores for each concept were compared for the two groups before and after the intervention. From the findings in Table 9.5 below, it is evident that both mean and median went up for average scores for all 36 women on understanding of randomisation, double-blinding and placebo use after the intervention. Table 9.7 shows the increases for the two groups before and after the intervention. There were increases in both the intervention and non intervention arm on understanding of randomisation, placebo use and double blinding. The non intervention arm experienced a decline in score on understanding of double blinding. The fact that both groups experienced increases in average scores, suggests the work of some confounding variables. The termination of the microbicide trial as well as dissemination of the microbicide study results could have served as confounders. The two could have reinforced the fact that the microbicide trial was indeed a study and not a programme. Study nurses reported that upon termination of the microbicide study, they invited the trial participants to bring back to the site any remaining gels, only to find that some of them had shared the gels with their colleagues. The increases for the non intervention arm were smaller than the increases experienced by the intervention arm. This

finding provides some evidence for the short-term usefulness of the intervention in improving understanding. The means and median values were only calculated for the 36 women who participated in the intervention phase.

Table 9.5:
Measures of central tendency before and after intervention for the two arms

Concept	Mean Before intervention	Mean intervention	Comment on change	Median before intervention	Median after intervention	Comment on change
Randomisation	78	78.42	Increase	75	90.00	Increase
Double-blinding	74.86	64.83	Decrease	78.00	67.00	Decrease
Placebo	56.11	78.67	Increase	60.00	83.00	Increase
Implications	42.92	58.17	Increase	44.00	55	Increase
Composite score	60.53	70.19	Increase	60.00	67.00	Increase

Table 9.6 shows that, before the intervention phase, all 36 women were in the low scoring category. Interestingly, after the intervention, 13 women moved to the high scoring category.

Table 9.6:
Distribution of Composite scores before and after intervention

Scores	Freq before intervention	Percent	Frequency after intervention	Percent
Low scores below 50%	3	8.3	5	13.9
Low scores 50-74	33	91.7	18	50.0
High scores 75+	0	0	13	36.1
Total	36	100	36	100.0

Table 9.7 below shows that the means and the medians for the intervention group increased in all the four areas under study, as did the composite score. Table 9.7 compares the mean and

median scores for the two groups after the intervention to the mean and median scores for the whole group of 36 before the intervention.

Table 9.7:
Mean and median scores by group before and after intervention

	Before intervention (*n*=36)		**Non Intervention Group after intervention (*n*=18)**		**Intervention Group after intervention (*n*=**	
	Mean	Median	Mean	Median	Mean	Median
Randomisation	78	75	78.42	90	92	100
Double-blinding	74.86	78.00	64.83	67	85.17	100
Placebo	56.11	60.00	78.67	83.0	91.61	100
Implications	42.92	44.00	58.17	55	74.11	78
Composite score	60.53	60.00	70.19	67	88.89	100

Before the intervention, there was no difference in terms of the distribution of scores between the intervention group and the non-intervention group as shown in Table 9.8 below.

Table 9.8:
Distribution of composite scores before the intervention

		low score 0-49%	**low score 50-74%**	**Total**
Non intervention	Count	2	16	18
	% within q161	11.1%	88.9%	100.0%
Intervention	Count	1	17	18
	% within q161	5.6%	94.4%	100.0%
TOTAL	Count	3	33	36
		8.3%	91.7%	100.0%

After the intervention, the distribution of scores on a three-category scale changed. In the intervention group, no participants remained in the 0-50 percent score category. In the non-intervention group, there were 5 women in the 0-49 percent category; no women from this group scored 75 percent and above. This clearly reflected the effectiveness of the intervention in improving understanding. Table 9.9 shows the new distribution after the intervention showing that, in the intervention arm, 13 women had moved from the low scorers category to the high scorers category (75 percent and above). None of the women in the non-intervention group moved to the high scorers category.

Table 9.9:
Distribution of composite scores after the intervention

		LOW SCORE BELOW 49%	LOW SCORE 74	HIGH SCORE 75+	
Non intervention	Count	5	13		18
	% within q161	27.8%	72.2%		100.0%
Intervention	Count		5	13	18
	% within q161		27.8%	72.2%	100.0%
TOTAL	Count	5	18	13	36
		13.9%	50.0%	36.1%	100.0%

To check for the effect of the intervention on understanding of randomisation, a cross tabulation was done. The cross tabulation showed that participants from the intervention arm were more likely to obtain higher scores on understanding of randomisation than participants from the non-intervention arm (Refer to Table 9.10). However, the Fischer's exact test revealed that the influence of the intervention on understanding of randomisation was not very strong. The Fischer's exact test yielded a *p*-value of .075, indicating that the relationship was not statistically significant.

Table 9.10:
Cross tabulation of intervention and understanding of randomisation

		Low Scorers 0-74%	High Scorers 75%+	Total
Non intervention	Count	9	9	18
	% within non intervention/ intervention	50.0%	50.0%	100.0%
Intervention	Count	3	15	18
	% within non intervention/ intervention	16.7%	83.3%	100.0%
TOTAL	Count	12	24	36
		33.3%	66.7%	100.0%

P=0.075

To assess the effectiveness of the intervention on improving understanding on placebo use, a *p*-value of .002 was obtained using the Pearson's chi-square test and .003 using Fischer's exact test. These *p*-values indicates that there was a statistically significant relationship between the intervention and improved understanding of placebo use. Table 9.11 below indicates that 15 of the 18 participants in the intervention arm scored higher on this measure, compared to only 6 on the non-intervention arm.

Table 9.11:
Cross tabulation of intervention by understanding on placebo use

		Low scorers 0-74%	**High scorers 75%+**	**Total**
Non intervention	Count	12	6	18
	% within non intervention/ intervention	66.7%	33.3%	100.0%
Intervention	Count	3	15	18
	% within non intervention/ intervention	16.7%	83.3%	100.0%
TOTAL	Count	15	21	36
		41.7%	58.3%	100.0%

p=.003

Cross tabulation of intervention by score on double-blinding also showed that the intervention had a significant effect on the scores that the women obtained. Fifteen women in the intervention arm scored highly as compared to only 6 women in the non intervention arm (Refer to Table 9.12). A *p*-value of *p*=.001 was obtained using both Pearson's chi-square and Fischer's exact test. This *p*-value indicates that there was a statistically significant relationship between the intervention and the improved scores on double-blinding.

Table 9.12:
Cross tabulation of intervention and understanding of double-blinding

		Low Scorers 0-74%	**High Scorers 75%+**	**Total**
Non intervention	Count	15	3	18
	% within non intervention/ intervention	83.3%	16.7%	100.0%
Intervention	Count	5	13	18
	% within non intervention/ intervention	27.8%	72.2%	100.0%
TOTAL		20	16	36
		55.6%	44.4%	100.0%

P=0.001

The effect of the intervention on the understanding of personal implications was also assessed. A *p*-value of .000 was obtained using Fischer's exact test and Pearson chi square test. This value confirmed that the intervention had a statistically significant impact on improved understanding of personal implications. The findings in Table 9.13 below indicate that 11 of the 18 women scored highly in contrast to only one woman in the non-intervention arm.

Table 9.13:
Cross tabulation of intervention and Understanding of personal implications

		Low scorers 0-74%	**High Scorers 75%+**	**Total**
Non intervention	Count	17	1	18
	% within non intervention/ intervention	94.4%	5.6%	100.0%
Intervention	Count	7	11	18
	% within non intervention/ intervention	38.9%	61.1%	100.0%
TOTAL	Count	24	12	36
		66.7%	33.3%	100.0%

P=0.0002

In an attempt to assess the impact of the intervention on overall understanding of all four areas under study, the independent variable (the intervention) was cross tabulated with the composite score. Table 9.14 below indicates that 13 of the participants in the intervention arm managed to obtain high scores, while no participant from the non-intervention arm managed to score 75percent and above. A *p*-value of 0.0002 was obtained using both Pearson's chi-square test and Fischer's exact test, signifying that there was a statistically significant relationship between the intervention and the composite scores obtained.

Table 9.14:
Cross tabulation of intervention and composite score

		Low Scorer 0-74%	**High Scorer 75%+**	**Total**
Non intervention	Count	18		18
	% within non intervention/ intervention	100.0%		100.0%
Intervention	Count	5	13	18
	% within non intervention/ intervention	27.8%	72.2%	100.0%
TOTAL	Count	23	13	36
		63.9%	36.1%	100.0%

P=0.0001

Table 9.15 below shows the *p*-values that were obtained using both Pearson's Chi Square test and Fischer's Exact test. The *p*-value of 0.0001 that was obtained confirms that the effect of the intervention on composite score was statistically significant.

Table 9.15:
Test results showing the effect of the intervention on composite score.

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	20.348	1	.000		
Continuity Correction	17.338	1	.000		
Likelihood Ratio	25.822	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	19.783	1	.000		
N of Valid Cases	36				

a Computed only for a 2x2 table
b 0 cells (.0%) have expected count less than 5. The minimum expected count is 6.50.

9.4 MATCHED PAIR ANALYSIS

Matched pair analysis of the scores of the participants in the intervention arm before and after the intervention indicates that all participants experienced some significant gains in scores except for one who experienced a drop of 2 percent from 65 percent before the intervention to 63 percent after the intervention. Nine of 18 respondents showed very large gains of 20 percent and above, while 8 of the 18 respondents experienced some gains of between 10 percent and 19 percent. Only one participant experienced a minimal loss of 2 percent (Refer to Table 9.16).

Table 9.16:
Matched pair analysis of composite scores for Intervention group before and after intervention for intervention group (n=18)

Participant Number	Composite Score after intervention	Composite Score before intervention	Difference	Negative/Positive Gain	Magnitude of gain
164	63	50	+13	Pos	Significant
093	70	65	+15	Pos	Significant
112	70	58	+12	Pos	Significant
150	70	58	+12	Pos	Significant
183	85	70	+12	Pos	Significant
136	89	68	+13	Pos	Significant
158	89	63	+13	Pos	Significant
184	89	60	+29	Pos	Very sig
191	89	60	+29	Pos	Very sig
179	93	68	+25	Pos	Very sig
083	96	70	+26	Pos	Very sig
157	96	58	+38	Pos	Very sig
198	96	40	+56	Pos	Very sig
063	100	58	+42	Pos	Very sig
202	100	50	+50	Pos	Very sig
096	81	68	+13	Pos	Significant
135	85	63	+22	Pos	Very Sig
070	63	65	-2	Neg	Minimal

Matched pair analysis of the scores of the participants from the non-intervention group before and after the intervention revealed that the majority of the participants scored lower during the second assessment. Twelve of the 18 respondents experienced negative gains ranging from -1 to as high as -28, and two respondents did not experience any gain in their scores. This finding confirms the suggestion that history and maturation of instrument had very minimal bias on the scores since the second assessment was done about 8 months after the first assessment. The difference between the gains of the intervention arms and those of the non intervention arm

also confirms that the placebo that was used for the non-intervention did not influence the scores of the non intervention arm in a significant way. Interestingly, 7 of the 18 non intervention respondents experienced losses of 10 percent and above. Such losses were classified as significant losses (10-19 percent) and very significant (20 percent and above). Only two respondents experienced significant gains of between 10-19 percent (Refer to table 9.17).

Table 9.17:
Matched pair analysis of composite scores for Non Intervention group before and after intervention (n=18)

Participant Number	Composite score after inter	Score before intervention	Net gain in scores	Negative/ Positive gain	Magnitude of gain /Loss
163	33	53	-20	Neg	Very significant
139	40	58	-18	Neg	Significant
116	44	48	-4	Neg	Minimal
089	55	70	-15	Neg	Significant
120	55	55	0	Zero	Nil
134	55	55	0	Zero	Nil
155	55	40	+15	Pos	Significant
168	55	53	+2	Pos	Minimal
105	59	60	-1	Neg	Minimal
085	63	68	-5	Neg	Minimal
181	63	73	-10	Neg	Significant
100	67	65	+2	Pos	Minimal
115	67	68	-1	Neg	Minimal
201	67	53	+12	Pos	Significant
094	70	65	+5	Pos	Minimal
124	48	73	-28	Neg	Very Significant
101	63	70	-7	Neg	Minimal
194	44	60	-14	Neg	Significant

9.5 GROUP STATISTICS AND INDEPENDENT SAMPLES TESTS

Table 9.18 and Table 9.19 below show the group statistics on all the categories that were scored after the intervention. Table 9.18 shows that the mean scores obtained by members from both groups before the intervention were almost similar. Table 9.19 shows that, after the intervention, the mean and median values for the intervention group were higher than those obtained by the non-intervention group for all areas under study.

Table 9.18:
Intervention and non intervention Group Statistics before the intervention

	Intervention/non intervention	**N**	**Mean**	**Std Deviation**	**Std error mean**
Composite score	Intervention	18	92.22	15.55	3.67
	Non intervention	18	60.39	9.26	2.18
Implications	Intervention	18	60.67	7.93	1.87
	Non intervention	18	41.78	9.99	2.36
Double-blinding	Intervention	18	44.06	16.40	3.87
	Non intervention	18	54.44	20.36	4.80
Placebo use	Intervention	18	57.78	22.64	5.34
	Non intervention	18	74.83	20.43	4.81
Randomisation	Intervention	18	74.89	15.42	3.63
	Non intervention	18	79.33	12.19	2.87
	Intervention	18	76.67	13.56	3.20

Table 9.19:
Intervention and Non-intervention group Statistics after the intervention

	Intervention/non intervention	N	Mean	Std. Deviation	Std. Error Mean
Composite score	Non intervention	18	55.72	10.45	2.46
	Intervention	18	84.67	12.36	2.91
Implications	Non intervention	18	42.22	13.36	3.15
	Intervention	18	74.11	19.60	4.62
Double-blinding	Non intervention	18	44.50	34.14	8.05
	Intervention	18	85.17	26.22	6.18
Placebo	Non intervention	18	65.72	21.81	5.14
	Intervention	18	91.61	13.14	3.10
Randomisation	Non intervention	18	64.61	29.17	6.88

Independent samples tests were done before and after the intervention to check on the usefulness of the intervention at group level. *P*-values above 0.005 were obtained for the scores before the intervention, and *p*-values below 0.005 were obtained for all the four scores after the intervention. This finding is very important as it shows that the samples were independent and that the intervention had a positive effect on understanding of all four areas under consideration in this study. Table 9.20 and Table 9.21 below show the results from the independent samples test before and after the intervention. They show that, before the intervention, there were no significant differences between the two groups. The significance values in indicated in **bold** in Table 9.20 are all greater than 0.05 while those in Table 9.21 (also indicated in **bold**) are all below 0.05 showing that there were some statistically significant differences between the two groups in terms of all the concepts that were being assessed in the

study (randomisation, double-blinding, placebo use, personal implications and composite score) following the intervention.

Table 9.20:
Independent samples tests results before intervention

		Levene's Test for Equality of Variances F	Sig.	t-test for Equality of Means t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference
Composite score (Q100B)	Equal variances assumed	1.017	0.320	-0.097	34	**0.924**	-.28	2.87	-6.12
	Equal variances not assumed			-0.097	33.207	**0.924**	-.28	2.87	-6.12
Implications Score (Q97B)	Equal variances assumed	1.361	0.251	-0.503	34	**0.618**	-2.28	4.53	-11.48
	Equal variances not assumed			-0.503	28.087	**0.619**	-2.28	4.53	-11.55
Blinding Score (Q96B)	Equal variances assumed	0.307	0.583	-0.465	34	**0.645**	-3.33	7.18	-17.92
	Equal variances not assumed			-0.465	33.624	**0.645**	-3.33	7.18	-17.92
Placebo use score (Q95B)	Equal variances assumed	2.941	0.095	-0.009	34	**0.993**	-5.56E-02	6.03	-12.31
	Equal variances not assumed			-0.009	31.622	**0.993**	-5.56E-02	6.03	-12.35
Randomisation score (Q94B)	Equal variances assumed	0.712	0.405	0.620	34	**0.539**	2.67	4.30	-6.07
	Equal variances not assumed			0.620	33.619	**0.539**	2.67	4.30	-6.07

Table 9.21:
Independent samples tests results after intervention

		Levene's Test for Equality of Variances F	Sig.	est for uality of eans t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
COMPOSITE SCORE %	Equal variance assumed	0.840	0.366	-7	34	**0.0001**	-28.94	3.82	-36.70	-21.19
	Equal variance assumed			-7	33.081	**0.0001**	-28.94	3.82	-36.71	-21.18
	Equal variance assumed			-3	24.821	**0.005**	-25.00	8.20	-41.89	-8.11
Implications score	Equal variance assumed	3.356	0.076	-5	34	**0.0002**	-31.89	5.59	-43.25	-20.53
	Equal variance assumed			-5	29.996	**0.0001**	-31.89	5.59	-43.31	-20.47
DOUBLE-BLINDING %	Equal variance assumed	1.700	0.201	-4	34	**0.0002**	-40.67	10.15	-61.28	-20.05
	Equal variance assumed			-4	31.878	**0.0001**	-40.67	10.15	-61.33	-20.00
PLACEBO MARKS %	Equal variance assumed	1.850	0.183	-4	34	**0.0002**	-25.89	6.00	-38.08	-13.69
	Equal variance assumed			-4	27.903	**0.0003**	-25.89	6.00	-38.18	-13.59
RANDOMISATION %	Equal variance assumed	4.950	0.033	-3	34	**0.001**	-27.61	7.79	-43.45	-11.78
	Equal variance assumed			-3	25.940	**0.002**	-27.61	7.79	-43.63	-11.59

9.6 EFFECT OF INTERVENTION ON ATTITUDES

In the intervention phase, some questions were included in the questionnaire to establish the attitudes of the respondents towards randomisation, double-blinding and placebo use. Before the intervention, 44.4 percent of all respondents had found randomisation to be unacceptable. Interestingly, after the intervention, 78.7 percent (n=14) of those on the intervention arm were in support of randomisation as compared to 33.3 percent (n=6) in the non-intervention arm (See Table 9.22). *P*-values of 0.007 and .009 were obtained using Pearson's chi square test and Fischer's exact test. These values indicate that the effects of the intervention in changing attitudes towards randomisation were statistically significant.

Table 9.22:
Cross tabulation of Intervention and attitude to placebo use

		Before intervention		**After Intervention**		
		Negative	Positive	Positive	Negative	**Total**
Non interventio	Count	16	2	6	12	18
	% within non intervention/interve n	88.9%	11.1%	33.3%	66.7%	100.0%
Interventic	Count	18		14	4	18
	% within non intervention/interve n	100.0%		77.8%	22.2%	100.0%
TOTAL	Count	34	2	20	16	36
		94.4%	5.6%	55.6%	44.4%	100.0%

P=0.009

A question was included on acceptability of placebo. After the intervention, about 66.7 percent (n=12) of those in the intervention arm showed a positive attitude to placebo use as they did

not see any problem with placebo use. About 44.4 percent (*n=8*) on the non-intervention arm found placebo use acceptable (See table 9.23). A *p*-value of 0.157 was obtained using Fischer's exact test, indicating that the effect of the intervention on attitude to placebo was not statistically significant.

Table 9.23:
Intervention and attitudes towards placebo use

		Before intervention		**After intervention**		
		Negative	Positive	Positive	Negative	**Total**
Non intervention	Count	16	2	8	10	18
	% within non intervention/intervention	88.9%	11.1%	44.4%	55.6%	100.0%
Intervention	Count	18		12	6	18
	% within non intervention/intervention	100.0%		66.7%	33.3%	100.0%
TOTAL	Count	34	2	20	16	36
		94.4%	5.6%	55.6%	44.4%	100.0%

p=0.157

A question was included to find out about the attitudes of the participants to double-blinding. About 77.8 percent (*n=14)* of those on the intervention arm thought that double-blinding was an important part of the trial. In the non intervention arm, only one person (5.6 percent) out of 17 found double-blinding to be acceptable. One respondent in the non intervention arm did not have a position (Refer to Table 9.24). A *p*-value of .000 was obtained using both Pearson's chi square test and Fischer's exact test. This value signifies a statistically significant relationship between the independent variable (the intervention) and the dependent variable (attitude towards double-blinding).

Table 9.24:
Intervention and attitudes towards double-blinding

		Before Intervention		After Intervention			
		Negative	Pos	Pos	Neg	Neutral	**Total**
Non intervention	Count	17	1	1	16	1	18
	% within non intervention/ intervention	94.4%	5.6%	5.6%	88.9%	5.6%	100.0%
Intervention	Count	17	1	14	4		18
	% within non intervention/ intervention	94.4%	5.6%	77.8%	22.2%		100.0%
TOTAL	Count	34	2	15	20	1	36
		94.4%	5.6%	41.7%	55.6%	2.8%	100.0%

P=0.0001

9.7 OBSERVATIONS DURING THE INTERVENTION PHASE

The intervention was presented in an environment that encouraged discussion and the participants were free to interrupt the presenter and make comments or seek clarification. Of interest were some of the comments that came from the participants during and after the intervention. Some of these comments are included below as they further reflect on the success of the intervention in improving understanding:

> *So the farmers who participated in the experiment are supposed to buy the new fertilizer at a reduced price. If the company was selling the fertilizer at K100, they should sell it to the farmers at K50 because the farmers would have assisted in the development of the fertilizer.*

This comment clearly showed that this particular woman had clearly realised that the farmers in Ncheu had been used as part of a study and the aim of the study was the generation of new information that could be used in establishing if the new fertilizer was effective. The issue of benefit sharing has been an area of serious debates in recent times. It was interesting that the participants could justify their claim to benefits in that way. The participants had clearly realised that, by participating in the research, they were going to assist others in future, just as the farmers participated in the research which eventually led to improvements in yields for the whole nation.

The majority of the women were grateful to the presenter for having presented the information in a way which was easy to understand.

> ***LLP7****: On behalf of my friends, I am grateful to you for your coming. To be frank we have learnt a lot from this discussion about the Microbicide study. Your questions made us think about what we went through during our participation in this study and it will help us to remember this study forever. So, we don't take our participation in the discussion for granted- we thank you so much!*

The majority of women were very appreciative of the microbicide study as they indicated that it had assisted them in learning about their status, and they were assisted by the staff whenever they had health problems.

9.8 SUMMARY

This chapter has presented the findings on the implementation of the intervention designed to improve understanding. The chapter has also presented the findings on the usefulness of the intervention in improving understanding. Overall, there was evidence that the intervention was effective in improving understanding of the concepts under study. Various statistical tests were conducted to test the effects of the intervention on the understanding of the concepts

under study. There were significant improvements in the test results for the participants in the intervention arm compared to those in the placebo arm. Regarding attitudes towards the three trial procedures, the data suggest that the intervention had a statistically significant impact on attitudes to randomisation and double-blinding, as most of the respondents in the intervention arm initially had negative attitudes, but ended up accepting randomisation and double-blinding as an important aspect of clinical trials after the implementation of the intervention. The impact of the intervention on placebo use was evident though not statistically significant.

CHAPTER 10

DISCUSSION OF FINDINGS ON THE IMPLEMENTATION AND EFFECTIVENESS OF THE PILOT INTERVENTION

10.0 INTRODUCTION

In this chapter, the implementation and usefulness of the intervention aimed at improving understanding are discussed. The discussion is aimed at explaining the results reported in the previous chapter. The findings are discussed under the main premise underlying the design and implementation of the pilot intervention. The findings are also specifically used to answer the research question on the usefulness of the pilot intervention that was introduced in the first chapter.

10.1 DISCUSSIONS ON PREMISE 4 - INTERVENTION TO IMPROVE UNDERSTANDING

Premise 4 related to the possibility of developing an intervention that could be used in improving understanding. According to this premise, if properly explained in lay-man's terms, trial participants can improve their understanding of the purpose and personal implications of trial procedures under study. Two assumptions were developed as a way of addressing this premise:

- Most interventions that are developed to improve understanding are merely a repetition of the information from informed consent documents using different media. There are no attempts to simplify the information or to present it in a way which makes more sense for the potential participants (Flory & Emanuel, 2004).
- Trial participants can understand trial procedures and their implications if the explanations they are given about the procedures include details on how the procedure

will be implemented, and the justification for and personal implications of those procedures (Lindegger & Richter, 2000).

The following sub-question was specifically put forward in order to examine this premise:

Can an intervention improve trial participants' understanding of research, randomisation, double-blinding and placebo use?

The findings reported in Chapter 9 suggest that understanding can be improved. It is important to highlight the possibility of some confounding biases:

History – Time is an important factor in any study which looks at a particular phenomenon over a period of time. With time, individuals learn more about research, about the products being studied. With more exposure, it means they are in a better position to give the correct answers when asked questions on the subject.

Instrument maturation – The two instruments used in the main study and intervention study covered similar questions. However, it is important to note that there was a time lag of more than 8 months between the first assessment and the second assessment. This time lag could have weakened the bias caused by instrument maturity. In any case the maturation would have affected the intervention and non intervention groups equally.

Dissemination of study results – Results from the microbicide study were disseminated to all participants around March 2009. The first assessment had been conducted between September and November 2008. The intervention was introduced and evaluated in July 2009, more than three months after the dissemination of the findings. It is therefore possible that the dissemination of findings could have significantly affected the impact of the intervention on understanding.

It is important to note, however, that the above confounders applied equally to both the intervention arm and the non-intervention arm. The women in the two groups were all familiar with the research procedures under study. As such, it can be safely concluded that any differences between the intervention and non-intervention arm must be attributable to the intervention.

The findings of the pilot study, which aimed to test the effectiveness of an intervention in improving understanding of the three concepts as well as their implications, suggest that the intervention was effective in improving understanding. Women in both the intervention and non-intervention arms were selected because they had obtained low scores in the initial field test. After the intervention, the majority of women on the intervention arm scored significantly higher on the understanding of all four areas under study (randomisation, double-blinding, placebo use and their personal implications) compared to those in the non-intervention arm.

The findings also suggest that the intervention had statistically significant effects on attitudes towards randomisation and double-blinding. The effect on attitude towards placebo use was not statistically significant, which implies that the intervention was not successful in changing attitudes towards placebo use in a statistically significant way. The findings on the impact of the intervention confirm findings by Kruse *et al*., 2000; Searight and Miller, 1996; Weston *et al.*, 1997. These authors found that provision of adequate information on a trial and its procedures increased positive attitudes towards the trial. These results imply that the women in the intervention arm began to appreciate the usefulness of randomisation and double-blinding after they had understood their justification.

Regarding the finding on attitude towards placebo use, one may attempt to explain the fact that the intervention did not significantly improve attitudes towards placebo use using the realities

in the healthcare environment. While there may be several explanations to this finding, the finding may also be explained as a reflection of the expectations of individuals in limited resource setting who associate health care institutions only with provision of care. Some of the individuals would be expecting to benefit from the product (test product) which is being provided through the study or from the good quality care that is offered as part of the study (Ndebele, Mfutso-Bengo & Mduluza, 2008). It is therefore difficult for such individuals to accept something that they find useless even if they understand the reason why it is being provided to them. These findings are consistent with findings by Masiye, Kass, Hyder, Ndebele & Mfutso-Bengo (2008). It is also possible that the explanation given on placebo was inadequate.

The effect of the intervention on recruitment and retention were not evaluated since the microbicide study had already come to an end. It would have been interesting to test the suggestion by Robinson *et al*. (2005) that provision of adequate information may actually lead to greater understanding, which may ultimately lead to lower consent rates.

10.2 POSSIBLE REASONS FOR SUCCESS OF INTERVENTION

The success of the intervention can be attributed to the following factors:

- Review of previous interventions – studies on previous intervention were reviewed and points taken on weaknesses, strengths and areas of improvement. All these were taken into consideration in the development of the intervention which was tested in this study. The reference studies are summarised in Chapter 2.
- Use of local language: The intervention was delivered in ChiChewa, which is the dominant language in Malawi. This was aimed at ensuring that the information

disclosed would be meaningful to all respondents, regardless of educational level (Cornelli *et al.,* 2006).

- Use of lay language and avoidance of technical terms – throughout the intervention, layman's language was used in explaining the procedures and their justifications. Examples were taken from agriculture since Malawi is an agriculture-based country and every individual is conversant with agriculture (Verheggen & Van Wijmen, 1996).
- Adequate time – adequate time was provided for the implementation of the intervention. In the research setting, staff at the sites may be aiming at meeting accrual targets rather than enhancing understanding. In this case, the aim was only to improve understanding.
- A hierarchic and modular approach to providing information. Information was provided in a hierarchic and modular approach. Care was taken to ensure that information was provided on each concept to cover all three areas, namely procedures, purpose, and personal implications (Jimison *et al*., 1998).
- Use of vignettes in explaining the trial concepts and research – The procedures were explained in the form of a story which is interesting and easy to follow and relate to (Verheggen & Van Wijmen, 1996). In Malawian culture, as in the majority of African cultures, folktales are used as a useful way of passing important lessons to individuals (Gecau, 1970).
- Materials were presented in a way which was easy to understand – a PowerPoint presentation, which included colourful pictures, was designed and used as a way of supplementing the information about research, the microbicide study and the procedures under study, as well as their implications (Colletti *et al*., 2003; Fureman *et al.*, 1997).
- Inclusion of purpose, justification and implications of the research procedures and research participation. The intervention not only focused on the three concepts but

brought the three concepts into context so as to make the information more meaningful (Kerr *et al*., 2004).

- Asking participants to repeat in their own words or explain to others. During the intervention, participants who had understood the concepts were asked to repeat what they had understood to the presenter or to their colleagues (Verheggen *et al*., 1996).
- Inviting research participants to discuss with other participants - participants were allowed to discuss among themselves during and after the intervention (Lindegger & Richter, 2000).
- Use of a neutral team of disclosure staff distinct from the research team - The intervention was presented by a staff member from Centre for Bioethics at the College of Medicine and was not in any way a part of the research team at the site. During the implementation of the intervention, the microbicide trial staff were also not invited. This ensured that the women would discuss issues freely during the intervention. The presenter was familiar with the microbicide project and had a lot of experience in clinical trial issues, including key methodologic aspects of research (Hellman & Hellman, 1991).

The findings on the effectiveness of the intervention are consistent with findings by Barnett *et al*. (2005) and Sastry *et al*. (2004). They found that story-based interventions were useful as they facilitated understanding of concepts and procedures.

10.3 OFFER OF INTERVENTION TO NON-INTERVENTION ARM

During the planning of the intervention, it had been planned and agreed that the intervention would be introduced to the 18 women in the non-intervention arm if it had been found to be acceptable. This plan was obviously overtaken by events as the

intervention was implemented well after the microbicide had been concluded. The reason why it had been decided that the intervention would be disseminated to the women in the non intervention arm in the first place was aimed at ensuring that those women also benefit directly from the intervention. Tracking of the women for the intervention phase had also proven difficult. It was therefore agreed that the findings from this study would be disseminated at the two sites so that the principal investigators could utilise the findings in other and future trials, if they wished. The dissemination of the intervention to the 18 in the non intervention arm was however not going to serve an important purpose since the microbicide study had already come to an end. More importantly however, the 18 women in the non intervention arm benefited from a session on cervical cancer that was conducted as part of the non-intervention package. Plans are in place for the researcher to disseminate the findings at the two sites in Malawi as well as to conduct a larger study. The dissemination of findings on the usefulness of the intervention to the 36 women would have been a good opportunity to document their views on the acceptability and challenges related to the intervention.

10.4 SUMMARY

This chapter discussed findings on the implementation and usefulness of the intervention which was designed as part of the current study. An intervention which was based on a narrative of the three concepts under study was designed. The narrative relied on daily examples relating to agriculture since Malawi is an agriculture based nation. The intervention was implemented with a group of 18 women, whilst another group of 18 women went through a placebo session. There was a period of about eight months before the pre-test and post-test. The narrative was relayed with the assistance of a power point presentation. The findings on the efficacy of the intervention suggest that the intervention positively impacted on understanding of trial

procedures under study, as the majority of women in the intervention arm got significantly higher scores after the intervention. The findings also suggest that the intervention was useful in changing participants' attitudes towards randomisation and double blinding. The intervention did not change attitudes towards placebo use in a statistically significant way. Overall, the findings confirmed the research premise number 4, thereby successfully answering the relevant research question. Initially, there were plans to introduce the intervention to participants in the non-intervention arm. These plans were changed for various reasons, including the fact that the intervention was introduced and tested about four months after the conclusion of the microbicide trial. In the interest of justice and improving informed consent, it was resolved that the findings would be disseminated to the two sites and others for possible adoption.

CHAPTER 11

INTERPRETATION AND GENERAL DISCUSSION OF MAIN FINDINGS

11.0 INTRODUCTION

Findings on the two phases of the present study were discussed separately in Chapters 7 and 9. In this chapter, an attempt is made to synthesise the two discussion chapters as a way of laying the foundation for the final chapter of this study. This chapter comprises various sections including testing hypotheses, responses to research questions, clarifications on main study premises, a general discussion of the main findings, challenges faced during the implementation of the study, and limitations of the study.

11.1 TESTING OF STUDY HYPOTHESES

Several hypotheses related to the specific objectives of the study were formulated. The testing of the hypotheses is an important step in ensuring that the main research question and the sub-research questions are answered. In this section, the study hypotheses are discussed.

Hypothesis A which states that i*nformed consent forms and materials provide adequate information on randomisation, double-blinding and placebo use*. This hypothesis was rejected as it was found that the informed consent document did not provide sufficient information for the understanding of the three procedures. Findings from document review of the informed consent documents were useful in testing this hypothesis.

Hypothesis B which postulates that r*esearch staff have a positive attitude regarding full disclosure of information on blinding, randomisation and placebos to research participants*. This hypothesis was supported as it was established that staff were very keen to disclose all the

information that was required of them. The adoption of comprehension exercises ensured that staff would be motivated to disclose the information. Staff followed study SOPs relating to disclosure of information and responded to all questions adequately. Data from the indepth interviews with research staff were used in testing this hypothesis.

Hypothesis C which states that t*rial participants are aware that the procedures of double-blinding, randomisation and placebo use are being used in the trial.* This procedure was supported by the findings. The majority of participants were aware that the three procedures were part of the study. Data from both the structured interviews and focus group discussions were used in testing this hypothesis.

Hypothesis D which states that t*rial participants are aware of the purpose of double-blinding, randomisation and placebo use in research*. This hypothesis was not supported as the majority of participants were not aware of the justifications for the three procedures. Data from structured interviews and focus group discussions were used in testing this hypothesis.

Hypothesis E which states that t*rial participants understand the personal implications of the trial procedures under study*. This hypothesis was rejected as the study established that the majority of respondents were not aware of the personal implications of the three procedures. Data from the structured interviews and focus group discussions were used in testing this hypothesis.

Hypothesis F which states that all respondents *do not believe that they are completely protected from HIV infection by the microbicide under study*. This hypothesis is rejected as there was evidence that some of the participants thought that the products they were being given would protect them against HIV infection. A small minority of the women had even convinced themselves that they were on the active product arms as they were looking forward to some kind of protection. Data from structured interviews and focus group discussions were used in testing this hypothesis.

Hypothesis G which states that t*rial participants have a positive opinion regarding double-blinding, randomisation, and use of placebos.* This hypothesis was rejected as the study established that the majority of respondents had negative attitudes towards the three procedures. Data from structured interviews and focus group discussions were used in reaching this conclusion.

Hypothesis H which states that r*esearch staff provide adequate information on double-blinding, randomisation and placebo use to trial participants*. This hypothesis was not supported as the study established that the information which was provided by staff was inadequate. The staff did not provide information on the justification of the study procedures of randomisation, double-blinding, as well as their personal implications. Data from indepth interviews with study staff were used in testing this hypothesis.

Hypothesis I which states that u*nderstanding of randomisation, double-blinding and placebo use can be improved by use of an intervention*. Using data from the intervention phase of the study, this hypothesis was supported as the study established that the intervention which was developed as part of this study, was useful in improving understanding of two of these concepts (randomization and double blinding).

11.2 RESPONDING TO RESEARCH QUESTIONS

The main research question was: *Are trial participants aware that they are participating in a trial which employs randomisation, double-blinding and placebo use, and are they aware of the purposes and personal implications of these procedures*?

The study established that a significant proportion of the microbicide trial participants had low levels of understanding of randomisation, double-blinding and placebo use. The majority of microbicide trial participants who participated in the current study were not aware of the personal implications of the three procedures

11.2.1 RESPONSES TO RESEARCH SUB-QUESTIONS

The main research question was broken down into several sub-questions. For each of the sub-questions, an attempt is made to provide the answer or to explain the lack of an adequate answer.

Sub-question 1: *How do trial related documents explain the concepts of randomisation, double-blinding and placebo use*? The study established that research documents mentioned the use of the three procedures in the microbicide study but did not adequately address the justification for or the personal implications of each procedure.

Sub-question 2: *How do study staff explain the concepts of randomisation, double-blinding and placebo use to prospective trial participants?* The study established that staff mentioned the fact that the three procedures were part of the study but did not adequately address the justification for their inclusion or the personal implications of the procedures. All study documents, including SOPs, did not require staff to address the justification and personal implications of the three procedures.

Sub-question 3: *Are participants aware of the purpose of the study?* The majority of the participants were aware that the study was aimed at testing PRO2000 and Buffergel. A small proportion of the respondents however were of the opinion that the study was a programme aimed at protecting them against HIV infection.

Sub-question 4: *Are participants aware that they are participating in a trial to test a product whose efficacy is not known?* Some of the participants were not aware that they were participating in a study aimed at testing a product whose efficacy was unknown. Some participants expected to benefit directly from the products through protection from HIV.

Sub-question 5: *Are participants aware that they are still exposed to HIV infection even though they are using the product they have been issued with?* The majority of participants

were aware that there were possibilities of becoming infected with HIV while participating in the study. Some respondents however, thought that they were protected against HIV infection as they thought that the products were aimed at protecting them.

Sub-question 6: *Are trial participants aware that randomisation, double-blinding and placebo use are part of the study?* A significant majority of participants were aware that these three procedures were being used in the study as this had been mentioned during the disclosure of information.

Sub-question 7: *Are trial participants aware of the reasons why randomisation, double-blinding and placebos are used in the study? A significant* majority of respondents were not aware of the justifications for the use of the three procedures in clinical trials.

Sub-question 8: *Are participants aware of the various study arms in the microbicide study?* The majority of respondents were aware of the various study arms. However, a significant majority of respondents could not correctly list all the four study arms.

Sub-question 9: *Are participants aware that they have been randomised into different groups?* A significant majority of participants were aware that they had been randomised to different groups. Some, however, thought they were aware of the specific group they had been assigned to.

Sub-question 10: *Are participants aware that they may be receiving a placebo?* Some participants were aware that they could be receiving placebo. A small proportion of the respondents were however convinced that they were on the active product arm of the study.

Sub-question 11: *Are participants aware that neither themselves nor the trial nurses and doctors (i.e., research personnel) are aware of the arms they are in?* Some participants were not aware that neither they nor staff were aware of their assignments. Some participants even approached trial staff to find out about which arm they were on.

Sub-question 12: *Are trial participants aware of the personal implications of randomisation, double-blinding and placebo use?* A significant majority of trial participants were not aware of the personal implications of the three procedures.

Sub-question 13: *Are participants aware of the implications of their participation regarding protection from infection by the product under test?* A significant majority of women were aware that there was a possibility that they could be infected with HIV during the study. Others, however, thought that they were protected against HIV by the products they had been given.

Sub-question 14: *What is the attitude of the trial participants regarding randomisation, double-blinding and placebo use?* A significant majority of trial participants had negative attitudes towards randomisation, double-blinding and placebo use.

Sub-question 15: *Can an intervention improve trial participants' understanding of research, randomisation, double-blinding and placebo use?* The study established that the intervention which was developed as part of this study was effective in improving understanding. The intervention also had an effect on the acceptability of double-blinding and randomisation. The intervention was not successful in impacting on attitudes towards placebo use.

11.3 CLARIFYING THE MAIN PREMISES AND ASSUMPTIONS

In this section, clarifications are provided of the four main premises underlying the study. The clarifications are based on the findings as well as the testing of the hypotheses:

Premise 1: The study supported the premise that the information that was provided through study documents was not adequate. It was evident that study documents did not adequately address the justification as well as the personal implications of the trial procedures under study.

Premise 2: The study supported the premise that the information disclosed by research staff did not adequately address the trial procedures under study and therefore could not facilitate complete understanding of the study procedures, their justifications and personal implications. It was also noted that research staff are guided by SOPs on informed consent, which generally do not emphasise the need to cover justification and implication of the individual trial procedures.

Premise 3: The study supported the premise as approximately two thirds of trial participants (61.1 percent) were identified as having low levels of understanding of randomisation, double-blinding, placebo use, and the personal implications of these procedures. For each of the three concepts, participants with limited understanding were identified.

Premise 4: The study supported the premise that if properly explained in lay terms, it is possible for trial participants to grasp information on the purpose and personal implications of trial procedures under study. After the intervention phase of the study, there was some evidence suggesting that levels of understanding improved for the majority of participants on the intervention arm compared to those on the placebo arm. Some of the participants on the placebo arm actually got scores which were lower than the ones they got during the first assessment eight months earlier.

11.4 GENERAL DISCUSSION OF THE OVERALL STUDY FINDINGS

Based on the findings from the two phases of the study, all the four major premises underlying this study were substantiated. The results from this study however need to be interpreted with due caution due to some of the weaknesses described in Section 11.7. Recruitment during an actual trial is necessary in order to rule out the confounding effects. Phase 2 of this trial was conducted after the termination of the microbicide trial and this turned the intervention phase from a practical exercise into a hypothetical one. This study can however be taken as a first step leading to a larger confirmatory study.

Based on literature reviewed, it was not surprising that some participants had low levels of understanding related to the three procedures under study as well as the implications of those procedures, despite all the steps that had been taken in the trial to ensure understanding of the trial. While it was clear to some that they were participating in research, for the majority, the personal implications were not clear. This can be attributed to many factors, including the fact that the personal implications were not adequately addressed by study documents and relevant study staff during the process of obtaining informed consent. Other factors such as trust in the staff and the research centres may also have contributed towards these findings.

Misunderstanding seems to emanate from participants' failure to realise why they are being randomised, why a placebo is used, and why there is double blinding. Understanding the reasons why these procedures are used can help participants to accept the fact that the purpose of the trial is the advancement of knowledge and not their own protection or treatment. Understanding the purpose of the trial procedures may assist the potential participant to take a

more scientific perspective instead of the treatment perspective which may be common among people who are not conversant with clinical trials.

Contrary to several studies which have shown that interventions aimed at improving understanding are not useful (Agre *et al*., 2003; Agre & Rapkin, 2003; Davis *et al*., 1998; Ellis Butow & Tattersall, 2002; Kripalani *et al*., 2008; Ryan *et al*., 2008; Wray *et al*., 2005), this study has suggested that a well tailored intervention can assist in improving understanding. As a result of the findings from this study, it can be argued that, while researchers and their teams are taking measures to ensure that participants better grasp issues concerning trial procedures, their actions are not designed in a way that makes them effective. It is possible that some researchers may simply assume that explaining scientific terms is difficult and never engage in serious efforts aimed at ensuring that the terms are simplified. Given that some of the participants who had lower levels of formal schooling managed to grasp the concepts as delivered through the intervention, it is evident that most people can understand these concepts if the information is presented in a manner which makes it easy to understand.

The intervention phase was implemented using a group of people who had had experience with research. The group had also previously received some explanations of research. The findings have suggested that research can be demystified and presented to so-called "lay" people in a way that they can still understand. The findings further suggest that it is possible to educate communities and the public at large about research and clinical trials so that they feel empowered when they are invited to participate in research. The discussions with the women in the intervention arm after the implementation of the intervention were revealing. It was interesting to note the questions and issues that the women were raising. The women in the intervention arm reported that they found the session very enlightening as it was presented in a simple and informal way compared to how information was presented during the recruitment

for the microbicide study. The intervention did not assume in any way that they were familiar with research procedures.

It is important to note that, while the improving of understanding of research purpose and trial procedures is desirable, it may cause some challenges for researchers. Improved understanding may lead to difficulties in accrual and may also diminish the trust that communities and individuals have in health workers. Potential research participants may adopt a questioning attitude, which may create problems for research staff who may be used to fast accruals in populations that do not have a questioning attitude. In this study, informed refusals or withdrawals which may have been attributable to improved understanding were not possible as the microbicide trial had already come to an end by the time the intervention was introduced. In future studies, it would be important to investigate the negative effects on accrual and retention that an intervention such as the one implemented in this study can pose on accrual rates and study withdrawals. Unfortunately the present study did not ask if women would have chosen to remain in the trial if the intervention had been seen earlier.

It is important to note that, while the intervention demonstrated some success in other areas, it was not successful in impacting in a statistically significant way on attitudes towards placebo. This finding may not be surprising in an area in which the public health care system is overburdened and some treatments are not readily available in some public health facilities. In such areas, people may rationally choose to participate in research as a way of accessing good quality treatment (Mfutso-Bengo *et al*., 2008). In such a situation, it is understandable that individuals would find placebo use to be unacceptable, even if they understand the reason why it is being used in the trial. In some cases, placebo use would itself defeat the participants' motive for enrolling. A comparative study that is conducted in a limited resource area and a well-resourced area might shed some more light on this finding.

From this work, further research is necessary. It would be appropriate to conduct a study of this nature using a large cohort which is in the process of considering enrolment into a real trial rather than a hypothetical or completed trial. Such an approach would ensure that the effects of confounding variables are minimised. The current study has laid a foundation for the future research as it has presented evidence of the challenge of limited understanding. The findings from the intervention phase also present evidence of the usefulness of the developed intervention in improving understanding about research participation, trial procedures and their personal implications.

11.5 DISCUSSION OF THE TAXONOMY FOR ANALYSING UNDERSTANDING

The conceptual framework designed for this study proved to be useful as it provided some direction during the data collection and data analysis. The theoretical framework led to the development of the taxonomy for analysing understanding of clinical trial concepts (see Figure 3.3). The findings from the study suggested that the proposed taxonomy was a useful tool in analysing understanding of trial concepts as it provided for different levels of understanding and what each level is capable of achieving. From the findings, it is evident that the majority of participants were operating at the basic level of understanding before the intervention. This level is associated with simple recall of disclosed information (Hochhauser, 2005). The findings after the intervention suggest that the intervention was useful in moving understanding levels for the majority of participants to level 3, which is important as it leads to level 4 which is about making a decision based on adequate understanding.

11.6 CHALLENGES FACED DURING THE IMPLEMENTATION OF THE STUDY

Several challenges were encountered by the researcher during the implementation of the study. The researcher took measures to decrease the likelihood that these challenges would significantly impact on the study. The challenges included the following:

11.6.1 Lack of cooperation by some principal investigators – this study was delayed by more than two years as the researcher met some resistance from some principal investigators of HIV vaccine and microbicide trials in Zimbabwe and in Malawi. The study was initially intended to be conducted in Zimbabwe and the investigator finally moved it to Malawi after facing some resistance from some principal investigators in Zimbabwe who were not prepared to have the present study conducted with participants from their sites. This challenge was also noted by Nattrass (2006) who observed that it is common for HIV clinicians to prevent social scientists from accessing their clients. Nattrass observed similar practices at HIV trial sites in South Africa and listed the following reasons that were given by the clinicians at the HIV clinics in South Africa:

- The population has been "over-researched"
- None of the investigators from the clinic have been included in the proposed study
- It has not been approved by the same ethics committee
- There are insufficient tangible benefits for the patients
- Concerns about the additional amount of time that the patients would spend
- Research does not address the needs of the clinic
- In the case of this study, the reason given was that the local investigators needed to obtain approval of the other investigators from the other sites who were part of the international study, and that these had not responded to the request for permission. The two PIs in Malawi kindly agreed to have the study conducted at their sites after noting

that the study was in effect going to strengthen their own studies by assessing how they were obtaining informed consent at their own sites.

11.6.2 Recruitment of participants was very difficult as the study was only approved by the UKZN Ethics Committee when the microbicide trial was reaching its planned end. The budget that was available could not adequately cater for tracing participants who had already exited from the microbicide trial.

11.6.3 Language barrier for the investigator – The investigator could not participate meaningfully in data collection as he was not conversant in ChiChewa, the local Malawian language used in data collection. The investigator, however, relied on three research assistants who were well experienced in collecting data using various methods. The three research assistants went through some intensive training.

11.6.4 Limited funding - The study mainly relied on two small grants obtained from various sources and personal funds.

11.6.5 Timing of the study and work commitments - The investigator had challenges balancing study and work commitments. The study was conducted in Malawi at the same time as the investigator was moving to Botswana from Malawi to take up a new position.

11.6.6 Refusals – Three women refused to respond to the questionnaire during the initial assessment due to research fatigue. They said that they had already responded to too many questions through the microbicide trial. Three women who came to the microbicide trial site during the intervention phase of the study indicated that they were not willing to participate as they had other demanding chores. Three women could not be included in the intervention phase as they arrived late at the trial site.

11.6.7 Recruitment of respondents for the intervention: Recruitment was very difficult as some of the respondents had already moved to new residences.

11.6.8 Remote supervision: After acceptance of the proposal for this study, all supervision was electronic due to distances involved. The distance also prevented the researcher from attending the PhD programme run by the UKZN School of Psychology.

11.7 LIMITATIONS OF THE STUDY

Some of the limitations of the current study are listed below. Some action was taken to minimise the effects of these on the study findings:

11.7.1 Conceptual difficulty with the three terms under study – The three terms that were the focus of the study are conceptually difficult terms to the extent that even some highly educated persons find them difficult to appreciate. During some seminars organized for both research staff and university students, it emerged that the concepts of randomisation, placebo use and double-blinding are difficult to understand even for people with higher levels of education. It was the aim of this study to establish if participants really understand them so as to identify ways of explaining them if difficulties are confirmed by the study.

11.7.2 Complex nature of understanding – Understanding in the strict sense of inter-subjective agreement is difficult to prove. It is possible that the respondents and the interviewers may be using different words to mean the same thing. Alternatively, an interviewer might feel that s/he has understood something and yet in reality it is the interviewee who has changed the subject during the course of the interview. Chances of this occurring were minimised by breaking down the meaning of "understanding" into various components which, when aggregated, would lead to a complete state of understanding which is scorable.

11.7.3 Timing of the intervention – The intervention was conducted with women after the microbicide study had ended. This made these women hypothetical rather than true

participants experiencing an intervention who were still participating in a study or who were considering enrolling into a study. This might have affected their understanding in various ways. The provision of the study results as well as the confiscation of unused gels may have confirmed to the respondents the fact that they were participating in a study to test the effectiveness of the gels.

11.7.4 Social desirability - As with any other social science research, there is the risk that some participants may give responses that they feel the researcher is looking for, irrespective of what they really understand about the nature of the study. In social science research, some individuals may give "the correct" responses in order to continue to receive attention or rewards irrespective of what they really understand about the nature of the study (Arnold & Feldman,1981; Denzin, 1994; Groves,1989). Respondents in the study could have tried their best to ensure that they gave answers that they thought that the investigator was looking for e.g., associating the study with the Medical School, they could have given responses that are aligned to healthcare provision.

11.7.5 Contextual messages: In social science research, it is also possible that some respondents may find some cues in the interviewer to guide their responses. These phenomena may lead to some wrong conclusions. It is acknowledged that, in this study, the invitation for women to participate in this study, could have passed a contextual message to the women which may have affected their responses. By being referred by the study staff to the current study, it is possible that the microbicide participants might have interpreted the current study as a part of the microbicide study. This in itself could have affected their response due to various factors including the social desirability effect.

11.7.6 Repetition of questions: Some cognitive experiments have revealed a phenomenon which may distort the effects of interventions being tested (Donaldson, 1992). It has been noted that after introducing an intervention, if asked the same question, respondents can infer

that a different answer is required from the first one they gave before the intervention was introduced.

11.7.7 Non Intervention arm – The women in the non-intervention arm may not have had a good or motivated team or person explaining since it was something done before. Importantly, interpersonal differences might have led to some of the significant differences between the two arms. It might also have been the case that this control group might have been confused by the additional layer of cancer information.

11.7.8 – Implementation of intervention- In the current study, the intervention was used as a top-up as study information has already been conveyed through other means. It is important to conduct a larger study in which he disclosed of information is managed in a defined manner.

11.7.9 Meaning of words: Understanding is also affected by the meaning that different individuals attach to words. This could also be in part due to differences in tribal languages. In this study, attempts were made to ensure that words used in the study were used in a stable way by assigning different individuals to translate and also during the pilot testing of the tools.

11.7.10 Contextual factors: Understanding can be affected by other contextual factors such as test anxiety, memory function, personal mood and others. It is very difficult to determine the effects of such contextual factors. During the collection of data, the research team members were encouraged to ensure that they limited the possibility of anxiety by making the participant feel comfortable to discuss freely.

11.7.11 Translation of FGDs from ChiChewa into English – translation could have resulted in some loss of meaning in some cases. This was minimised by using experienced assistants to do the transcriptions.

11.7.12 Long term effects of the intervention could not be evaluated due to logistical challenges. This is suggested as an item for future research. It would be important to test

how well an intervention such as this one works much later after the intervention e.g. after three months, as was done by the researcher in the first phase of the current study.

11.7.13 Effects of time. It is possible that understanding may have been high on enrolment but might have faded by the time the assessment for the current study was conducted. If this was the case, that type of understanding would be classified as short term recall. While the current study did not assess long term recall, the use of a life story (comparable to biblical parables) was aimed at creating long term recall (Calvert & Tart, 1993).

11.7.14 Generalisability of findings: The study was only conducted in Malawi, which has its own unique social settings. The findings can therefore not necessarily be generalized to other HPTN035 sites or to HIV prevention sites in general.

11.7.15 Effects of rural vs urban areas: The two sites in Malawi are situated in urban areas. As such, all the respondents who participated in both the microbicide study and this study were based in urban areas. The findings can therefore not necessarily be generalized to rural environments.

11.7.16 A small number of study staff was involved. At each site, informed consent was the responsibility of a select few staff members who had been trained to administer the informed consent process. These staff may not have been representative of all study staff, so their role must be viewed with some caution.

11.7.17 Exclusion of participants from no-treatment arm – Participants from the no treatment arm were excluded from both phases of the study since the procedures did not apply to them. They might have had very different understanding and attitudes to the trial and might have been valuable to include even if not able to participate in all aspects of the trial.

11.7.18 Negative trial – The microbicide trial participants experienced what can be termed a negative trial. The results were negative and the participants were apprised on the findings.

This reality went against what they could have expected or assumed. The negative results could have improved their understanding about research.

11.8 SUMMARY

In this chapter, the study hypotheses were presented against the findings and research questions were answered. A brief discussion of the main findings from the two phases of the current study was also presented. The chapter also presented clarifications of the four main premises on which the study was based. Overall, the findings from the study led to the confirmation of all premises and assumptions. The chapter also discussed usefulness of the proposed taxonomy for understanding clinical trial procedures. The findings from the study confirm the usefulness of the proposed taxonomy as a tool that can be used in understanding of the concepts under study. During the implementation of the study, there were various challenges that the researcher faced. These challenges were highlighted in the chapter, including the various ways in which some of the challenges were addressed by the research. The final section in the chapter presented some limitations of the current study. While the study had its own limitations, the findings may nonetheless be valuable as they present some important lessons in efforts to improve informed consent, more importantly, in an African clinical trials setting.

CHAPTER 12

MAJOR CONCLUSIONS AND RECOMMENDATIONS

12.0 INTRODUCTION

In this chapter, an overview of the main findings, major conclusions and recommendations are presented. This chapter comprises different sections, including an overview of study findings, implications of the findings towards informed consent, and recommendations for practice, policy and further research.

12.1 OVERVIEW OF MAIN STUDY FINDINGS

This research arose from considerable evidence from literature and the field that, despite efforts to simplify language and clarify trial information, participants in clinical trials still seem to have challenges in understanding clinical trial procedures. The primary objective of the study was to assess HIV preventive microbicide trial research participants' understanding of randomisation, double-blinding and the use of placebo in the microbicide trial. The study was also aimed at assessing trial participants' awareness of personal implications of the procedures under study, as well as their attitudes towards the three trial procedures. The study identified about two thirds of the microbicide study participants who had low levels of understanding of the concepts under study. The study also established that more than half of respondents had negative attitudes towards the three concepts. The study has confirmed findings from other studies that have found that many participants do not understand randomisation, double-blinding and placebo use. An intervention which was developed and implemented as part of this study had some positive findings. Findings from the evaluation of the intervention suggest that it was useful in improving understanding of the key concepts under study. The findings also suggest that the intervention was useful in changing respondents' attitudes towards

randomisation and double-blinding. The impact on attitudes towards placebo use was positive but not statistically significant.

This study has illustrated the importance of adequate information and explanation in facilitating understanding, which is important in the making of an informed decision. The pattern of the results on the three concepts suggests that providing information to participants in the way that is currently accepted as best practice by both research ethics committees and IRBs, is unlikely to be helpful if not accompanied by more innovative ways of ensuring that the information is accessible. More importantly, the study has proven that, if information on these scientific procedures is provided in a meaningful, structured and complete way, it is possible to facilitate adequate understanding. Based on the findings, some conclusions and recommendations for theory, practice and further research are presented in the next sections.

12.2 CONCLUSIONS AND IMPLICATION OF FINDINGS FOR INFORMED CONSENT

This research, the first phase of which was carried out in real research settings (within the context of a real trial), has confirmed the challenges that researchers have in explaining trial procedures and research in general. The second (intervention) phase was implemented after the microbicide trial had come to an end was hypothetical in nature. The findings from both the first and second phases of this study have implications for informed consent. Informed consent is taken to be a process during which individuals are empowered to make decisions that are meaningful to themselves and that are based on adequate information. The findings have confirmed the important role that information disclosure plays in facilitating understanding. Faden and Beauchamp (1980) have emphasised the role of information disclosure in ensuring comprehension essential for informed consent. The study has confirmed that, while trial

information that is provided through various means (written and verbal form) conforms to current best practices, the information does not necessarily enable potential participants to adequately understand important aspects of the research and therefore make adequately informed judgements (Agre *et al*., 2003; Agre & Rapkin, 2003; Davis *et al*., 1998; Ellis *et al.* 2002; Kripalani *et al*., 2008; Ryan *et al*., 2008; Wray *et al*., 2005).

The findings from the study further confirm that the consent that some trial participants granted cannot be regarded as truly informed, as the study found that about two-thirds of the respondents had inadequate understanding of the procedures of randomisation, double-blinding and placebo use, all of which are important in understanding the study itself and the personal implications of participation. The findings from the intervention phase are a clear empirical demonstration that it is possible to disclose technical information about research procedures using terms that can be clearly understood. The results indicate that clear descriptions of study procedures need to be supplemented with accessible explanations for the potential research participants to understand a research perspective, rather than treatment perspective (Robinson *et al*., 2005). While in the assessment before the intervention, the study found that formal education did have a statistically significant effect on understanding, the findings after the intervention confirm that research participants with or without some formal education are capable of understanding research procedures if these are explained adequately.

The majority of participants in this study indicated that they benefited most from orally provided information. Currently, sponsors and GCP guidance emphasise written information. Ethics committees also put a lot of effort into the review of informed consent documents and it is possible that very little scrutiny is placed on orally provided information. Some of the supplementary materials (including videos) that were reviewed by the researcher were mere repetitions of the information that is provided through the written documents. Written

information cannot be tailored to a specific individual and yet oral information can be adjusted to suit the needs of a specific individual (Robinson *et al*., 2005). This emphasis on written information by sponsors, GCP guidance and research ethics committees, while it ensures that there is legal proof of the information having been disclosed, is not based on the best practices according to the expectations of potential and current research participants.

The findings on understanding of trial procedures that are presented may be important for researchers, research team members and research ethics committees. By highlighting the fact that some participants have challenges understanding of the concepts under study, these findings emphasise the need for researchers and ethics committee members to think about ways in which the understanding can be improved. The intervention which was tested through this study may guide other researchers in thinking about how understanding can be improved. More importantly, the evidence from the intervention is encouraging as it serves as empirical proof that understanding can be improved if researchers use accessible language and examples that demystify research, and present it as a tool which is aimed at improving health care decisions and tools. The findings regarding the effect of the intervention on attitudes is also an important message for researchers. It shows that if potential research participants are adequately apprised on the study and all its procedures, they will appreciate the usefulness of the procedures, even if some of the procedures may not benefit them as individuals. The important issue is for the participants to be clear that they are being invited to participate in a study involving certain procedures so they become aware of the procedures and their personal implications. That way, when the individuals are making decisions, their decisions are better informed and more rational. The findings suggest that expectations about normal treatment decisions may make it difficult for participants to appreciate information about trial procedures. Innovative ways have to be identified to deal adequately with these expectations.

Data should be collected to monitor participants' understanding of the study and to guide additional efforts where necessary. Participants' understanding should continue to be evaluated and, where necessary, measures put in place to address deficiencies. Questions on comprehension can be included in the regularly administered data collection questionnaires. Study monitors and research ethics committee members can assist in conducting this assessment. The tests that are often employed by researchers in assessing participants' understanding of studies are more appropriate for assessing short term recall, which is not an adequate indication of understanding (Wendler, 2004). Assessments need to include checklists of understanding of technical information, as well as responses to narratives or vignettes related to participation. Lindegger and Richter (2000) caution, however, that research staff need to be aware of the phenomenon of social desirability – the tendency of participants to respond in a way that wins them the approval of the investigators.

While all the above recommendations may take up time and resources, they are important since study participants need to be informed so as to be in a better position to protect themselves. While improving informed consent may not necessarily reduce the risks involved in a particular study, it helps to ensure that people are responsible for their participation, as well as for their health. Participants' understanding is very important in microbicide studies in particular, where participants themselves must administer the study product before each sex act. Well informed participants are more likely to be adherent to follow-up schedules and microbicide application procedures (Kilmarx *et al*., 2001). With all the problems and controversies surrounding microbicide studies (Singh & Mills, 2005; Slack et al., 2005; Wassenaar & Ijsselmuiden, 2007; Vallely et al., 2009), there remains a need to ensure that participants adequately understand essential study concepts.

Finally and more importantly, the results from this study may encourage researchers to engage in efforts aimed at evaluating their informed consent procedures and documents instead of just relying on documents that are based on institutional templates or some readability scores, which may not mean much when the same documents will be translated into a local language. It is not possible to tailor written information to the needs of a specific individual but it is possible to tailor it to the needs of a specific group after conducting a needs assessment study of that group. Research ethics committees should move beyond simply requiring evidence of an informed consent document based on a template, to focusing on documents that meet the information needs of the groups on which the study will be conducted. Research ethics committees may ask for evidence of the evaluation of informed consent documents.

12.3 RECOMMENDATIONS

While the findings of this study have limited generalisability, it is hoped that the study indicates possible ways of improving future studies. Based on the above findings and their interpretation, it is possible to provide some recommendations. The recommendations below are presented with caution due to some of the study weaknesses that have been highlighted in Section 11.7:

12.3.1 Theoretical recommendations

- Some informed consent practices which are driven by trial sponsors and national laws may emphasise fulfilling legal aspects of informed consent without necessarily focusing on adequate understanding. It is important to note that while these practices are accepted legally, they may not lead to adequate informed consent, which is a moral, not a legal requirement. Research on informed consent needs to focus on the need for fulfilling both legal and moral requirements.

- Some literature that has been cited in the literature review has not addressed the question of the cut-off point regarding how much information is adequate to be labeled as having understood the clinical trial procedures. This study has suggested a standard of 75 percent that can be used in assessing understanding of the three procedures under study as it addresses what needs to disclosed. Research on informed consent needs to come up with some reliable criteria for adequate understanding of study purpose, procedures and implications.
- Several studies have confirmed that some participants find it difficult to understand trial procedures. The current study has provided evidence that individuals can understand scientific procedures if appropriately assisted to do so. There is a need for informed consent researchers to go beyond the identification of challenges to the identification of solutions. This study has attempted to illustrate one such possible solution.
- The current study has suggested the usefulness of the taxonomy on the understanding of clinical trial procedures. In this study, it was found to be useful in explaining various levels of understanding. The taxonomy is offered for further testing and use.

12.3.2 Recommendations for practice and policy

- The results of the study confirm other findings from other studies reviewed in Chapter 2 and suggest that there is a need to improve informed consent practices in HIV preventive microbicide clinical trials and research in general. Researchers need to develop informed consent documents which are based on the needs of the target groups, and develop orally provided information to supplement the written information.
- Research ethics committees need to develop ways of encouraging and monitoring the information that is provided orally. From the researcher's interactions with research

ethics committees, it is evident that research ethics committees are mostly interested in written information.

- Researchers are encouraged to use an intervention such as the one used in this study before obtaining informed consent and during long trials, so that they can satisfy themselves that the consent to be granted will be based on improved understanding.
- Researchers need to continuously find better ways of explaining concepts that are culturally acceptable and appropriate.
- Staff and researchers need to be sensitised to the importance of providing information on justification of and personal implications of research participation and study procedures to participants. By improving levels of understanding among trial participants, researchers may also play an important role in influencing potential trial participants' understanding of the personal implications of the procedures, as well as attitudes towards the trial procedures.
- Researchers conducting research on sensitive areas such as HIV vaccine and microbicide trials may need to involve other parties such as research participant advocates, CABs, NGOs and others in informed consent to minimise conflict of interest.

12.3.3 Recommendations for further research

Due to the limitations of the current study, further research should focus on the following areas:

- There is a need for further research to identify effective ways of helping participants to understand research and be able to distinguish between research and routine treatment.
- There is a need for further testing of this intervention with a larger group, using various designs and in various settings. For example, a new study may test the intervention at

various sites with some sites having two arms and some having a single arm. This can assist in addressing confounders. The approach and tools can be modified and tested in other types of research such as behavioural studies.

- The method used in this study assessed understanding in the short term since the impact of the intervention was tested immediately after implementation. There is a need for further research to test understanding in ongoing trials in the long term rather than in the short term. Participants in both arms can be tested after six months and one year. Long term understanding may be important for longitudinal studies such as vaccine and microbicide studies.
- There is a need to investigate the effect of improved understanding on accrual. This study did not impact on accrual or retention in any way as the intervention was implemented at the end of the microbicide trial.
- This study has amplified the call for more studies in African settings. The majority of studies on informed consent have been conducted in developed country settings.
- Given the diversity of cultural beliefs, traditions and values, future studies may need to consider the complex mix of possible influences on decision making. Such studies for example could look at the role of Ubuntu, hierarchical society and other cultural practices including culture specific behaviours in informed consent.

REFERENCES

Abdool Karim, Q., Abdool Karim, A.S., Coovadia, H., & Susser, M. (1998). Informed consent for HIV testing in a South African Hospital: Is it truly informed and voluntary? *American Journal of Public Health, 88*, 637-640.

Abdool Karim, Q., Abdool Karim, P.S., Hoge, S.K., & Leadbetter, R.A. (2003). Competence to contest to research among long-stay inpatients with chronic schizophrenia. *Psychiatric Services, 54*. Retrieved October 2, 2008, from http://psychservices.psychiatryonline.org.

Abdool Karim, Q., Abdool Karim, S.S., Frohlich, J.A., Grobler, A.C., Baxter, C., Mansoor, L.E., Kharsany, A.B., Sibeko, S., Mlisana, K.P., Omar, Z., Gengiah, T.N., Maarschalk, S., Arulappan, N., Mlotshwa, M., Morris, L., & Taylor, D., (2010). Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. *Science, 329.* 1168 – 1174.

Abdool Karim, S.S., & Baxter, C. (2009). Antiretroviral prophylaxis for the prevention of HIV infection: future implementation challenges. *HIV Therapy, 3*, 3-6.

Abebe, S. (1996). Physician-patient interaction in a prenatal clinic in Addis Ababa, Ethiopia: A study to assess the communication style of the physicians and its effect on patient outcome. Unpublished doctoral dissertation, Johns Hopkins University, Baltimore, Maryland USA.

Abrahams, R. (1983). *African folktales: Traditional stories of the black world*. New York: Pantheon Books.

Agard, A., Hermeren, G., & Herlitz, H. (2001). Patients' experiences of intervention trials on the treatment of myocardial infarction: Is it time to adjust the informed consent procedure to the patients' capacity? *Heart, 86*, 632-637.

Agre, P., Campbell F.A., Goldman, B.D., Boccia, M.L., Kass, N., McCullough ,L.B., Merz, J.F., Miller, S.M., Mintz, J, Rapkin, B, Sugarman, J, Sorenson, J., & Wirshing, D. (2003). Improving informed consent: The medium is not the message. *IRB: Ethics and Human Research*, *25*, S11-S19.

Agre, P., & Rapkin, B. (2003). Improving informed consent: A comparison of four consent tools. *IRB: Ethics and Human Research*, *25*, 1-7.

Alliance for Microbicide Development. (2007). *The Microbicide Quarterly, 5*, 11-12.

Annas G., & Grodin M. (1998). Human Rights and Maternal-Fetal HIV Transmission Prevention Trials in Africa. *American Journal of Public Health, 88,* 562.

Arnold, J. H., & Feldman, D.C. (1981). Social desirability response bias in self-report choice situations. *Academy of Management Journal, 24,* 377-385.

Appelbaum, P. S. (2002). Clarifying the ethics of clinical research: A path toward avoiding the therapeutics misconception. *American Journal of Bioethics, 2,* 22-23.

Appelbaum, P.S., Grisso, T., Frank, E., O'Donell, S., & Kupfer, D.J. (1999). Competence of depressed patients for consent to research. *American Journal of Psychiatry*, *156,* 1380-1380.

Appelbaum, P.S., Roth, L.H., Lidz, P., & Winsdale, W. (1987). False hopes and best data: Consent to research and the therapeutic misconception. *Hastings Center Report, 17,* 20-24.

Babbie, J., & Mouton, J. (2001). *The practice of social research*. Cape Town. Oxford University Press.

Barnett, K, Harrison, C., Newman, F., Bentley, C., & Cummins, C. (2005). A randomised study of the impact of different styles of patients' leaflets for randomised controlled trials on children's understanding. *Archives of Diseases in Childhood, 90*, 1097-1098

Barrett, R. (2005). Quality of informed consent: Measuring understanding among participants in oncology clinical trials. *Oncology Nurse Forum*, *32*, 751-755

Barron, J. S., Duffey, P. L., Byrd, L. J., Campbell, R., & Ferrucci, L. (2004). Informed consent for research participation in frail older persons. *Aging Clinical & Experimental Research Journal*, *16*, 79-85.

Barsdorf, N., Maman, S., Kass, N., & Slack, C. (2009). Access to treatment in HIV prevention trials: Perspectives from a South African community. *Developing World Bioethics.* Retrieved on 10 January 2010 from http://www3.interscience.wiley.com/journal/122610532/. doi:10.1111/j.1471-8847.2009.00265.x

Bartholow, B.N., Buchbinder, S., Celum, C., Goli, V., Koblin, B., Para, M., Marmor, M., Novak, R.M., Mayer, K., Creticos, C., Orozco-Cronin, P., Popovic, V., & Mastro, T.D. (2005). HIV sexual risk behavior over 36 months of follow-up in the world's first HIV vaccine efficacy trial. *Journal of Acquired Immune Deficiency Syndrome, 39*, 90-101.

Barouch, D.H. (2008). Challenges in the development of an HIV-1 vaccine. *Nature*, *455*, 613-619.

Bartlett, J., Kotrlik, J., & Higgins, C. (2001). Organisational Research: Determining appropriate sample size in survey research. *Information Technology, Learning and Performance Journal, 19*, 43-50.

Baskin, S.A., Morris, J., Ahronheim, J.C., Meier, D.E., & Morrison, H.R.S. (1998). Barriers to obtaining informed consent in dementia research: Implications for surrogate-decision making. *Journal of American Geriatric Society, 46*, 287-290.

Beauchamp, T.L., & Childress, J.F. (2001). *Principles of biomedical ethics.* 4th ed. New York: Oxford University Press.

Belkin, G.S. (2006). Misconceived bioethics? The misconception of the “therapeutic misconception”. *International Journal of Law and Psychiatry. 29,* 75-85.

Benhardt, B.A., Geller, G., Strauss, M., Helzlsouer, K.J., Stefanek, M., Wilcox, P.M., & Holtzman, N.A. (1997). Toward a model informed consent process for BRCA1 testing: A

qualitative assessment of women's attitudes. *Journal of Genetic Counselling, 6*, 207-222.

Berkley, S. (2003). Thorny issues in the ethics of AIDS vaccine trials. *Lancet, 362,* 992.

Bernard, H.R. (2000). *Social research methods: Quantitative approaches*. London: Sage Publications.

Bernstein, A. (2008). An HIV/AIDS vaccine: Where do we go from here? *Trends in Microbiology*, *16,* 553-554.

Bhutta, Z. (2004). Beyond informed consent. *Bulletin of the World Health Organization*, *82,* 771-777.

Bjorn, E., Rossell, P., & Holm, S. (1999). Can written information to research subjects be improved? An empirical study. *Journal of Medical Ethics*, *25,* 263-267.

Blayne, C., & Justman, J. (2008). Vaginal microbicides and the prevention of HIV transmission. *Lancet Infectious Diseases, 8,* 685 – 697.

Brahams, D. (1988). Randomised trials and informed consent. *Lancet*, *8618,* 1033-1034.

Brehaut, J.C., Lott, A., Fergusson, D. A. Shojania, K.G., Kimmelman, J., & Saginur, R. (2008). Can Patient decision aids help people make good decisions about participating in clinical trials? A study protocol. *Implementation Science, 3* (38) Retrieved 16 September 2009, from http://www.implementationscience.com/content/3/1/38/abstract

Brody, H., & Miller, F.G. (2003). The clinician-investigator: Unavoidable but manageable tension. *Kennedy Institute of Ethics Journal, 13*(4), 329-346.

Buchbinder, S., Wheeler, S., Vittinghoff, E., McKirnan, D., Celum, C., Mayer, K., Fuchs, J., Para, M., Novak, R., & Barthlow, B. (2003). *Declines in risk behaviour are small in Phase III vaccine trial participants than in a non-vaccine trial control group.* Abstract of paper presented at AIDS Vaccine Conference, September 2003, New York.

Busby-Grant, J., Mackinnon, A.J., Christensen, H., & Walker, J. (2009). Participants' perceptions of motivation, randomisation and withdrawal in a randomised controlled trial of interventions for prevention of depression. *Journal of Medical Ethics, 35,* 768-773.

Calvert, S.L., & Tart, M. (1993). Song versus verbal forms for very-long-term, long-term, and short-term verbatim recall. *Journal of Applied Developmental Psychology, 14*, 245-260

Campbell, F.A., Goldman, B.D., Boccia, M.L., & Skinner, M. (2004). The effect of format modifications and reading comprehension on recall of informed consent information by low-income parents: A comparison of print, video, and computer-based presentations. *Patient Education Counselling, 53,* 205-216.

Cassel, M.M., Halperin, D.T., Shelton, J.D., & Stanton, D. (2006). Risk compensation: the Achille's heel of innovations in HIV prevention? *British Medical Journal*, *332*, 605-607. Retrieved on 17 March 2006, from www.bmj.bmjjournals.com/cgi/content/full/332/7541/605.

Cates, W., & Feldblum, P. (2008). HIV prevention research: The ecstasy and the agony. *Lancet, 372*, 1932-3.

Charmaz, K. (2005). Grounded theory in the 21st Century: Applications for advancing Social Justice Studies. In Denzin, N. and Lincoln, Y. (Eds.) *Handbook of qualitative Research*. 3rd Edition. London: Sage Publications.

Chingono, A., Lane, T., Chitumba, A., Kulich, M., & Morin, S. (2008). Balancing science and community concerns in resource-limited settings: Project ACCEPT in rural Zimbabwe. *Clinical Trials, 5*, 273-276.

Christakis, N. (1988). The ethical design of an AIDS vaccine trial in Africa. *Hastings Center Report, 18,* 142-147.

Coggins, C., & Elias, C. (2000). Safety of three formulations of nonoxynol-9 containing vaginal spermicides. *International Journal of Gynaecology and Obstetrics, 68,* 267-8.

Cohen, J. (2000). AIDS Researchers Look to Africa for New Insights. *Science,* 287, 942.

Cohen J. (2005). Cameroon Suspends AIDS Study. *Science Now*, 2005. Feb. 4, 2005.

Colletti, A.S., Heagerty, P., Sheon, A.R., Gross, M., Koblin, B.A., Metzger, D.S., & Seage, G.R. (2003). Randomised controlled evaluation of a prototype informed consent process for HIV vaccine efficacy trials. *Journal of Acquired Immune Deficiency Syndrome,* 32, 161-169.

Coplan, P., Mitchnik, M., & Rosenberg, Z. (2004). Regulatory challenges in microbicide development. *Science*, *304,* 1911-1912.

Cornelli, A.C., Bentley, M.E., Sorenson, J.E., & Henderson, G.E. (2006). Using formative research to develop a context-specific approach to informed consent for clinical trials. *Journal of Empirical Research on Human Research Ethics*, *1,* 45-60.

Coyne, C.A., Xu, R., Raich, P., Plome, K., Dignan M, Wenzel, L.B., Fairclough, D., Haberman, T., Schnell, L., Quella, S., & Cella, D. (2003). Randomised controlled trial of an easy to-read informed consent statement for clinical trial participation: a study of the Eastern Cooperative Oncology Group. *Journal of Clinical Oncology, 21,* 836-842.

Cracowski J.L., & Paris, A. (2005). How to improve patients' understanding in biomedical research. *Archives of Diseases in Childhood*, *90,* 1097-1098.

Creed – Kanashiro, H., Ore, B., Scurrah, M., Gil, A., & Penny, M. (2005). Conducting research in developing countries: experiences of the informed consent process from community studies in Peru. *Journal of Nutrition*, *135*, 925 – 928.

Creswell, J.W. (2003). *Research Design. Qualitative, quantitative and mixed methods approaches.* 2nd Edition. London: Sage Publications.

Creswell, J.W., & Plano Clark, V.L. (2007). *Designing and conducting mixed methods research.* Thousand Oaks: Sage Publications.

Daugherty, C.K. (1999). Impact of therapeutic research on informed consent and the ethics of clinical trails: A medical oncology perspective. *Journal of Clinical Oncology*, 17, 1601-1617.

Daugherty, C.K., Fitchett, G., Murphy, P.E., Peterman, A.H., Banik, D.M., Hlubocky, F., & Tartaro, J. (2005). Trusting God and medicine: spirituality in advanced cancer patients volunteering for clinical trials of experimental agents. *Psycho-oncology, 14,* 135-46.

Davis, T.C, Holcombe, R.F., Berkel, H.J., Pramanik, S., & Divers, S.G. (1998). Informed consent for clinical trails: a comparative study of standard versus simplified forms. *Journal of the National Cancer Institute*, *90,* 668-674.

Dawes, P.J.D., O'keefe, L., & Adcock, S. (1992). Informed consent: The assessment of two structured interview approaches compared to the current approach. *The Journal of Laryngology and Otology*, *106,* 420-424.

Dawson, L., & Kass, N.E. (2005). Views of US researchers about informed consent in international collaborative research. *Social Science & medicine*, 61, 1211-1211.

Denzin, N.K. (1994). Triangulation in educational research. In T. Husen T. and T.N., Postlewaite. (Eds.) *The international encyclopedia of Education.* Oxford: Pergamon.

Denzin, N.K., & Lincoln, Y.S. (Eds.) (1994). *Handbook of qualitative research*. Thousand Oaks: Sage Publications.

Descombe, M. (1998) *The good research guide for small-scale social research projects.* Buckingham: Open University Press.

de Zoysa, I., Ellias,C.J., & Bentley, M.E. (1998). Ethical challenges in efficacy trials of vaginal microbicides for HIV prevention. *American Journal of Public Health*. *88,* 571-75.

Di Blasi, Z., Kaptchuk, T.J., Weinman, J., & Kleijnen, J. (2002). Informing participants of allocation to placebo at trial closure: Postal survey. *British Medical Journal, 325*, 1329. Retrieved on 29 October 2005, from www.British Medical Journal.com on 29 October 2005. doi: 101136/*British Medical Journal,325*.7376.1329.

Donaldson, M. (1992). *Human Minds*, London: Allen Lane

Doumbo, O.K. (2005). It takes a village: Medical research and ethics in Mali. *Science 307*, 679-681.

Dunn, L.B., & Jeste, D.V. (2001). Enhancing informed consent for research and treatment. *Neuropsychopharmacology, 24*, 595-607.

Dunn, L.B., & Jeste, D.V. (2003). Problem areas in the understanding of informed consent for research: study of middle-aged and older patients with psychotic disorders. *Psychopharmacology*, *171*, 81-85. Doi: 10.1007/500 213-003-1501-3.

Dunn, L.B., Lindamer, L.A, Palmer, B.W., Golshan, S., Schneirderman, L.J., & Jeste, D.V. (2002). Improving understanding of research consent in middle-aged and elderly patients with psychotic disorders. *American Journal of Geriatric Psychiatry*, *10,* 142-150.

Dunn, L.B.,Nowrangi, M.A., Palmer, B.W., Jeste, D.V., & Saks, E.R. (2006). Assessing decisional capacity for clinical research or treatment: a review of instruments. *American Journal of Psychiatry, 163*, 1323-1334.

Dunn, L.B., Palmer, B.W., & Keehan, M. (2006). Understanding of placebo controls among order people with schizophrenia. *Schizophrenia Bulletin, 321,* 137-146.

Dunn, L.B., & Palmer, B.W., Keehan, M., Jeste, D.V., & Appelbaum, P.S. (2006). Assessment of therapeutic misconception in older schizophrenia patients with a brief instrument. *American Journal of Psychiatry*, *163,* 500-506.

Eder, M.L.,Yamokoski, A.D, Wittman, P.W., & Kodish, E.D. (2007). Improving informed consent: Suggestions from parents of children with leukemia. *Pediatrics, 119,* e849-

e859. Retrieved November 2, 2008 from http:// www.pediatrics.org/cgi/concent/ full/119/4/e849

Edwards, S.J.L., Lilford, R.J., & Hewison, J. (1998). The ethics of randomised controlled trials from the perspectives of patients, the public, and healthcare professionals. *British Medical Journal*, *317,* 1209-1212.

Elbourne, D, Snowdon,C., & Garcia, C. (1997). Subjects may not understand concept of clinical trials. *British Medical Journal, 315,* 247.

Ellenberg, S.S., & Temple, R. (2000). Placebo controlled trials and active-control trials in the evaluation of new treatments. *Annals of Internal Medicine*, *133*, 464-470

Elliott, C., & Abadie, R. (2008). Exploiting a research underclass in Phase 1 clinical trails. N*ew England Journal of Medicine, 358*, 2316-2317.

Ellis, P.M., & Butow, P.N. (1998). Focus group interviews examining attitudes to randomised trials among breast cancer patients and the general community. *Australia New Zealand Journal of Public Health, 22,* 528-531.

Ellis, P., Butow, P., Tattersall, S., Dunn, S., & Houssami, N. (2001). Randomised clinical trials in oncology: Understanding and attitudes predicts willingness to participate. *Journal of Clinical Oncology*; *19*, 3554-3561.

Ellis, P.M., Butow, P.N., & Tattersall, M.H.N. (2002). Informing breast cancer patients about clinical trials: a randomised clinical trail of an educational booklet. *Annals of Oncology, 13,* 1414-1423.

Ellis, P.M., Dowsett, S.M., Butow, P.N., & Tattersall, M.H.N. (1999). Attitudes to randomised clinical trials amongst out-patients attending a medical oncology clinic. *Health Expectations, 2,* 33-43.

Emanuel, E.J., & Miller, F.G. (2001). The ethics of placebo-controlled trials: A middle ground. *New England Journal of Medicine, 345*:915–919.

Eriksson, S., & Helgesson,G. (2005). Keep people informed or leave them alone? A suggested tool for identifying research participants who rightly want only limited information. *Journal of Medical Ethics*, *31,* 674-678.

Esparaza, J., & Bhamarapravati, N. (2000). Accelerating the development of future availability of AIDS vaccines. *Lancet, 355*, 206-216.

Excler. J. Rida, W. Priddy, F. Fast, P., & Koff, W. (2007). A strategy for accelerating the development of preventive AIDS vaccines. *AIDS, 21,* 2259-2263.

Faden, R., & Beauchamp, T.L. (1980). Decision making and informed consent: A study of the impact of disclosed information. *Social Indicators Research, 7*, 313-336.

Feartherstone, K., & Donovan, J. (1998). Random allocation or allocation at random? Patient's perspectives of participation in a randomised controlled trial. *British Medical Journal, 317,* 1177-1180.

Featherstone, K., & Donovan, J.L. (2002). Why don't they just tell me straight, why allocate it? The struggle to make sense of participating in a randomised controlled trial. *Social Science & Medicine*, *55,* 709-719.

Feldblum, P.J., Welsh, M. J., & Steiner, M.J. (2003). Don't overlook condoms for HIV prevention. *Sexually Transmitted Infections, 79*, 268-9.

Ferguson, P.R. (2000). Patients' perceptions of information provided in clinical trails. *Journal of Medical Ethics, 28,* 45-48.

Ferguson, P.R. (2003). Information giving in clinical trails: The view of medical researchers. *Bioethics, 17,*101-111.

Fitzgerald, D.W., Marotte, C., Verdier, R.I., Johnson, W.D., & Pape, J.W. (2002). Comprehension during informed consent in a less-developed country. *Lancet, 26,* 1301-1302.

Flory, J., & Emanuel, E. (2004). Interventions to improve research participants understanding in informed consent for research- A systematic review. *Journal of American Medical Association*, *292,* 1593-1601.

Foss, A.M., Vickerman, P.T., Heise, L., & Watts, C.H. (2003). Shifts in condom use following microbicide introduction: Should we be concerned? *AIDS, 17*, 1227-1237.

Freedman, B. (1990). Placebo controlled trails and the logic of clinical purpose. *IRB: A review of Human subjects Research*, *12,* 1-6.

Freedman, B., Fuks A., & Weijer, C. (1992). Demarcating research and treatment: a systematic approach for the analysis of the ethics of clinical research. *Clinical Research*, *40,* 653–660.

Friedland, B., De Kock, A.., Marumo,P.M., Ngcozela, V., Monedi C., Skoler, S., McGrory, E., & Van De Wijgert, J. (2004). Development of recruitment video for a phase 3 trial of Carraguard (abstract). *International Conference on AIDS*, 2004 Jul, 1-16; 15 (Abstract Number ThPeC7585).

Fureman, I., Myers, K., Mcllellon, T., Metzger, D., & Woody, G. (1997). Evaluation of a video supplement to informed consent: Injecting drug users and preventive HIV vaccine efficacy trials. *AIDS Education and Prevention*, *9,* 330-341.

Gay, L.R., & Airasian, P. (2003). *Educational research: Competencies for analysis and applications.* New Jersey: Prentice Hall

Gecau, R. (1970). *Kikuyu folktales: Their nature and value.* Nairobi: East African Literature Bureau.

Geissler, W.P., Kelly, A., Imoukhuede, B., & Pool, R. (2008). 'He is like a brother, I can give him some blood' – Relational ethics and material exchanges in a malaria vaccine 'trial community' in the Gambia. *Social Science & Medicine, 67*, 696-707.

Gikonyo, C., Bejon, P., Marsh,V., & Molyneux, S. (2008). Taking social relationships seriously: Lessons learned from the informed consent practices of vaccine trials on the Kenyan coast. *Social Science & Medicine, 67*, 708-720.

Goodyear, M.D., Lemmens, T., Sprumont, D., & Tangwa, G. (2009). Does the FDA have the authority to trump the Declaration of Helsinki? *British Medical Journal, 338*: b1559.

Glogowska, M., Roulstone, S., Enderby, P., Peters, T., and Campbell, R. (2001). Who's afraid of the randomised controlled trial? Parents views of an SLT research study. *Journal of Language and Communication Disorders, 36*, 499-504.

Green, J., and Thorogood, N. (2004). *Qualitative methods for health research*. London: Sage Publications.

Greene, J.C., & Caracelli, V.J. (2003). Making paradigmatic sense of mixed-method practice. In Tashakkorri. A., and Teddlie, C. (Eds). *Handbook of mixed methods in social and behavioural research.* Thousand Oaks: Sage.

Greenhalgh, T., & Taylor, R. (1997). How to read a paper: Papers that go beyond numbers (qualitative research). *British Medical Journal, 315*, 740-743.

Grisso, T., and Appelbaum, P.S. (1998). *Assessing competence to consent to treatment: A guide for physicians and other health professionals*. New York: Oxford University Press.

Grossman, S.A., Piantadosi, S., & Covahey, C. (1994). Are informed consent forms that describe clinical oncology research protocols readable by most patients and their families? *Journal of Clinical Oncology*, *12,* 211-2215.

Groves, R.M. (1989). *Survey errors and survey costs.* New York: Wiley.

Hanson, W.E., Creswell, J.W., Plano-Clark, V.L., Petska, K.S., & Creswell, J.D. (2005). Mixed methods research designs in counselling psychology, *Journal of Counselling Psychology, 52,* 224-235.

Harries, A.D., Libamba, E., Schouten, E.J., Mwansambo, A., Salaniponi, F.M., & Mpazanje, R. (2004). Expanding antiretroviral therapy in Malawi: drawing upon the country's experience of tuberculosis. *British Medical Journal, 329*, 1163-6.

Harrison, K., Vlahov, D., Jones, K,. Charron, K., & Clements, M.L. (1995). Medical eligibility, comprehension of the consent process, and retention of injection drug users recruited for an HIV vaccine trial. *Journal of Acquired Immune Deficiency Syndrome, 10,* 386-390.

Hearst, N., & Chen, S. (2004). Condom promotion for AIDS prevention in the developing world: Is it working? *Studies in Family Planning. 35,* 39-47.

Heitenan, P., Aro, A.R., Holli, K., & Absetz, P. (2000). Information and communication in the context of a clinical trial. *European Journal of Cancer*, *36,* 2096-2104.

Hellman, S., & Hellman, D.S. (1991). Sounding board: Of mice but not men: Problems of the randomised clinical trial. *New England Journal of Medicine*, *324,* 1585-1589.

Henderson, G.E., Esther, M.M., Zimmer, C., King, N.M., Davis, A.M., Rothschild, B.B., Churchill, L.R., Wilfond, B.S., & Nelson, D.K. (2005). *Social Science & Medicine*. *62,* 239-253.

Hill, Z., Tawiah-Agyemang, C., Odei-Danso, S., & Kirkwood, B. (2008). Informed consent in Ghana: What do participants really understand? *Journal of Medical Ethics*, *34,* 48-53.

Hochhauser, M. (2005). The multiple comprehensions of informed consent. *Drug Information Association Forum*, *41,* 22-23.

Hochhauser, M. (2008). Consent comprehension in the 21st century: What is missing? *Drug Information Journal*, *42,* 375-384.

Howze, E. (2009). Building Health Promotion Capacity in Developing Countries: Strategies From 60 Years of Experience. *United States Health Education & Behavior*, *36,* 464-475.

Hunt, L.M., & de Vougd, K.B. (2007). Are good intentions good enough? Informed consent without trained interpreters. *Journal of General Internal Medicine*, *22,* 598-605.

Hyder, A.A., & Wali, S.A. (2006). Informed consent and collaborative research: Perspectives from the developing world. *Developing World Bioethics, 6,* 33-40.

IAVI (2010). *IAVI Report*, *14* (2), Published: March-April 2010

IJsselmuiden, C., & Faden, R. (1992). Research and informed consent in Africa - Another look. *New England Journal of Medicine, 326*, 830-834.

Indiana University. (2004). *Internal Audit*. Retrieved 26August 2006, from http://indiana.edu/~iaudit/glossary.html

Israel, G.D. (1992). *Determining sample size*. Retrieved on 21 April 2006, from http://edis.ifas.ufl.edu

Jefford, M., & Moore, R. (2008). Improvement of informed consent and the quality of the informed consent documents. *Lancet Oncology*. *9*, 485-493.

Jimison, H., Sher, P., Appleyard, R., & Le Vernois, Y. (1998). The use of multimedia in the informed consent process. *Journal of the American Medical Informatics Association*, *5*, 245-256.

Joffe,S., Cook, E.F., Clearly, P.D., Clark, J.W & Weeks, J.C. (2001a). Quality of informed consent in cancer clinical trials: A cross-sectional survey. *Lancet*, *358*, 1772-1777.

Joffe, S., Cook, F., Cleary, P., Clark, J., & Weeks, J. (2001b). Quality of informed consent: A new measure of understanding among research subjects. *Journal of the National Cancer Institute, 93,* 139-147.

Johnson, B.R., and Onwuegbuzie, A.J. (2004). Mixed methods research: A research paradigm whose time has come, *Educational Researcher*, *33,* 14-26.

Johnston, M., & Fauci, A.S. (2008). An HIV vaccine — Challenges and prospects. *New England Journal of Medicine, 359*, 888-890.

Juraskova, I., Butow, P., Lopez, A., Seccombe, M., Boyle, F., McCarthy, N., & Forbes, J.F. (2007). Improving informed consent in clinical trials: Successful piloting of a decision aid. *Journal of Clinical Oncology*, *25,* 1443-1444.

Kass, N., Maman, S., & Atkinson, J. (2005). Motivations, understanding and voluntariness in international randomised trials. *IRB: Ethics and Human Research, 27* , 1-8.

Kass, N.E., Sugarman, J., Medley, A.M., Fogarty, L.A., Taylor, H., Daugherty, C., Emerson M.R., Goodman, S.N., Hlubocky, F.J., Hurwitz, H.I., Carducci, M., & Goodwin-Landler, A. (2009). An intention to improve cancer patients' understanding of early-phase clinical trials. *IRB: Ethics & Human Research, 31* (3), 1-10.

Keller, D.M (2010). Tenofovir vaginal gel first microbicide to prevent HIV, HSV infections. AIDS XVIII International AIDS Conference: Abstract TUSS0504. Retrieved from: http://www.medscape.com/viewarticle/725583 2010: Presented July 19, 2010. Retrieved on 29 October 2010.

Kenya Ministry of Health. 2005. *Kenya National guidelines for research and development of HIV/AIDS vaccines*. Nairobi: Ministry of Health.

Kerr, C., Robinson, E., Stevens, A., Braunholtz, D., Edwards, S., & Lilford, R.J. (2004). Randomisation in trials: Do potential trial participants understand it and find it acceptable? *Journal of Medical Ethics, 30,* 80-84.

Khalil, S.S., Silverman, H.T., Raafat, M., El-Kamary, S., & El-Setouhy, M. (2007). Attitudes, understanding, and concerns regarding medical research among Egyptians: a qualitative pilot study. *BMC Medical Ethics,* 8(9). Retrieved May11,2007, from htt//www.biomedcentral.com/1472-6939/8/9.

Kilmarx, P.H., Ramjee, G., Kitayaporn, D., & Kunasol, P. (2001). Protection of Human subjects rights in HIV preventive clinical trials in Africa and Asia: Experiences and recommendations. *AIDS, 15* (Sup.4), 501-507.

Kimmelman, J. (2007). The therapeutic misconception at 25: Treatment, research, and confusion. *Hastings Center Report*, *37,* 36-42.

Kimmelman, J, Weijer, C, & Meslin, E.M. (2009). Helsinki discords: FDA, ethics, and international drug trials. *Lancet, 373,* 13–4.

King, N.M.P., Henderson, G.E., Churchill, L.R., Davis, A.M., Hull, S.C., Nelson, D.K., Parham-Vetter, P.C., Rothschild, B.B., Easter, M.M., & Wildfond, B.S. (2005). Consent forms and the therapeutic misconception: The example of gene transfer research. *IRB: Ethics & Human Research, 27,* 1-8.

Kitamura, T., & Kitamura, F. (2000). Reliability of clinical judgement of patients' competency to give informed consent: A case vignette study. *Psychiatry and Clinical Neurosciences, 54*, 245-247.

Klasse, P.J., Shattock, R., Moore, J.P., & Phillips, P. (2008). Antiretroviral drug–based microbicides to prevent HIV-1 sexual transmission. *Annual Review of Medicine*, *59*, 455-471.

Kon, A., & Klug, M. (2006). Method and practices of investigators for determining participants decisional capacity and comprehension. *Journal of Empirical Research on Human Research Ethics*, *1*, 61-68.

Kovnick, J., Appelbaum, P.S., Hoge, S.K., & Leadbetter, R.A. (2003). Competence to consent to research among long-stay inpatients with chronic schizophrenia. *Psychiatric Services*. *54,* 1247-1252.

Kripalani, S., Bengtzen, R., Henderson, L.E., & Jacobson, T.A. (2008). Clinical research in low-literary population; using teach back to assess comprehension of informed consent and privacy information. *IRB: Ethics & Human Research, 30,* 13-19.

Krosin, .T., Klitzman, R., Levin, B., Cheng, J., & Ranney, M.L (2006). Problems in comprehension of informed consent in rural and peri-urban Mali, West Africa. *Clinical Trials*, *3*, 306-313.

Kruse, A.Y., Kjoergaard, L.L., Krogsgaard, K., Gluud, C., Mortensen, E.L., Gottschau, A., & Bjerg, A.M. (2000). A randomised trial assessing the impact of written information on outpatients' knowledge about and attitude towards randomised clinical trials. *Controlled Clinical Trials*, *21,* 223-240.

Lansimies-Antikainen, H., Laitinen, T., Rauramaa, R., & Pietila, A.M. (2009). Evaluation of informed consent in health research: a questionnaire survey. *Scandinavian Journal of Caring Science*. *R*etrieved September 16,2009 from http://www.ncbi.n\m.nih.gov/pubmed/19552792?

Lainsimies-Antikainen,H., Pietila, A.M., Laitinen,T., Schwab,U., Rauramaa, R., & Lansmies,E., (2007). Evaluation of informed consent: a pilot study. *Journal of Advanced Nursing, 59,* 146-154.

Landro, L. (2008). The informed patient: Consent forms that patients can understand. *Wall Street Journal*. Retrieved February 21 2006, from htt://online.wsj.com/artcle/SB120224055438544931.HTML

Lange, J.M.A. (2005). We must not let the protestors derail trials of pre-exposure prophylaxis for HIV (tenofovir). *Plos Medicine, 2* (9). Retrieved October 30, 2005, from http:/www.atap.org/2005/HN/072205-02htm

Lavery, J.V., Grady, C., Wahl, E.R., & Emanuel, E.J. (2007). *Ethical issues in international biomedical research: A casebook.* Oxford: Oxford University Press.

Lavori, P.W., Sugarman, J., Hays, M.T., & Feussner, J.R. (1999). Improving informed consent in clinical trials: A duty to experiment. *Control Clinical Trials, 20,* 187-193.

Leach, A., Hilton, S., Greenwood, B.M., Manneh, E., Dibba, B., Wilkins, A., & Mulholland, E.K. (1999). An evaluation of the informed consent procedure used during a trial of a Haemophilus influenza type B conjugate vaccine undertaken in the Gambia West Africa. *Social Science & Medicine, 48,* 139-148.

Leedy, P.D., & Ormrod, J.E. (2001). *Practical research: Planning and design.* (7th Ed.). Upper Saddle River, NJ: Merrill Prentice.

Levine, R.J. (1985). The use of placebos in randomised clinical Trials. *IRB: A Review of Human Subjects Research*, *7*, 1-3.

Levine, R.J. (1991). Informed consent: Some challenges to the universal validity of the western model. *Law and Medical Healthcare*, *19*, 207-213.

Lewens, T. (2006). Distinguishing treatment from research: A functional approach. *Journal of Medical Ethics*, *32,* 424–429.

Ritchter, L.M., Lindegger, G., Addool Karim, S., & Gasa, L. (2002). *Guidelines for the development of culturally sensitive approaches to obtaining informed consent for participation in HIV vaccine related trials.* School of Psychology. University of KwaZulu Natal (Discussion Document). Available at http:// http://www.avac.org/pdf/primer2/AVH_CH16.pdf (accessed 10 March 2006).

Lindegger, G., Milford, C., Slack, C., Quayle, M., Xaba, X., & Vardas, E. (2006). Beyond the checklist – Assessing understanding for HIV vaccine trial participation in South Africa. *Acquired Immune Deficiency Syndrome, 43,* 560-566.

Lindegger, G., & Richter, L.M. (2000). HIV vaccine trials: Critical issues in informed consent. *South African Journal of Science. 96,* 313-317.

Llewellyn-Thomas, H.A., McGreal, M.J., Theil, E.C., Fine, S., & Erlichman, C. (1991). Patients' willingness to enter clinical trials: Measuring the association with perceived benefit and preference for decision participation. *Social Science & Medicine*, *32,* 35-42.

Loh, W.Y., Butow, P.N., Brown, R.F., & Boyle, F. (2002). Ethical communication in clinical trials: Issues faced by data managers in obtaining informed consent. *Cancer, 95,* 2414-2421.

Lynöe, N., Sandlund, M., Dahlqvist, G., & Jacobsson, L. (1991). Informed consent: Study of quality of information given to participants in a clinical trial. *British Medical Journal, 303*, 610-613.

Manafa, O., Lindegger, G., & IJsselmuiden, C. (2007). Informed consent in an antiretroviral trial in Nigeria. *Indian Journal of Medical Ethics*, *4*, 26-30.

MacQueen, K.M., Abdool Karim, Q., & Sugarman, J. (2003). Ethics guidance for HIV prevention trials. *British Medical Journal*, *327*,340.

Madsen, S.N., Holm, S., & Riis, P. (2007). Attitudes towards clinical research among cancer trial participants and non-participants: An interview study using a grounded theory approach. *Journal of Medical Ethics. 33*, 234-240.

Mantell, J.S., Morar, N.S., Myer, L. & Ramjee, G. (2006). "We have our protector": Misperceptions of protection against HIV among participants in a microbicide efficacy trial. *American Journal of Public Health*, 96, 1073-1077

Masiye, F., Kass, N., Hyder, A., Ndebele, P., & J. Mfutso-Bengo. Why mothers choose to enrol their children in malaria clinical studies and the involvement of relatives in decision making: Evidence from Malawi. *Malawi Medical Journal, 20,* 50-56.

Mason, S.A., & Allmark, P.J. (2000). Outstanding informed consent to neonatal randomised controlled trials: Interviews with parents and clinicians in the Euricon study. *Lancet. 356,* 2045-2051.

Mcgrath, J., George, K., Svilar, G., Ihler, E., Mafigiri, D., Kabugo, E., & Mugisha, E. (2001). Knowledge about vaccine trials and willingness to participate in an HIV/AIDS vaccine study in the Ugandan military. *Journal of AIDS, 27,* 381-388.

McQuellon, R.P., Muss, H.B., Hoffman, S.L. Russell, G., Craven, B., & Yellen, S.B. (1995). Patient preferences for treatment of mestatic breast cancer: A study of women with early-stage breast cancer. *Journal of Clinical Oncology, 13*, 858-868.

Meade, C.D. (1999). Improving understanding of the informed consent process and document. *Seminars on Oncology Nursing*, *15,* 124-137.

Medical Research Council of South Africa. (2003).*Guidelines on ethics for medical research: HIV/AIDS preventive vaccine trials*. Retrieved on 19 October 2007, from www.mrc.ac.za/ethics/ethicsbook5.pdf.

Melby, T., Mendelson, J.E., & Jones, R.T. (1996). Patients' understanding of consent form should be checked before participation in trial. *British Medical Journal,* 312 (7034), p847

Mfutso-Bengo, J., Ndebele, P., Jumbe, V, Mkunthi, M., Masiye, F., Molyneux, S., & Molyneux, M. (2008). Why do individuals agree to enrol in clinical trials? A qualitative study of health research participation in Blantyre, Malawi. *Malawi Medical Journal, 20* (2), 37-41.

Microbicide Trials Network [MTN]. (2009). *Backgrounder: HPTN035: A multi-center clinical trial evaluating the candidate microbicides Buffergel and Pro 2000 for prevention of HIV*. Retrieved on 3 January 2010, from http://www3.niaid.nih.gov/.

Miller, T., & Boulton, M. (2007). Changing constructions of informed consent: Qualitative research and complex social worlds. *Social Science & Medicine*, *65,* 2199-2211

Minnies, D., Hawkridge,T., Hanekom,W., Ehrlich,R., London, L., & Hussey, G. (2008). Evaluation of the quality of informed consent in a vaccine field trial in a developing country settling. *BMC Medical Ethics*. 9(15). Retrieved on 16 August 2009, from http://www.biomedcentral.com/1472-6939/9/15.

Molyneux, S., Gikonyo, C,. Marsh, K., & Bejon, P. (2007). Incorporating a quiz into informed consent process: qualitative study of participants' reaction. *Malaria Journal, 10,* 145.

Molyneux, C.S, Peshu, N., & Marsh, K., (2004). Understanding of informed consent in a low-income setting: Three case studies from the Kenyan coast. *Social Science & Medicine, 59*, 2547-2559.

Molyneux, C.S., Wassenaar, D.R., Peshu, N., & Marsh, K. (2005). "…even if they ask you to stand by a tree all day, you will have to do it (laughter)…!" Community voices on the notion and practice and practice of informed consent for biomedical research in developing countries. *Social Science & Medicine, 61*, 443-454.

Moodley K. (2002). HIV vaccine trial participation in South Africa: An ethical assessment. *Journal of Medicine & Philosophy*, *27*, 197–215.

Moodley K. (2007). Microbicide research in developing countries: Have we given the ethical concerns due consideration? *BMC Medical Ethics. 19*, 10.

Morgan, D.L. (2007). Paradigms and pragmatism regained: Methodological implications for combining qualitative and quantitative methods. *Journal of Mixed Methods Research*, *1,* 48-76.

Morreim, H. (2009). The dirty little truth: We want them to understand but not really. A*merican Journal of Bioethics, 9*, 9-11.

Morris, N., & Balmer, B. (2006). Volunteer human subjects' understandings of their participation in a biomedical research experiment. *Social Science &Medicine, 62,* 998-1008.

Morrow, G., Gootnick, J., & Schmale, A. (1978). A simple technique for increasing cancer patients' knowledge of informed consent to treatment. *Cancer, 42,* 793-799.

Mortensen, M.G., Kiyak, H.A., & Omnell, L. (2003). Patient and parent understanding of informed consent in orthodontics. *American Journal of Orthodontics & Dentofacial Orthopedics*, *124*, 541-550.

Moustakas, C. (1994). *Phenomenological research methods*. London: Sage Publications.

National Statistical Office Malawi [NSO]. (2004). *Malawi Demographic and Health Survey 2004.* Zomba, Malawi.

Nattrass, N. (2006). When HIV clinicians prevent social scientists from accessing "their" patients: Some ethical concerns. *The Southern African Journal of HIV Medicine*, March 2006. pp.16-18.

Ndebele, P., Mfutso-Bengo, J., & Mduluza, T. (2008). Compensating clinical trial participants from limited resource settings in internationally sponsored clinical trials: A proposal. *Malawi Medical Journal, 20*, 42-45.

Newman, P.A., Duan, N., Lee, S., Rudy, E., Seiden, D., Kakinami, L., & Cunningham, W. (2007). Willingness to participate in HIV vaccine trials: The impact of trial attributes. *Preventive Medicine, 44,* 554-557.

Nicholson, R.H., & Crawley, F.P. (1999). Revising the Declaration of Helsinki: A fresh start. *Bulletin of Medical Ethics, 151*, 13–7.

Nunnaly, J. (1978). *Psychometric theory.* New York: McGraw

Nyika, A., Wassenaar, D.R., & Mamotte, N. (2009). The effect of relationships on decision-making process of women in Harare, Zimbabwe. *Ethics & Behavior*, *19,* 184-200.

Oduro, A.R., Aborigo, R.A., Amugsi, D., Anto, F., Anyorigiya, T., Atuguba, F., Hodson, A., & Koram, K.A. (2008). Understanding and retention of the informed consent process among parents in rural Northern Ghana. *BMC Medical Ethics,* 19 (9), 12. Retrieved on 13 July 2008, from http://www.biomedcentral.com/1472-6939/9/12

Olatoye, O. (2005). Features and controversies in community based education. *Archives of Ibadan Medicine,* 6, 24-28.

Pace, C., & Emanuel, E. (2005). The ethics of research in developing countries: Assessing voluntariness. *Lancet, 365*, 11-12.

Pace, C., Emanuel, E., Chuenyam, T., Duncombe, C., Bebchuk, J.D., Wendler, D., Tavel, J., McNay, L., Phanuphak, P., Foster, H., & Grady, C. (2005). The quality of informed consent in a clinical study in Thailand. *IRB Ethics and Human Research, 27(1)* 9-17.

Palmer, B.W., Dunn, L.B., Appelbaum, P.S., Mudaliar, S., Thal, V., Henry, R., Golshan, S., & Jeste, D.V. (2005). Assessment of capacity to consent to research among older persons with Schizophrenia, Alzheimer disease, or diabetes mellitus: Comparison of

a 3-item questionnaire with a comprehensive standardised capacity instrument. *Archives of General Psychiatry, 62,* 726-733.

Peterson, R.A. (2000). *Constructing effective questionnaires*. California: Thousand Oak.

Polit, D.F., & Beck, P.B. (2004). *Nursing research: Principles and methods*. Philadelphia: Lippicott Company.

Preziosi, M., Yam, A., Ndiaye, M., Simaga, A., & Simondon, F. (1997). Practical experiences in obtaining informed consent for a vaccine trial in rural Africa. *New England Journal of Medicine*, *336*, 370-373.

Pucci, E., Belardinelli, N., Signorino, M., & Angeleri, F. (1999). Patients' understanding of randomised controlled trials depends on their education. *British Medical Journal*, *318*, 875.

Quieroz da Fonseca, O., & Lie, R.K. (1995). Informed consent to AIDS-vaccine Trials in Brazil: A pilot study. *AIDS and Public Policy Journal, 10,* 22-26.

Quieroz da Fonseca, O., &. Lie, R.K. (1999). Comprehension of the informed consent form and general knowledge of vaccines among potential participants for an HIV vaccine trial. *International Journal of Pharmaceutical Medicine, 13*, 233-260.

Ramjee. G. (2007). Ethical Challenges in the N-9 Trial: The Investigator's Perspective. In J. Lavery, C. Grady, E. Wahl & E. Emanuel (Eds.) *Ethical issues in international biomedical research*: *A casebook.* (pp. 314-318). New York: Oxford.

Ramjee, G., Morar, N.S., Alary, M., Mukenge-Tshibaka, L., Vuylsteke, B., Ettiegne-Traore, V, Chandeying, V, Abdool Karim, S., & Van Damme, L. Challenges in the conduct of vaginal microbicide effectiveness trials in the developing world. (2000). *AIDS,* 14, 2553-7.

Record, R., & Mohiddin, A. (2006). An economic perspective on Malawi's medical "brain drain". *Globalization and Health*, 2(12). Retrieved 22 August 2008, from http://www.globalizationandhealth.com/content/2/1/12.

Redman, B.K. (2006). Review of measurement instrument in clinical and research ethics, 1999-2003. *Journal of Medical Ethics*, *32,* 153-156

Resnick, B., Gruber-Baldini, A.L., Pretzer-Aboff, I., Galik,E., Buie, V.C., Russ, K., & Zimmerman, S. (2007). Reliability and validity of the evaluation to sign consent measure. *The Gerontologist. 47*, 69-77.

Ritchter, L.M., Lindegger, G.C., Abdool Karim, Q., & Gasa, N. (1999). *Discussion Document:Guidelines for the development of culturally sensitive approaches to obtaining informed consent for the participation in HIV vaccine-related trials*. Unpublished paper. University of KwaZulu-Natal.

Robb, M. (2008). Failure of the Merck HIV vaccine: An uncertain step forward. *Lancet*, *372*, 1857–1858.

Robinson, E.S., Kerr, C., Stevens, A., Lilford, R., Braunholtz, D., & Edwards, S. (2004). Lay conceptions of the ethical and scientific justifications for random allocation in clinical trials. *Social Science & Medicine, 58,* 811-824

Robinson, E.J., Kerr, C.E., Stevens, A.J., Lilford, R.J., Braunholt, D.A., Edward, S.J., Beck, S.R., & Rowley, M.G. (2005). Lay publics' understanding of equipoise and randomisation in randomised controlled trials. *Health Technology Assessment Journal*, *9,* 1-192.

Rothman, K., & Michels, K. (1994). Sounding Board: The continuing unethical use of placebo controls. *New England Journal of Medicin,. 331*(6). 394-397.

Ryan, R.E., Prictor, M.J., McLaughing, K.J., & Hill, S.J. (2008). Audiovisual presentation of information for informed consent for participation in research. *Cochrane Database of Systematic Reviews.* 23, (1): Abstract number CD003717. Retrieved on 13 May 2009, from http.www.nvbi.nlm.nih.gov/pubmed/18254029.

Sachs, G.A., Hougham, G.W., Sugarman, J., Agre, P., Broome, M.E., Geller,G., Kass, N., Kodish,E., Mintz,J., Roberts,L.W., Sankar, P., Siminoff, L.A., Sorenson, J., &

Weiss, A (2003). Conducting empirical research on informed consent. *IRB: Ethics & Human Research supplement,* Sept-Oct, S4-S10.

Saelens, A. (1998). *The science, technology and ethics of HIV vaccine research*. Retrieved October 30th 2005, from http//www. Georgetown. Edu/sts/programs/ stia/ students/ vol.1/ saelensa.htm

Sarkar, R., Grandin, E. W., Gladstone, B. P., Muliyil, J., & Kang, G. (2009). Comprehension and recall of informed consent among participating families in a birth cohort study on diarrhoeal disease. *Public Health Ethics, 2*, 37-44.

Sastry, J., Pistal, H., Sutar, S., Kapadia-Kundu, N., Joshi, A., Suryavanshi, N., Bharucha, K.E., Shrotri, A. Phadke, M.A., Bollinger, R.C., & Shankar, A.V. (2004). Optimizing the HIV/AIDS informed consent process in India. *BMC Medicine,* 2 (28). Retrieved November 11, 2005, from http://www.biomedicentral.com/1741-7015/2/28

Schafer, A. (1982). The ethics of the randomised clinical trial. *New England Journal of Medicine. 307,* 719-724.

Schuklenk, U. (n.d). *An introduction to bioethics.* Retrieved October 30th, 2005 from http// sunsite. Wits .ac. za/ bio/ intro11. Htm

Schuklenk, U., & Ashcroft, R. (2000). International research ethics. *Bioethics, 14,* 158-172.

Searight, H.R., & Miller, C.K. (1996). Remembering and interpreting informed consent: a qualitative study of drug trial participants. *Journal of American Board of Family Practitioners, 9*, 14-22.

Senn S.J. (1997). *Statistical issues in drug development*. Chichester: John Wiley.

Shapiro, H.T., & Meslin, E.M. (2001). Ethical issues in the design and conduct of clinical trials in developing countries. *New England Journal of Medicine, 345*, 139-142.

Sharp, S. M. (2004). Consent documents for oncology trials: Does anybody read these things? *American Journal of Clinical Oncology, 27,* 570-575.

Silverman, D. (2004). Who cares about experience? In Silverman, D. (Ed). *Qualitative research: Theory, method and practice.* 2nd Edition. London: Sage Publications.

Simes, R.J., Tattersall, M.H.N., Coates, A. S., Raghavan, D., Solomon, H. J., & Smartt, H. (1986). Randomised comparison of procedures for obtaining informed consent in clinical trials of treatment of cancer. *British Medical Journal*, *293,* 1065-1068.

Siminoff, L.A. (2003). Toward improving the informed consent process in research with humans. *IRB: Ethics & Human Research Supplement, 25*, S1-S3

Singh, J.A., & Mills, E.J. (2005). The abandoned trials of tenofovir for pre-exposure prophylaxis for HIV: What went wrong? *HIV and AIDS*. Retrieved September 10, 2005, from htt://www.hivandhepatitis.com/recent/ad/072205-a.html

Slack, C.M., Lindegger, G.C., Vardas, E., Richter, L.M., Strode, A., & Wassenaar, D.R. (2000). Ethical issues in HIV vaccine trials in South Africa. *South African Journal of Science*, *96,* 291-312.

Slack, C., & Stobie. M. (2008) Response to "HIV vaccine trials: Reconsidering the therapeutic misconception and the question of what constitutes trial related injuries". *Developing World Bioethics*, *2*, 159-161.

Slack, C.M., Stobie, M., Milford, C., Lindegger, G.C., Wassenaar, D.R., Strode, A., & IJsselmuiden, C.B. (2005). Provision of treatment in HIV vaccine trials: A developing country perspective. *Social Science & Medicine*. *60,* 1197-1208.

Slevin, M., Mossman, J., Bowling, A., Leonard, R., Steward, W., Harper, P., Mclllmurray, M., & Thatcher, N. (1995). Volunteers or victims: Patients' views of randomised cancer clinical trials. *British Journal of Cancer, 71,* 1270-1274.

Snowdon, C., Garcia. J., & Elbourne, D. (1998). Reactions of patients to the results of a randomised controlled trial: Exploratory study. *British Medical Journal, 317*, 21-26.

Speziale, H., & Carpenter, D. (2003). *Qualitative research in nursing* (3rd edition). Philadelphia: Lippincott.

Spicer, N. (2004). Combining qualitative and quantitative methods. In Seale, C. (Ed.) *Researching society and culture.* pp 293-303. 2nd Edition. London: Sage Publications.

Spiro, H. M. (1986). *Doctors, patients and placebos.* New Haven: Yale.

Sreenivasan, G. (2003). Does informed consent to research require comprehension? *Lancet, 362*, 2016-2018.

Stafford, M.K., Ward, H, Flanagan, A., Rosenstein, I.J., Taylor-Robinson, D., Smith, J.R., Weber, J., & Kitchen, V. (1998). Safety study of Nonoxynol-9 as a vaginal microbicide: Evidence of adverse effects. *Journal of Acquired Immune Deficiency Syndromes & Human Retrovirology*, *17*, 327-331.

Stead, M., Eadie, D., Gordon, D., & Angus, K. (2005). "Hello, hello – it's English I speak": A quantitative exploration of patients' understanding of the science of clinical trials. *Journal of Medical Ethics, 31*, 664-669.

Stobie, M.L., Strode, A., & Slack, C. (2005). The dilemma of enroling children in HIV vaccine research in South Africa: What is in a child's best interest? In A.A. Van Niekerk, & L.M. Kopelman, L.M. (Eds.) *AIDS in Africa.* Pp. 190-207. Cape Town: David Philip/New Africa Books

Stolte, I.G., Duker, N.H., Geskus, R.B., Coutinho, R.A., & de Wit, J.B. (2004). Homosexual men change to risky sex when perceiving less threat of HIV/AIDS since availability of highly active antiretroviral therapy: A longitudinal study. *AIDS*, *18,* 303 309.

Sugarman, J., McCrory, D.C., & Hubal R. C. (1998). Getting meaningful informed consent from older adults: A structured literature review of empirical research. *Journal of American Geriatric Society, 46,* 517-524.

Sullivan, T., Monette, D., & DeJong, C. (Eds.) (1998). *Applied social research: A tool for the human sciences.* 4th edition. Port Worth: Harcourt College Publishers.

Taiwo, O.O., & Kass, N. (2009). Post consent assessment of dental subjects' understanding of informed consent in oral health research in Nigeria. *BMC Medical Ethics*, *10*,11.

Tarantola, D., Macklin, R., Reed, Z., Kieny, M.P., Osmanov, S., Stobie, M., & Hankins, C. (2007). Ethical considerations related to the provision of care and treatment in vaccine trials. *Vaccine*, *25*(26), 4864-4874.

Tashakkori, A., & Creswell, J.W. (2007). The new era of mixed methods. *Journal of Mixed Methods Research, 1*, 3-7.

Tashakkori, A., & Teddlie, C. (1998). *Mixed methodology: Combining qualitative and quantitative approaches.* Thousand Oaks, CA: Sage.

Taylor, H. (1999a). *The recruitment of HIV-infected children into clinical research: An exploration of factors that influence decision-making.* Unpublished doctoral dissertation, Johns Hopkins University, Baltimore, Maryland USA.

Taylor, H. (1999b). Barriers to informed consent. *Seminars in Oncology Nursing*, 15, (2). Retrieved September 16, 2009 from http//www.ncbi.n/m.nih.gov/pummed/10222580?odinalpos=1&itool=entrenzsystem 2.Pent

Teddlie, C., & Tashakkori, A. (2006). A general typology of research designs featuring mixed methods. *Research in the Schools,* 13, 12-28.

Tindana, P.O., Kass, N., & Akweongo, P. (2001). The informed consent process in a rural African Setting: A case study of the Kassena – Nankana District of Northern Ghana. *IRB: Ethics and Human Research,* May-June 2006; *28,* 1-6.

Tomamichel, M.,. Jaime, H., Degrate, A., de Jong, J., Pagani, O., Cavalli, F., & Sessa, C. (2000). Proposing phase I studies: Patients', relatives' nurses' and specialists' perceptions. *Annals of Oncology, 11,* 289-294.

Tomamichel, T., Sessa, C., Herzig, S., de Jong, J., Pagani, O., Willems, Y. & Cavalli F. (1995). Informed consent for phase I studies: Evaluation of quantity and quality of information provided to patients. *Annals of Oncology, 6*, 363-369.

Tucker, T., & Slack, C. (2003). Not if, but how? Caring for HIV-1 vaccine trial participants in South Africa. *Lancet, 362*, 955.

Ubel, P.A., & Lowenstein, G. (1997). The role of decision analysis in informed consent: choosing between intuition and systematicity. *Social Science & Medicine, 44,* 647-656.

Uganda AIDS Commission. (2006). Uganda guidelines for HIV vaccine research. Retrieved from http://www.aidsuganda.org/ . Retrieved on 31 August 2010.

UNAIDS. (2000). *Ethical considerations in HIV Preventive vaccine research: UNAIDS Guidance Document*: Geneva: UNAIDS

UNAIDS. (2007). *Ethical considerations in biomedical HIV Prevention trials: UNAIDS Guidance Document*: Geneva: UNAIDS

US Department of Health and Human Services. (2009). *Anti-HIV gel shows promise in large scale study in women*. Retrieved 10 April 2009 from http;//www.niad.nih.gov.

US Department of Health and Human Services. (2009). *45 CFR 46 Revised January 15, 2009. Effective July 14, 2009*. Retrieved on 13 June 2009, from http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm.

Vallely, A., Snagi, C., Lees, S., Shapiro, K., Masanja, J., Nikolau, L., Kazimoto, J., Mclormack, S., & Hayes, R.J. (2009). Microbicides development programme: Engaging the community in the standard of care debate in a vaginal microbicides trial in Mwanza, Tanzania. *BMC Medical Ethics, 10*, 10 – 17

Van Damme, L., Chandeying, V., Ramjee, G., Rees, H., Sirivongrangson, P., Laga, M., & Perriens, J.H. (2000). Safety of multiple daily applications of COL-1492, a nonoxynol-9 vaginal gel among female sex workers. *AIDS. 14,* 85-88.

Van Damme, L., Niruthisard, S.,Atisook, R., Boer, K., Dally, L., Laga M., Lange, J.M., Karam, M., & Perriens, J.H. (1998). Safety evaluation of nonoxynol-9 gel in women at low risk of HIV infection. *AIDS*, *12*, 433-437

Van Damme L, Ramjee G, Alary M, Vuylsteke B, Chandeying V, Rees H, Sirivongrangson P, Mukenge-Tshibaka L, Ettiègne-Traore V, Uaheowitchai C, Karim S, Mâsse B, Perriens, J., & Laga M. (2002). Effectiveness of COL-1492, a nonoxynol-9 vaginal gel, on HIV-1 transmission in female sex workers: a randomised controlled trial. *Lancet*, *360*, 971-977.

Varmus H., & Satcher, D. (1997). Ethical complexities of conducting research in developing countries. *New England Journal of Medicine*, *337,* 1003.

Verheggen, F.W., & van Wijmen F C. (1996). Informed consent in clinical trials. *Health Policy, 36,* 131-53.

Wade, J., Donavan J.L., Lane J.A., Neal, D.E., & Hamdy, F.C. (2009). It's not just what you say it is how you say it: Opening the "the black box" of informed consent appointments in randomised controlled trials. *Social Science & Medicine*, *68*, 2018-2028.

Warzaify, M., Khalil, S.S., & Silverman, H.J. (2009) Expression of therapeutic misconception amongst Egyptians: A qualitative pilot study. *BMC Medical Ethics* 10 (7). Retrieved on 19 December 2009, from http://www.biomedcentral.com/1472-6939/10/7 . doi: 10. 1186/1472-6939-10-7.

Wassenaar, D.R., & IJsselmuiden, C.B. (2007). Obligations to participants harmed in the course of the N-9 multicenter vaginal microbicide trial in South Africa: Commentary 19.2: Was the N-9 trial ethical? Questions and lessons. In J. Lavery, C. Grady, E. Wahl & E. Emanuel (Eds.) *Ethical issues in international biomedical research: A casebook* (pp. 319-325) . New York: Oxford.

Weijer, C. (1999). Placebo controlled trials in Schizophrenia: Are they ethical? *Schizophrenia Research, 35*, 211-218.

Weijer, C., & LeBlanc, G. (2005). *Revisiting the ethics of HIV prevention in developing countries.* Paper Commissioned by UNAIDS on June 7, 2005.

Wendler, D. (2004). Can we ensure that all research subjects give valid consent? *Archives of Internal Medicine, 164*, 2201- 2204.

Wendler, D., & Grady, C. (2008). What should research participants understand to understand they are participants in research? *Bioethics, 22,* 203-208

Weston, J., Hannah, M., & Downes, J. (1997). Evaluating the benefits of a patient information video during the informed consent process. *Patient Education and Counselling*, *30,* 239-245.

WHO/UNAIDS/IAVI Expert Group. (2007). Executive summary and recommendations from the WHO/UNAIDS/IAVI expert group consultation on 'Phase IIB-TOC trials as a novel strategy for evaluation of preventive HIV vaccines, 31 January-2 February 2006, IAVI, New York, USA. *AIDS, 21*, 539-546

Wirshing, D., Wirshing,W., Marder, S., & Liberman, R., & Mintz, J. (1998). Informed consent: Assessment of comprehension. *American Journal of Psychiatry*, *155*, 1508-1511.

Wolf, L.E., & Lo, B. (2001). *Ethical dimensions of HIV/ AIDS*. Retrieved 30th October, 2005, from http// hivinsite. Ucsf. Edu/ insite. Jsp? Page= kb – 08- 01-05

Wood, L., & Harber, J. (2002). *Nursing research: Methods critical appraisal and utilisation.* Missouri: Mosby Inc.

Woodsong, C. (2005). Informed consent kits improve process globally. *Clinical Trials Administrator*. May 2005: pp55-56

Woodsong, C., & Abdool Karim, Q. 2005. A model designed to enhance informed consent: Experiences from the HIV Prevention Trials Network. *American Journal of Public Health, 95*, 412–419.

World Medical Association (WMA). (2000). *Declaration of Helsinki – Ethical principles for medical research involving human subjects*. As amended by the 52nd WMA General Assembly, Edinburgh, October.

World Medical Association (WMA). (2002). *Declaration of Helsinki – Ethical principles for medical research involving human subjects*. As amended by the 53rd WMA General Assembly, Washington (note of Clarification on paragraph 29 added).

World Medical Association (WMA). (2004). *Declaration of Helsinki – Ethical principles for medical research involving human subjects*. As amended by the 55th WMA General Assembly, Tokyo (note of Clarification on Paragraph 30 added).

World Medical Association (WMA). (2008). *Declaration of Helsinki – Ethical principles for medical research involving human subjects*. As amended by the 59th WMA General Assembly, Seoul, October.

Wray, R.J., Stryke, J. E., Winer, E., Demetri, G., & Emmons, K. M., (2007). Do cancer patients fully understand clinical trial Participation? A pilot study to assess informed consent and patients expectations. *Journal of Cancer Education*, *22*, 22-24.

Yoder, S.P., & M.K. Konate (2002). *Obtaining informed consent for HIV testing: The DHS experience in Mali.* Maryland: ORC Marco.

Yuval, R., Halon, D., Merdler, A., Khader, N., Karkabi, B., Uziel, K., & Lewis, B. (2000). Patient Comprehension and reaction to participating in a double-blind randomised clinical trial (ISIS-4) in acute myocardial infarction. *Archives of Internal Medicine, 160*, 1142-1146.

APPENDICES

APPENDIX 1: GLOSSARY OF IMPORTANT TERMS

The following terms which are commonly used in everyday language are used frequently in this thesis. For each term, the meaning as used in this study is presented:

Clinical trials: A study conducted to allow safety and efficacy data to be collected for new drugs or devices. These trials can only take place once satisfactory information has been gathered on the quality of the product and its non-clinical safety, and Health Authority/Ethics Committee approval is granted in the country where the trial is taking place.

Disinhibition: The adoption of high risk behaviours or reduction of preventive actions by trial participants in HIV prevention trials as a result of the belief that they are protected by the product they would have received (test product).

Double blinding: Term used to described a study in which both the investigator or the participant are blind to (unaware of) the nature of the treatment the participant is receiving. Double-blind trials are thought to produce objective results, since the expectations of the researcher and the participant about the experimental treatment such as a drug do not affect the outcome. Also called double-masked.

Microbicide: A microbicide is any compound or substance whose purpose is to reduce the infectivity of microbes, such as viruses or bacteria.

Placebo: In a clinical trial, a placebo is An inactive substance resembling a medication, given for psychological effect or as a control in evaluating a medicine believed to be active. It is usually a tablet, capsule or injection that contains a harmless substance but appears to be the same as the medicine being tested. It is important for comparing the effects of a given treatment with no treatment.

Placebo effect: The placebo effect is the measurable, observable, or felt improvement in health or behavior not attributable to a medication or invasive treatment that has been

administered. Patients can also be biased. Many feel better if they believe they have taken something to make them feel better even if they have only taken a tablet made of white chalk or sugar.

Phase I trials: Are the first stage of testing in human subjects. Normally, a small (20-50) group of healthy volunteers will be selected. This phase includes trials designed to assess the safety (pharmacovigilance), tolerability, pharmacokinetics, and pharmacodynamics of a drug. These trials are often conducted in an inpatient clinic, where the subject can be observed by full-time staff. Phase I trials also normally include dose-ranging, also called dose escalation, studies so that the appropriate dose for therapeutic use can be found.

Phase II: Once the initial safety of the study drug has been confirmed in Phase I trials, Phase II trials are performed on larger groups (20-300) and are designed to assess how well the drug works, as well as to continue Phase I safety assessments in a larger group of volunteers and patients. When the development process for a new drug fails, this usually occurs during Phase II trials when the drug is discovered not to work as planned, or to have toxic effects. Phase II studies are sometimes divided into Phase IIA and Phase IIB. Phase IIA is specifically designed to assess dosing requirements (how much drug should be given). Phase IIB is specifically designed to study efficacy (how well the drug works at the prescribed dose(s)). Some trials combine Phase I and Phase II, and test both efficacy and toxicity.

Phase III: Phase III studies are usually randomized controlled multicenter trials on large patient groups (300–3,000 or more depending upon the disease/medical condition studied) and are aimed at being the definitive assessment of how effective the drug is, in comparison with current 'gold standard' treatment.

Phase IV: Phase IV trial is also known as Post Marketing Surveillance Trial. Phase IV trials involve the safety surveillance (pharmacovigilance) and ongoing technical support of a drug after it receives permission to be sold. Phase IV studies may be required by regulatory authorities or may be undertaken by the sponsoring company for competitive or

other reasons. The safety surveillance is designed to detect any rare or long-term adverse effects over a much larger patient population and longer time period than was possible during the Phase I-III clinical trials. Harmful effects discovered by Phase IV trials may result in a drug being withdrawn from the market, or restricted to certain uses.

Randomisation: Randomisation is a method that is used for assigning individuals participating in a trial into treatment groups. It is an effective method for balancing confounding factors between treatment groups

Randomised controlled trial (RCT): Is a type of scientific experiment most commonly used in testing the efficacy or effectiveness of interventions such as medical drugs, , medical devices or surgery). RCTs involve the random allocation of different interventions (treatments or conditions) to subjects. Numbers of subjects should be sufficient to balance for confounding factors between treatment groups.

Therapeutic misconception: Is the belief by microbicide trial participants that they are protected from HIV infection by the microbicide under study.

Trial participants: Individuals participating in a clinical trial or a research study.

Subject: Same as trial participant

APPENDIX 2: RESEARCH PARTICIPANTS QUESTIONNAIRE (ENGLISH VERSION)

UNIVERSITY OF KWAZULU-NATAL
SARETI
SCHOOL OF PSYCHOLOGY

MICROBICIDE TRIAL PARTICIPANTS' QUESTIONNAIRE

Title of Study: A study of trial participants' understanding and attitudes towards randomisation, double blinding and placebo use – A pilot intervention in a microbicide Trial in Malawi

START TIME :……..

MICROBICIDE TRIAL PARTICIPANTS' QUESTIONNAIRE

001 QUESTIONNAIRE NUMBER	
002 INTERVIEWER	
003 PARTICIPANT IDENTIFIER	
004 SITE CODE	
005 DATE	

SECTION 1 D*EMOGRAPHIC INFORMATION*

006 How old are you? (write down age) _____

1 Below 20
2 20-25
3 26-30
4 31-35
5 36-40
6 41+

007 In what month and year were you born? (verify with answer above)

1. Correct ____/____
2. Not sure
3. Corrected after probing.

008 What language do you mostly speak at home? (ethnicity)

1 Chewa/Nyanja
2 Yao
3 Lomwe
3 English
4 Other (specify)……..

009 How long have you stayed in this area?

1 Past 1 year
2 past 2 years
3 past three – 5 years
4 past 6- 10 years
5 more than 10 years

010 Where have you been staying during the past one year?

1 Urban
2 Rural
3 Peri-urban
4 Township
5 Farming area

011 In what kind of residence do you currently live?

1 Tenant
2 Lodger
3 Owner
4 Stay with family/relative
5 Stay with employer
6 unknown

012 What is your marital status?

1 Married
2 Single
3 Widowed
4 Divorced

013 What is the last grade or year that you completed in school?

1 None
2 Standard 1-4
3 Standard 5-8
4 Form 1-4
5 A level and Tertiary

014 What was your main economic activity during the past twelve months?

1 Student
2 housewife
3 formal employment
4 informal employment (selling goods)
5 Not employed

015 Do you currently have a permanent job?

1 Yes
2 No

016 What kind of work do you do?

1 Bar/hotel/restaurant
2 Office/factory
3 Housemaid
4 Child care
5 Patient care
6 Casual worker
7 Own business
8 Street vending
9 Sex work
10 Student/scholar/learner
11 Agriculture
12 Other(Specify)……

017 Are you on any medical aid scheme?

1 Yes
2 No

018 How do you normally pay your medical bills?

1 Pay myself

2. Medical Aid scheme
3. Someone pays for me
4. Other means (specify)……

019 What is your religion?

1 Traditional
2 Roman catholic
3 Protestant (Anglican, United Methodist, Lutheran, Baptist)
4 Pentecostal
5CCAP
6 Apostolic sect
8 Other Christian (Specify)……..
9 Moslem
10 Other religion (specify)……..
11 No religion

SECTION 2: GENERAL QUESTIONS CONCERNING RESEARCH

020 Tell me a bit about the programme you are currently participating in here.

1. Study to test microbicides
2. Programme to protect women against HIV infection
3. Other (specify)……..
4. Don't know

021 What is the main purpose of this study?

1. To test new microbicides
2. To protect women from HIV infection
3.. Other (specify)……..
4. Don't know

022 What do you think of when you hear the term research?

1. Testing of new interventions
2. Health care provision
3. Other (specify)……..
4. Don't know

023 Describe what you think is the difference between a clinical trial and regular medical care.

1. Trial is for research of new interventions and health care for cure or prevention of sickness
2. The same thing
3. Other (specify)……..
4. Don't know.

024 Briefly describe the experience you had when you were invited to participate in this study.

1. Visited at home by study staff
2. Referred by relative or friend.
3. Heard about programme through other source
4. Other (specify)……..……

025. How satisfied were you by the information you were provided with about the study?

1. Not at all satisfied
2. Somewhat satisfied
3. Moderately satisfied
4. Very satisfied
5. Don't know
6. Decline

026. What kinds of questions did you ask about the trial?(Circle all answers)

1. Trial procedures

2. Microbicide
3. Placebo use
4. Randomisation
5. Double blinding
6. Other (specify)…….
7. No questions.

027. How satisfied were you by the answers you were given?
1. Not at all satisfied
2. Somewhat satisfied
3. Moderately satisfied
4. Very satisfied
5. Don't know
6. Decline

028 What one thing did you want to know and understand the most?
1. Trial procedures
2,. Microbicide
3. Placebo use
4. Randomisation
5. Double blinding
6. Other (specify)…….
7. No questions.

029. Does the study involve anything new or special?
1. Yes
2. No

030. If yes state
1. Microbicide
2. condoms
3. other (specify)……...

031 What was the main reason that made you decide to join?
1 persuaded to join by other (specify)……
2 respect for the researchers
3 wanted to know my HIV/status
4 wanted to access free medical care
5 benefit mankind
6 other (specify) ……

032. How long did you take to decide?
1 Decided on first day
2 After one week
3 two – four weeks
4 more than 4 weeks
5 DK/forgotten

033. Was it hard or easy to decide?
1 Hard
2 Easy

034. Did you talk to anyone about the decision
1 Yes
2 No

035. If yes Who? Tell me about those talks
1Partner
2 Aunt
3 Parents
4 Friend
5 Other (specify)……

036. Who thought it was a good/bad idea for you to join?

1 Self
2 Other (specify)…….

037. Why did they think so?

1 respect for the researchers
2 wanted to know my HIV/status
3 wanted to access free medical care
4 benefit mankind
5 other (specify …….
8 Not applicable

038. In general, why do you think people should participate in research?

1 respect for the researchers
2 wanted to know my HIV/status
3 wanted to access free medical care
4 benefit mankind
5 other (specify)…….

TABLE 1 - QUESTIONS ON RANDOMISATION,

039. Are you aware that participants in this study are allocated into different groups? …….	Yes No	1 0
040. Describe the groups that participants in this study are allocated to. ……. ……..	4 correct arms 3 arms (2 gels + placebo) 2 arms (gel + placebo) 1arm /DK	3 2 1 0
041. Describe the way participants are assigned into the groups. ……	1 Describes the process of randomisation 2 Other/DK	1 0
042. Why do you think that participants are randomly allocated to these groups? ……	1 similar samples 2 DK/other wrong answer	1 0
043. Of the groups you mentioned, which group where you assigned to?.....	1 Not aware 2 list…….	1 0
044. Why do you say so? ……	1.Gel works 2. Not sure about group.	0 1
045. TOTAL SCORE FOR THIS TABLE (OUT OF 8)		

046. What is your opinion regarding randomisation into the various study groups without your choice?

1 to ensure scientific validity
2 indifferent
3 negative

047. If you were to be re-assigned, which group would you want to be reassigned to?

1 indifferent
2 active study arm
3 placebo

048. Why do you say so?

1 protection from HIV and Sexually transmitted infections

2 To see if the product works
3 Other (specify)……..

TABLE 2 - QUESTIONS ON PLACEBO USE

049. Describe the products that are being used in this study …….	1. Two gels plus 1 placebo gel 2. Microbicide + placebo 3. Microbicide only	2 1 0
050. What do you understand by the word 'placebo'	– A thing that looks like product under test 2 wrong answer	1 0
051.Are you aware that some participants in this study are being given something that looks and feels like the product under study? ……	1 yes 2 No	1 0
052. Why do you think some participants are being given such a product as part of this study? …….. ……..	1 comparison easy 2 wrong answer	1 0
052. How are different products assigned to study participants in this study? …….	randomly By need or any wrong answer	1 0
053. Is the study microbicide given to those who are at high risk and the placebo to those at low risk?.	1. Yes 2. No	0 1
054. Which study product do you think you are receiving? …….. ……..	1Donk know 2.List	1 0
055. What do you think are some of the implications of the use of the placebo to you as a participant? ……. ……..	1. Aware 2. Not aware	1 0
056. TOTAL SCORE FOR THIS TABLE (OUT OF 9)		

057. (**If mentioned a particular product in Q051 above)** Why do you think that you are currently receiving this particular product.

1 I feel it
2 Never had an STI since I started using it
3 Other (specify)…….
8 Not applicable

058. What is your opinion regarding the giving of a product which just looks like the product under study to some of the participants.

1 It's a very bad practice (very negative)
2 Negative
3 No problem with it
4 Don't know
5. Other (specify)……..

059. If told latter that you were receiving a product which looks like a microbicide but is not really a microbicide, how would you feel?

1 Cheated
2 Betrayed
3 Indifferent/Nothing
4 Ok because its part of the study
5 Other (specify)……

060. Why would you feel that way?

1 Thought I was being given the active product
2 throught I was being protected from HIV
3 Other (specify)……

061. If the microbicide is later proven to be effective, would you be upset with the researchers if you were informed later that you were being given something which looks like the microbicide (placebo)?

1 Yes
2 No
3 Don't know

062. If the microbicide is later proven to be ineffective, would you be upset with the researchers if you were informed later that the product does not protect women against HIV infection?

1 Yes
2 No
3 Don't know

TABLE 3 - QUESTIONS ON BLINDING

		Scor
063. Do you think the doctor knows which product you will receive?.....	Yes No	0 1
064. What do you think the term "blinding" means?	Both researcher and participant not aware Don't know + wrong answer	1 0
065. To whom is the placebo given? ……	Anyone 1 Other 2	1 0
066. Why do you think that neither you, the doctors nor the research staff should know at first about whether you are being given the trial microbicide or placebo? ……	1.Avoid researcher bias 2 Other/DK	1 0
067. What are some of the disadvantages of the double blind procedure with regards to your protection? …… …….	1 Delayed identification and reporting of drug reactions or SAEs 2DK other	1 0
068. TOTAL SCORE FOR THIS TABLE (OUT OF 5)		

069. What is your opinion regarding the possibility that you might be given either the study product or something that looks like the study product but is not the real study product, without your knowing which one you are getting?

1. Its appropriate for science
2. Very bad
3. Indifferent

070. What is your opinion regarding the possibility that you might be given either the study product or something that looks like the study product but is not the real study product, without the doctors or nurses knowing which one you are getting?

1. Its appropriate for science
2. Very bad
3. Indifferent

TABLE 4: PLEASE INDICATE WHETHER THESE STATEMENTS ARE TRUE OR FALSE

071. The microbicide that is being tested prevents you against HIV infection.	**T** **F**	0 1
072. Everybody who participates in this study will receive the microbicide under study.	**T** **F**	0 1
073. In order to protect themselves against HIV, microbicide trial participants can use condoms.	**T** **F**	1 0
074. People who join the microbicide trial will never again have to worry about HIV infection, no matter what they do.	**T** **F**	0 1
075. People in the microbicide trial will need to worry less than people not in this study about catching HIV if they forget to use a condom with a new sex partner.	**T** **F**	0 1
076. People who join this study might catch HIV anyway.	**T** **F**	1 0
077. The microbicide that is being tested is 100% effective in preventing HIV infection.	**T** **F**	0 1
078. Trial participants need to continue taking precautions against risky behaviour.	**T** **F**	1 0
079. It is impossible to catch HIV whilst you are using the microbicide.	**T** **F**	0 1
080. TOTAL SCORE FOR THIS TABLE (out of 9)		

TABLE 5 - PLEASE INDICATE YES OR NO

081. In this trial, some women are given the study microbicide and others are given a product which looks like the study microbicide.	**Yes** **No**	1 0
082. You have a one in three chance of receiving a placebo.	**Yes** **No**	1 0
083. The staff are not aware whether they are giving you the real microbicide or the one that looks like the real microbicide.	**Yes** **No**	1 0
084. You cannot make a choice whether you receive the real microbicide or the other product that looks like the real one.	**Yes** **No**	1 0
085. TOTAL SCORE FOR THIS TABLE (OUT OF 4)		

TABLE 6 - PLEASE INDICATE WHETHER YOU AGREE OR DISAGREE WITH THE FOLLOWING STATEMENTS

086. Researchers should advise participants whether they are on the placebo or actual study product	Disagree 1 Agree 0	
087. Participants should be allowed to choose which study group they want to join.	Disagree 1 Agree 0	
088. Doctors and nurses should know which product each participant is receiving.	Disagree 1 Agree 0	
089. The active product should be given to those with high risk behaviours.	Disagree 1 Agree 0	
090. The placebo should be given to those with minimal risk behaviours.	Disagree 1 Agree 0	
091. TOTAL SCORES (OUT OF 5)		

092. Do you have any advice for others trying to make the decision to join a similar study?
……
……

093. Can you share with us any comments that you have about the microbicide study?
……..

……
……

Thank you for taking your time to speak to me. The information you have given me will be very useful.

End time:……

TABLE 7 : COMPOSITE SCORE CALCULATION AND CATEGORY CLASSIFICATION

TABLE	POSSIBLE SCORE	SCORE	%	CATEGORY
094 Table 1 Randomisation	8			
095. Table 2 Placebo use	9			
096. Table 3 Blinding	5			
097. Table 4 Implications	9			
098. Table 5 Knowledge	4			
099. COMPOSITE SCORE	40			
100. **CATEGORY**				

CATEGORY CLASSIFICATION

0%-50% = CATEGORY 1
51%-74% =CATEGORY 2
75% + = CATEGORY 3

NOTES:……

……

……

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……

APPENDIX 3: INFORMED CONSENT DOCUMENT FOR PARTICIPANTS (ENGLISH VERSION)

UNIVERSITY OF KWAZULU-NATAL

SARETI
School of Psychology

MICROBICIDE TRIAL PARTICIPANTS' CONSENT FORM

Title of Study: A study of trial participants' understanding and attitudes towards randomisation, double blinding and placebo use – A pilot intervention in a microbicide Trial in Malawi

---

Explanation of the Research project
I am part of a team conducting a study to assess microbicide trial participants' understanding of trial procedures. The study will be part of a doctoral degree for Paul Ndebele at the University of KwaZulu-Natal. We are not members of staff at this clinic. This study is part of the training that is being offered by the University of KwaZulu-Natal aimed at promoting the ethical conduct of research. We invite you to participate in this research study. You are being asked to join this study as you are participating in the microbicide trial. The purpose of the study is to assess microbicide trial participants' understanding and attitudes towards clinical trial procedures. We would like to find out what you understand about these trial procedures as well as your opinions concerning these procedures and there are no wrong or right answers. If you agree to participate in this study, we will note your answers to assist with our analysis of the data. If we happen to identify any shortcomings in your knowledge, we will initiate some activities in future aimed at improving your knowledge. All participants in the microbicide trial who joined the trial during the period before the last 3 months are eligible to participate in this study.

Procedures
We plan to enrol a total of 218 microbicide trial participants for this study. If you agree to participate in this study, you will be asked several questions relating to your microbicide trial participation. The discussion will last at least 40-50 minutes and will be held in a private room. We are also requesting your permission to have the discussion audio-taped so that the contents of the tape may be analysed later. The tapes will be destroyed after the data has been captured on computer.

Risks and Discomforts
There are no physical risks to you for participating in this study. The only risks we can foresee include a minor invasion of your privacy since we are going to ask you questions about your participation in the microbicide trial. The other risk is that of anxiety or upset that may result from talking about your participation. If you feel distressed please tell me and I will make sure that you are referred to appropriate trial support services.

You will also receive MK500 for each interview that you complete to cover your travel, time and inconvenience.

Benefits
You will not directly benefit from participating in this study. This study may benefit the microbicide trial investigators as well as future trial participants through the new knowledge that it will generate. If we identify some needs for addional knowledge, we will develop, and ask you to participate in, an intervention which will be aimed at improving understanding of trial procedures. We will provide you with feedback on these discussions as well as our findings during some meetings to be held at the end of the study.

Alternatives to Participation
Your participation in this study is entirely voluntary. You have the right to refuse or to withdraw from this study at any time. If you do not want to join the study, or if you withdraw from the study, this will not affect your participation in the microbicide trial neither will it affect the quality of care you receive at this health institution. You may even choose to decline to respond to specific questions if you feel that you are not comfortable with them.

If you have not yet made a decision regarding your participation in this study, we request permission to contact you again on the day of your next clinic visit for a further discussion. We also request permission to contact you again in future for intervention activities if this study identifies some knowledge gaps that need to be filled. If you agree to the request, the follow-ups will be conducted during days that you will visit this centre as part of the microbicide trial.

Confidentiality
No reports will identify you in any way. You will be allocated with a study number that will be used to identify you. This study number rather than your name will be used to label all study questionnaires. Our research staff will maintain a confidential list linking all participants' names with their study numbers. The list will enable us to contact you for follow - up activities and interviews.

Whom to Contact
For any questions you may have regarding this study, you are please advised to contact Paul Ndebele who is the person in charge of this study at 09619937. If for any reason you want to talk to anyone else about this study besides the person in charge, you can contact Mrs Thandizo Kamwendo, the administrator at the College of Medicine Ethics Committee on 01871911 Fax 01874700. Paul Ndebele's academic supervisor is Prof D Wassenaar who can be contacted at +27 33 2605373 or Wassenaar@ukzn.ac.za .

DECLARATION

I……(full names of participant) hereby confirm that I understand the contents of this document and the nature of the research project, and I consent to participating in the research project. I am willing to be re-contacted and to participate in future activities related to this study

I understand that I am at liberty to withdraw from the project at any time, should I so desire.

SIGNATURE OF PARTICIPANT DATE

……
……

NOTE TO THE INTERVIEWER:

Potential participants should be given time to read, understand and question the information given before giving consent. This should include time out of the presence of the investigator and time to consult friends and/or family. Please hand to the participant one copy of this information sheet.

Appendix 4: Research participants Questionaire in Chichewa

UNIVERSITY OF KWAZULU-NATAL

SARETI

School of Psychology

CHIKALATA CHA MAFUNSO KWA OTENGA MBALI MUKAFUKUFUKU WA MANKHWALA OVALIRA

001 QUESTIONNAIRE NUMBER .	
002 INTERVIEWER	
003 PARTICIPANT IDENTIFIER .	
004 SITE CODE .	
005 DATE	

SECTION 1: MAFUNSO OZINDIKILIRA OTENGA MBALI

006 Muli ndi zaka zingati? (Write down age) _____

1 Below 20
2 20-25
3 26-30
4 31-35
5 36-40
6 41+

007 Munabadwa mchaka ndi mwezi wanji? (tsimikizani ndi yankho lapamwambali)

1. Correct ____/____
2. Not sure
3. Corrected after probing.

008 Kodi mumayankhula chinenero chanji mukakhala kunyumba ndipo mtundu wanu ndi uti?

1 Chewa/Nyanja
2 Yao
3 Lomwe
3 English
4 Other (specify)……..

009 Kodi mwakhala kudera lino kwa nthawi yaitali bwanji?

1 Past 1 year
2 past 2 years
3 past 3 – 5 years
4 past 6- 10 years
5 more than 10 years

010 Kodi m'makhala kuti mchaka chimodzi chapitachi?

1 Urban
2 Rural
3 Peri-urban
4 Township
5 Farming area

011.Kodi panopa mumakhala pakhomo pa ndani?

1 Tenant
2 Lodger
3 Owner
4 Stay with family/relative
5 Stay with employer
6 unknown

012 Kodi muli pa banja?

1 Married
2 Single
3 Widowed
4 Divorced

013 Kodi sukulu munalekeza kalasi yanji?

1 None
2 Standards 1-4
3 Standards 5-8
4 Form 1-4
5 A level and Tertiary

014. Kodi mumapanga chiyani kuti mupeze mchere miyezi khumi ndi iwiri yapitayo?

1 Student
2 housewife
3 formal employment
4 informal employment (selling goods)
5 Not employed

015 Kodi panopa muli pantchito yokhazikika?

1 Yes
2 No

016. Kodi panopa mumagwira ntchito yanji?

1 Bar/hotel/restaurant
2 Office/factory
3 Housemaid
4 Child care
5 Patient care
6 Casual worker
7 Own business
8 Street vending
9 Sex work
10 Student/scholar/learner
11 Agriculture
12 Other(Specify)…….

017. Kodi muli mubungwe lirilonse lokuthandizani kulipira mabilo akuchipatala?

1 Yes
2 No

018. Kodi mumapereka bwanji mabilo anu akuchipatala?

1 Pay myself
2. Medical Aid scheme
3. Someone pays for me
4. Other means (specify)……

019 Kodi mumapemphera mpingo wanji?

1 Traditional
2 Roman catholic
3 Protestant (Anglican, United Methodist, Lutheran, Baptist)
4 Pentecostal
5 CCAP
6 Apostolic sect
8 Other Christian (Specify)…….
9 Moslem
10 Other religion (specify)……..
11 No religion

SECTION 2: MAFUNSO OKHUZA KAFUKUFUKU

020 Tandiuzanikoni mwachidule zokhuza chilinganizo cha kafukufuku amene mukutenga nawo mbali.

1. Study to test microbicides
2. Programme to protect women against HIV infection
3. Other (specify)……..
4. Don't know

021. Kodi kafukufukuyu cholinga chake nchiyani?

1. To test new microbicides
2. To protect women from HIV infection
3.. Other (specify)……..
4. Don't know

022. Kodi inu mukamva mau oti kafukufuku mumaganizanji (mumamvetsa bwanji mawuwa)?

1. Testing of new interventions
2. Health care provision
3. Other (specify)……..
4. Don't know

023. Kodi pali kusiyana kotani pakati pa kafukufuku ndi kupereka mankhwala pofuna kuchiza kapena kupewa matenda?

1. Trial is for research of new interventions and health care for cure or prevention of sickness
2. The same thing
3. Other (specify)……..
4. Don't know.

24. Tafotokozaniko mwachidule zimene zinachitika nthawi imene mumapemphedwa kuti mulowe mkafukufukuyu.

1. Visited at home by study staff
2. Referred by relative or friend.
3. Heard about programme through other source
4. Other (specify)……..……

025. Kodi inu munali okhutisidwa bwanji ndi chidziwitso chimene munapatsidwa?

1. Not at all satisfied
2. Somewhat satisfied
3. Moderately satisfied
4. Very satisfied

5. Don't know
6. Decline

026. Kodi ndimafunso otani amene munafunsa zokhuza kafukufukuyu?
1. Trial procedures
2. Microbicide
3. Placebo use
4. Randomisation
5. Double blinding
6. Other (specify)…….
7. No questions.

027. Kodi inu munali okhutira bwanji ndi mayankho amene munalandira?
1. Not at all satisfied
2. Somewhat satisfied
3. Moderately satisfied
4. Very satisfied
5. Don't know
6. Decline

028. Kodi nchiyani chimene munkafuna kumvetsa bwino lomwe? Tchulani chinthu Chimodzi.
1. Trial procedures
2,. Microbicide
3. Placebo use
4. Randomisation
5. Double blinding
6. Other (specify)…….
7. No questions.

029. Kodi kafukufukuyu akufufuza chirichonse chachilendo kapena chapadela?
1. Yes
2. No

30. Ngati ndi choncho, fotokozani.
1. Microbicide
2. Condoms
3. Other (specify)……...

031. Kodi nchifukwa chiyani munaganiza kuti mulowe mkafukufukuyu?
1 persuaded to join by other (specify)……
2 respect for the researchers
3 wanted to know my HIV/status
4 wanted to access free medical care
5 benefit mankind
6 other (specify) ……

032. Kodi zinakutengerani nthawi yaitali bwanji kuti muganize kuti mulowe mkafukufukuyu?
1 Decided on first day
2 After one week
3 two – four weeks
4 more than 4 weeks
5 DK/forgotten

033. Zinali zovuta kuti mupange chisankho chanu?

1 Hard
2 Easy

034. Munamuuzako aliyense za maganiza anuwo?

1 Yes
2 No

035. Ngati ndi eya tandifotokozereni za zokambiranazanuzo?

1Partner
2 Aunt
3 Parents
4 Friend
5 Other (specify)……

036. Ndi ndani yemwe anakuuzani kuti mwaganiza bwino kapena ayi kusankha kuti mulowe mkafukufukuyu?

1 Self
2 Other (specify)…….

037. Nchifukwa chiyani anaganiza/munaganiza choncho?

1 respect for the researchers
2 wanted to know my HIV/status
3 wanted to access free medical care
4 benefit mankind
5 other (specify …….
8 Not applicable

038. Mukuganiza kuti nchifukwa chiyani anthu ali woyenera kutenga mbali mkafukufuku?

1 respect for the researchers
2 wanted to know my HIV/status
3 wanted to access free medical care
4 benefit mankind
5 other (specify)…….

TABLE 1 - MAFUNSO OKHUZA ZA KASANKHIDWE KA ANTHU MWA PATALIPATALI

039. Kodi inu mukudziwa kuti wotenga mbali mukafukufukuyu akugawidwa m'magulu osiyanasiyana?	Yes No	1 0
040. Fotokozani magulu amene wotenga mbali mukafukufukuyu agawidwa.	4 correct arms 3 arms (2 gels + placebo) 2 arms (gel + placebo) 1arm /DK	3 2 1 0
041. Fotokozani mmene anthu amagawidwira m'magulu mmenemu.	1 Describes the process of randomisation 2 Other/DK	1 0
042. Mukuganiza kuti nchifukwa chiyani wotenga mbali mukafukufukuyu amayikidwa mmagulu mwapatalipatali?	1 similar samples 2 DK/other wrong answer	1 0
043. Mwamagulu amene anasankhawo inuyo munayikidwa mgulu liti?	1 Not aware 2 List…….	1 0
044. Mwadziwa bwanji? ……	1.Gel works 2. Not sure about group.	0 1
045. Malikisi onse kuonkhesera pamodzi (pa 8)		

046. Maganizo anu ndi otani pa kagawidwe ka magulu kosankha anthu mwa patalipatali mopanda inu kusankha mbali imene mukufuna.

1 to ensure scientific validity
2 indifferent
3 negative

047. Kodi atati akugaweninsoni inu mungafune kuti mukhale mgulu liti?

1 indifferent
2 active study arm
3 placebo

048. Chifukwa chiyani?

1 protection from HIV and Sexually transmitted infections
2 To see if the product works
3 Other (specify)……..

TABLE 2 – MAFUNSO OKHUZA KUGWIRITSA NTCHITO PULASIBO

049. Tafotokozani zinthu zimene zikugwiritsidwa ntchito Mukafukufukuyu.	1.Two gels plus 1 placebo gel 2. Microbicide + placebo 3. Microbicide only	
050. Kodi mumamvetsa bwanji mau oti pulasibo (amatanthauza chiyani)?	– A thing that looks like product under test 2 wrong answer	
051. Mukudziwa kuti anthu ena mukafukufukuyu akulandira zinthuzowoneka chimodzimodzi ngati zimene zikuyesedwa mukafukufukuyu koma zisali izo?	1 yes 2 No	
052. Inu mukuganiza kuti ndi chifukwa chiyani anthu ena akumapatsidwa zinthu zimenezo ngati mbali imodzi yakafukufukuyu?	1 comparison easy 2 wrong answer	
052. Kodi zinthuzi zimaperekedwa bwanji kwa anthu wotenga mbali mu kafukufukuyu?	randomly By need or any wrong answer 1.	
053. Kodi mankhwala ovalira amene akuyesedwawo amapatsidwa kwa anthu omwe angathe kutenga matenda mosavuta ndipo pulasibo imapatsidwa kwa anthu amene sangathe kutenga matenda mosavuta?	1. Yes 2. No	
054. Kodi inu mukuganiza kuti mukulandira chiyani?	1Donk know 2.List	
055. Kodi inu mukuganiza kuti kugwiritsa ntchito pulasibo kukutanthauzanji kwa inu monga otenga mbali mukafukufukuyu? …… ……..	3. Aware 2. Not aware	
056. KUONKHESA PAMOZI MALIKISI ONSE (PA 9)		

057. (Ngati atchula chinthu china mu funso 54) mukuganiza kuti nchifukwa chiyani mukulandira zimene mwatchula zija

1 I feel it
2 Never had an STI since I started using it
3 Other (specify)…….
8 Not applicable

058. Maganizo anu ndi wotani pa zomapereka zinthu zooneka ngati zimene zilikuunikidwa mukafukufuku kwa anthu ena otenga mbali mukafukufuku

1 It's a very bad practice (very negative)
2 Negative
3 No problem with it
4 Don't know
5. Other (specify)……..

059. Kodi inu mutadzauzidwa mtsogolo muno kuti mumalandira zinthu zonga mankhwala ovalira koma si mankhwala ovalira mungamve bwanji?

1 Cheated
2 Betrayed
3 Indifferent/Nothing
4 Ok because its part of the study
5 Other (specify)……

060. Muzamva choncho chifukwa chiyani

1 Thought I was being given the active product
2 throught I was being protected from HIV
3 Other (specify)……

061. Zikazapezeka kuti mankhwala ovalira ndithudi ndi amphamvu ndi wogwira ntchito koma inu mumapatsidwa zinthu zina osati mankhwalawa (pulasibo) mudzakhala okwiya ndi anthu wopangitsa kafukufukuyu kapena ayi

1 Yes
2 No
3 Don't know

062. Kukazapezeka kuti mankhwala ovalirawa sateteza kumatenda, inu mudzakhala okwiya ndi ofufuza pamene azakuuzani kuti mankhwalawa sateteza azimayi ku HIV

1 Yes
2 No
3 Don't know

TABLE 3 – MAFUNSO OKHUZA KABISIDWE

		Score
063.Mukuganiza kuti adokotala akudziwa chimene inu mukulandira?.....	Yes No	0 1
064. Kodi mawu oti bulaindi (chibisa) akutanthauza chiyani?	Both researcher and participant not aware Don't know + wrong answer	1 0
065. Kodi pulasibo imaperekedwa kwa yani? ……	1. Anyone 1 2. Other 2	1 0
066. Mukuganiza kuti nchifukwa chiyani kuli kofunika kuti inu adokotala komanso ofufuza asadziwe kuti inu mukulandira pulasibo kapena mankhwala enieni amene akuunikidwawo? …….. …….	1.Avoid researcher bias 2 Other/DK	1 0
067. Ndi kuipa kotani kumene inu mukuganiza kuti kulipo pa mbiso oti onse ofufuza ndi otenga mbali asadziwe zimene wotenga mbali akulandira pa chitetezo ? …… …….	1 Delayed identification and reporting of drug reactions or SAEs 2DK other	1 0
068. MALIKISI ONSE KUONKHESERA PAMODZI (PA 5)		

069. Kodi inu maganizo anu ndi wotani pankhani yoti nzotheka kuti inu mukhoza kumalandira zinthu zenizeni zimene zikuunikidwa mukafukufuku kapena zina zooneka chimodzimodzi ngati zimene zikuunikidwazo koma zisali izo popanda inu kudziwa chimene mukulandira

4. It's appropriate for science
5. Very bad
3. Indifferent

070. Kodi inu maganizo anu ndi wotani pankhani yoti nzotheka kuti inu mukhoza kumalandira zinthu zenizeni zimene zikuunikidwa mukafukufuku kapena zina zooneka chimodzimodzi ngati zimene zikuunikidwazo koma zisali izo popanda adokotala kapena anamwino amene akuperekawo kudziwa chimene mukulandira?

1. It's appropriate for science
2. Very bad
3. **Indifferent**

TABLE 4: CHONDE NENANI NGATI ZIGANIZOZI ZILI ZOWONA KAPENA ZABODZA

071. Mankhwala ovalira amene akuunikidwa mukafukufukuyu amateteza ku kachirombo ka HIV	**T** **F**	
072. Aliyense amene akutenga mbali mukafukufukuyu alandira mankhwala ovalira amene akuunikidwawo	**T** **F**	
073. Pofuna kuziteteza okha kukachirombo ka HIV wotenga mbali mukafukufuku akhoza kugwiritsa ntchito ma kondomu	**T** **F**	
074. Anthu wotenga mbali mukafukufuku wa mankhwala ovalira sayenera kudandaula za HIV posayang'anira chirichonse chimene angachite.	**T** **F**	
075. Anthu wotenga mbali mukafukufukuyu sayenera kudandaula kwambiri ngati sanagwiritse ntchito kondomu pamene agonana ndi bwenzi la tsopano poyerekeza ndi anthu amene sali mukafukufukuyu.	**T** **F**	
076.Anthu amene analowa mukafukufukuyu ndi woti akhozabe kutenga matenda kale	**T** **F**	
077. Mankhwala ovalira ndi amphamvu kwambiri (ali 100/100 mphamvu zake) poteteza kukachirombo ka HIV	**T** **F**	
078. Wotenga mbali mukafukufuku ayenera kusamala pochita zinthu zimene zingathe kuononga moyo wawo	**T** **F**	
079. Nzosatheka kutenga kachirombo ka HIV pamene munthu akugwiritsa ntchito mankhwala ovalira	**T** **F**	
080. MALIKISI ONSE KUONKESERA PAMODZI (PA 9)		

TABLE 5 – YANKHANI KUTI EYA KAPENA AYI KUZIGANIZO ZOTSATIRAZI

081. Mukafukufukuyu azimayi ena akulandira mankhwala ovalira akuunikidwayo ndipo ena akulandira zinthu zooneka ngati mankhwala ovalirawo koma asali omwewo	**Yes** **No**	1 0
082. Muli ndi mwayi umodzi pa katatu kalikonse kuti mukhoza kulandira polasibo	**Yes** **No**	1 0
083. Ogwira ntchito sakudziwa ngati akukupatsani mankhwala amankhwala ovalira enieni kapena zinthu zonga mankhwala ovalira	**Yes** **No**	1 0
084. Simungathe kusankha kuti muzilandira mankhwala ovalira enieni kapena zinthu zooneka ngati mankhwala ovalira koma zisali izo	**Yes** **No**	1 0
085. MALIKISI ONSE KUONKHESERA PAMODZI (PA 4)		

TABLE 6 CHONDE NENANI NGATI MUKUGWIRIZANA NDI ZIGANIZO ZILI MMUSIZI KAPENA AYI

086. Wopanga kafukufuku aziwauza anthu otenga mbali ngati akulandira pulasibo kapena zinthu zenizeni zimene zikuunikidwazo	Disagree 1 Agree 0	1 0
087. Wotenga mbali aziloledwa kusankha gulu limene akufuna kukhala	Disagree 1 Agree 0	1 0
088. Madokotala ndi anamwino akuyenera kudziwa chinthu chimene munthu aliyense wotenga mbali mukafukufuku akulandira	Disagree 1 Agree 0	1 0
089. Mankhwala enieni akuunikidwawo akuyenera kumaperekedwa kwa anthu amakhalidwe amene angawapangise kutenga matenda mosavuta	Disagree 1 Agree 0	1 0
090. Pulasibo akuyenera kuperekedwa kwa anthu amene makhalidwe awo sangawapangise kwenikweni kutenga matenda mosavuta	Disagree 1 Agree 0	1 0
091. MALIKISI ONSE KUONKHESERA (PA 5)		

092. Muli ndi malangizo ali wonse kwa anthu ena amene akufuna kupanga chisankho choti alowe mkafukufuku ngati ameneyu.

……
……

……
……

093. Muli ndi ndemanga ina iliyonse imene mukufuna kugawana nafe yokhuza kafukufuku wa mankhwala ovalira

……
……
……

Zikomo kwambiri potenga nthawi yanu kuyankhula nafe. Zimene mwatiuzazi zitithandiza kwambiri pa kafukufuku wathuyu.

Nthawi yomalizira: …….

TABLE 7: KUONKHEZERA MALIKISI ONSE PAMODZI NDI KUWAIKA/KUWAGAWA MMAGULU

TABLE	MALIKISI ONSE	MALIKISI AMENE APEZA	MALIKISI PA 100	GULU
094 Table 1 Randomisation	8			
095. Table 2 Placebo use	9			
096. Table 3 Blinding	5			
097. Table 4 Implications	9			
098. Table 5 Knowledge	4			
099. COMPOSITE SCORE	40			
100. **CATEGORY**				

CATEGORY CLASSIFICATION

0%-50% = CATEGORY 1
51%-74% =CATEGORY 2
75% + = CATEGORY 3

Mau owonjezera:...……

……

……

……

……

……

……

Appendix 5: Informed Consent form for participants (Chichewa)

UNIVERSITY OF KWAZULU-NATAL
SARETI
School of Psychology

CHIKALATA CHA CHILOLEZO CHA WOTENGA MBALI MUKAFUKUFUKU WA MANKHWALA OVALIRA (MAIKUROBISAIDI)

MUTU WAKAFUKUFUKU:

Kafukufuku ofuna kudziwa za momwe anthu otenga mbali mu kafukufuku wa mankhwala ovalira (maikurobisaidi) amvetsera ndi umo amaonera zokhuza kasankhidwe ka patali patali ka otenga mbali (randomaizeshoni), kubisa kwa mbali ziwiri (otenga mbali kapena ofufuza sadziwa zimene otenga mbali akulandira) ndi kugwiritsa ntchito mankhwala owoneka ngati ndi enieni amene akuwunikidwa mukafukufuku koma zisali choncho (pulasibo).

Kufotokoza mvemvemve weniweni wa kafukufuku.

Zikomo, ine ndine m'modzi wa gulu limene likupanga kafukufuku ofuna kudziwa mmene anthu amene akutenga nawo mbali mukafukufuku wa mankhwala ovalira akumvetsera za ndondomeko ya kafukufukuyo. Kafukufukuyu ndi mbali imozi ya maphunziro apamwamba aukachenjede waung'anga wa a Paul Ndebele pa sukulu yaukachenjede ya KwaZulu-Natal. Ife sindife wogwira ntchito pachipatala pano. Kafukufukuyu ndi mbali imodzi ya maphunziro amene akuperekedwa pa sukulu ya ukachenjede ya KwaZulu-Natal omwe cholinga chake ndi kulimbikitsa umunthu pakapangidwe ka kafukufuku. Tikukupemphani kuti mutengeko mbali mukafukufukuyu. Mukupemphedwa kutenga nawo mbali pokhalanso inu otenga mbali mukafukufuku wa mankhwala ovalira.

Kafukufukuyu akufuna kufufuza za mamvetsedwe ndi m'mene otenga mbali mu kafukufuku wa mankhwala ovalira akuwonera za njira ineme ikugwiritsidwa ntchito mu kafukufukuyu. Tikungofuna kudziwa mmene mukumvetsera za ndondomeko ya kafukufuku amene inu mukutenga mbali komanso maganizo anu pa ndondomekoyo. Palibe yankho lolondola kapena losalondola. Ngati mulola kutenga nawo mbali tidzatenga mayankho anuwo ndipo akatithandiza pamene tikaunika zotsatira za kafukufuku ameneyu. Tikapeza kupelewera mukudziwa kwanu tizachitapo kanthu pakuyambisa machitochito mtsogolo muno amene azakuthandizani inu kudziwa. Anthu onse amene analowa kafukufuku miyezi itatu yapitayo kupita m'mbuyomu ndiwo ali woyenera kutenga nawo mbali mukafukufukuyu.

Ndondomeko ya momwe tipangire kafukufukuyu.

Takonza kuti tilembe anthu 218 omwe atenge mbali mukafukufukuyu ndipo anthu wonse ndi omwe akutenga mbali mu kafukufuku wa mankhwala ovalira. Ngati mukuvomera kutenga nawo mbali muzafunsidwa mafunso okhuzana ndikutenga kwanu mbali mu kafukufuku wa mankhwala ovalira. Kukambirana kwathu kuzitha mphindi makumi anayi kapena asanu (40-50 minutes) ndipo tizikumana muchipinda chodukamphepo. Tikupemphani chilolezo chanu kuti tijambule zokambirana zathu pa chojambulira mawu kuti tikathe kuziunika bwino lomwe nthawi ina. Titatha kulowetsa zokambirana zathuzo pa makina a kompyutala makasetiwo tizawaononga.

Zolowa za mkafukufukuyu.

Palibe cholowa chenicheni chimene muchipeze chifukwa cha kutenga nawo mbali pakafukufukuyu. Komano chovuta chimene tikuchiwona nchakuti mwina tilowako pang'ono mkati mwa moyo wanu wachinsinsi pamene tizikufunsani za kutenga kwanu mbali mukafukufuku wa mankhwala ovalira. China nchakuti mwina mukhoza kukhala osasangalala kapena kukhumudwa pamene tikambirana za kutenga mbali kwanu mu kafukufuku wa mankhwala ovalira. Pamene zokambirana zili mkati ngati penapake muona kuti simukumva bwino, chonde ndiuzeni ine ndipo ndidzayesetsa kuti mwalondoleredwa kwa anthu oyenera omwe azakusamalirani.

Pomaliza pa zokambirana zathuzi muzalandira K500 imene izakuthandizani inu pa mayendedwe anu ndi zina zotero.

Phindu lanu

Palibe phindu lenileni limene muzapeza pakutenga nawo mbali mukafukufukuyu. Kafukufukuyu adzapindulira omwe akupanga kafukufuku wa mankhwala ovalira ndi wotenga mbali mukafukufukuyu a mtsogolo muno kupyolera mu chidziwitso chatsopano chimene chipezeke kuzera mu kafukufukuyu. Ngati tipeza kuti pakusoweka chidziwitso chowonjezera, tizayambitsa zichitochito zomwe zizakuthandizani inu kumvetsetsa ndi kudzindikira ndondomeko ya kafukufukuyu ndipo tidzakupemphani inu kuti mutengeko mbali. Tizakudziwitsani inu za zotsatira za zokambiranazi komanso zotsatira za kafukufukuyu kupyolera mu misonkhano imene izachitike kumapeto kwa kafukufukuyu

Ngati muli osasangalatsidwa kutenga mbali

Dziwani kuti kutenga mbali mukafukufukuyu ndimwakufuna kwanu. Simukuumirizidwa kutenga nawo mbali ayi. Muli ndi ufulu wosankha kutenga mbali kapena ayi ndipo pamene mwasankha kutenga mbali ndipo pazifukwa zina mwaganiza zosintha maganizo anu wotenga nawo mbali mkafukufukuyu, muli ndi ufulu wotero nthawi ina iliyonse. Ngati simukufuna kulowa mkafukufukuyu, kapena ngati mulowa koma nthawi ina muganiza zosiya kutenga mbali mukafukufukuyu muli womasuka ndipo izi sizikukhuzana munjira iliyonse ndikutenga kwanu mbali mukafukufuku wa mankhwala wovalira kapena chithandizo chimene mumalandira pachipatala pano. Muzapitiriza kutenga mbali mukafukufuku wa mankhwala ovalira monga kale komanso mudzapitiriza kulandira chithandizo pachipatala pano ngati kale. Pamene inu mukutenga mbali mukafukufuku ameneyu muli ndi ufulu wosayankha mafunso ena ngati simuli womasuka kuyankha mafunsowo.

Ngati simunapangebe chisankho chotenga nawo mbali mkafukufukuyu tikupemphani kuti mutilole tizakuoneninso tsiku lina limene mudzabwere kuchipatala kuno kuti tidzakambiranenso bwino. Tikupemphanso chilolezo chanu kuti tizathe kukupezani

mtsogolo muno pankhani ya zichitochito zimene tidzayambitse ngati kupyolera mkafukufukuyu tipeza kupelewera muchidziwitso zimene ziri zofunika kukonza. Ngati mukuvomera kutenga nawo mbali tidzakumana nanu matsiku akubwerawa kuchipatala kunkuno ngati mbali imodzi yakafukufuku wa mankhwala ovalira.

Chinsinsi

Simuzadziwika munjira iliyonse ndi maganizo anu chifukwa sitizafuna dzina lanu koma m'malo mwake mudzapatsidwa nambala imene muzadzindikiridwa nayo kotero kuzakhala kovuta kuti aliyense adziwe kuti maganizo amenewo ndi anu. Nambalayi izagwiritsidwa ntchito ngati chidzindikiro pa mapepala amafunso onse amene muzayankhe. Ogwira ntchito athu adzasunga ndandanda wa manambala ndi maina a anthu amene atenge nawo mbali mukafukufukuyu mwachinsinsi ndithu. Izi zizatithandiza ife kulumikizana nanu pamene tifuna kukupezaninso mwapadera ndikucheza nanunso.

Amene mungampeze

Ngati pali zofunsa zina zokhuzana ndi kafukufukuyu, mukhoza kuwapeza a Paul Ndebele amene ali oyang'anira zakafukufukuyu panambala iyi 09619937. Ngati pazifukwa zina mukufuna kuyankhula ndi munthu wina osati a Ndebele zokhuza kafukufukuyu mukhoza kuyankhula ndi Mrs Thandizo Kamwendo amene ndi wamkulu wa komiti ya ethics pa sukulu ya ukachenjede ya College of Medicine pa nambala iyi 01871911 kapena pangani fax pa nambala iyi 01874700. Amene akuwayang'anira kapena kuti kuwathandiza a Ndebele pa maphunziro awo ndi Prof D. Wassenaar amene akupezeka pa nambala iyi +27 33 2605373 kapena email iyi wassenaan@ukzn.ac.za

Chigamulo

Ine……(maina onse a otenga mbali)

ndiri pano kutsimikizira kuti ndamvetsetsa zomwe ziri muchikalata ichi komanso ndamvetsetsa tsatanetsatane wa kafukufuku uyu ndipo ndikuvomera kutenga nawo mbali mkafukufuku ameneyu. Kuonjezera apo ndikuvomera kupezedwa nthawi ina iliyonse ndikutenga mbali mumachitochito amtsogolo okhuzana ndi kafukufukuyu

Ndamvetsetsa kuti ndiri ndi ufulu osiya kutenga mbali mukafukufukuyu nthawi ina iliyonse imene ndikufuna

Saini ya wotenga mbali tsiku

……. **……**

Kwa ofunsa mafunso

Chonde zindikirani kuti munthu amene akufuna kutenga mbali ayenera kupatsidwa nthawi yoti awerenge ndi kumvetsa chikalata cholongosola za kafukufukuyu. Ngati angakhale ndi mafunso pa ndondomeko ya kafukufukuyu afunse asanavomere kutenga nawo mbali. Izi zikuyenera kuchitika nthawi zonse ngakhale pamene wopangitsa kafukufuku palibe komanso nthawi yoti akhoza kufunsa abale.. Chonde mpatseni otenga mbali aliyense chikalatachi.

NTHAWI YOYAMBIRA: .....

Appendix 6: Research staff questionnaire in English

UNIVERSITY OF KWAZULU-NATAL

SARETI

School of Psychology

A study of trial participants' understanding and attitudes towards randomisation, double blinding and placebo use – A pilot intervention in a microbicide trial in Malawi

MICROBICIDE TRIAL STAFF QUESTIONNAIRE

Study participant identifier:……

Section 1 – Gathers demographic information

Tell me briefly about yourself

……
……
……

001 Sex …….
002 Age…….
003 Job Designation …….
004 Training Academic Qualifications ……..
005 Professional Qualifications ……..
006 In-house training ……..
007 Other relevant training ……..
008 Prior relevant experience ……..

Section 2 – Information on the microbicide trial, formal protocols, experience in obtaining informed consent, randomisation double blinding and placebo use

009 Tell me about a typical day for you at this clinic.

……
……
……

010 Tell me in brief what your responsibilities are in the recruitment of participants.

……

011 What do you think when you hear the term research?

……

012 What do you think participants think when they hear the term research?

……..
……..

013 If I was a participant and was not familiar with the term research, how would you describe it to me?

……
……

014 What part of this protocol is hardest for participants to understand?

……
……

015 What do you think is the most important thing a participant needs to understand about this research protocol before they make their decision to enroll?

……..

……

016 How would you explain the difference between enrolling in a research protocol and coming to the clinic for routine care?

……

……

017 Do you think participants understand the difference?

……

018 What do you think are some of the benefits of enrolling in this research protocol for the participants?

……..

……

……..

019 What do you think are some of the disadvantages or burdens of enrolment in this research protocol?

……

……

020 I know that sometimes people enroll in research protocols to get access to medical care. Do you think some participants enroll in this study to get access to care?

……

……

021 How often do participants hesitate/refuse to participate in this study?

……..…

022 Why do you think they hesitate or refuse?

……

023 What steps if any are taken to encourage participants to participate?

……

……

024 For those participants who initially refuse to participate but change their mind later and agree, what do you think would have made them change their mind?

……

……

Recruitment process

025 Could you share how your conversations with prospective research participants usually go.

……

……

026 What types of questions do participants ask most often?

……

……

……

027 What issues do they focus on?

……

……

028 How do you assess a participant's understanding of the research protocol?

……

……

029 When are you comfortable that they know enough to provide their consent?

……..

……..

Factors in decision making

030 What factors do you think participants consider before they decide to enroll in the study?

031 How often do participants agree to enroll?

…….

……

032 Why do you think they say yes?

……

……

033 How often do participants who agree initially, refuse in future?

…….

034 Do they provide reasons?

……

……

035 Are there any notable differences between those who agree to participate and those who refuse?

……..

…….

Questions on randomisation, placebos, and blinding

036 Can you please describe the groups of participants in this study?

……..

……..

037 Describe the way participants are assigned into the groups.

……..

……..

038 How are different products assigned in this study?

……

……..

039 Does the doctor or clinic staff know which product a participant will receive?

…….

……..

…….

…….

040 To whom is the placebo given?

…….

……

Generally how do the women respond when you tell them about

041 Randomisation …….

042 Placebo use ……..

043 Double blinding ……

044 Have you had a participant asking whether he/she had received the actual product or placebo?

……

045 What was your response?

…….

046 What was their reaction?

……

047 If a participant would demand to know the treatment they are receiving what would you do?

……
……

048 Do some participants ask to be put on a specific product including those products that are not part of the protocol?

……

If I was a potential participant, how would you describe the following terms:

049 Placebo

……
……
……

050 Randomisation

……
……
……

051 Double Blinding

……
……
……

Why do you think these procedures are part of this study?

052 Placebo use

…….

053 Randomisation

…….

054 Double Blinding

…….

What are the implications/disadvantages of these procedures to the individual participants?

055 Placebo use

…….

056 Randomisation

…….

057 Double blinding

…….

058 Have you come across any participants who have refused to participate because they were afraid of receiving the placebo?

…….

059 Generally do you think that participants understand the concepts of randomisation, double blinding and placebo use?

……..
……..
……..

060 What are some of the challenges in obtaining informed consent that you have faced since you joined this study?

…….
…….

…….

061 What would you change to improve trial participants understanding of the trial purpose and trial procedures?

……..
……..
……..
……..

062 Do you have any questions or comments you would want to make about our conversation today?

…….

…….

……

……

Thank you for taking your time to answer these questions. The information you have provided is very useful.

End time……

Appendix 7: Informed consent form for staff (English)

UNIVERSITY OF KWAZULU-NATAL

SARETI
School of Psychology

MICROBICIDE TRIAL STAFF CONSENT FORM

Title of Research project : A study of trial participants' understanding and attitudes towards randomisation, placebo use and double-blinding – A pilot intervention in a microbicide trial in Malawi

---

Explanation of the Research project
I am part of a team carrying out a study to assess trial participants' understanding of trial procedures. The study will be part of Paul Ndebele's Doctoral Degree at the University of KwaZulu-Natal. Our team is not in any way affiliated with this microbicide project. This study is a part of the training that is being offered by the University of KwaZulu-Natal aimed at promoting the ethical conduct of research in Africa. We would like to ask you to participate in this research study. The purpose of the study is to assess microbicide trial participants' understanding and attitudes towards clinical trial procedures. We would like to find out from you how you explain these procedures to potential trial participants. There are no wrong or right answers. If you agree to participate, the answers that you provide will be noted while we talk, for analysis later on. All staff members on the microbicide study who are responsible for recruiting trial participants are eligible to participate in this study. You are being invited to join this study because you are one of the staff members responsible for recruiting trial participants into the microbicide trial.

Procedures
We plan to enrol all the staff members responsible for recruiting trial participants as well as a total of 218 microbicide trial participants. If you agree to participate in this study, you will be asked several questions relating to your work. The discussion will last an hour or less and will be held in a private room. We are also requesting your permission to have your interview audio-taped so that the contents of the tape may be analysed later. Your identity will not be on the tape or transcriptions. The tapes will be erased once the data has been transcribed.

Risks and Discomforts
There are no physical risks to you for participating in this study. The other risks we can foresee are those of anxiety or upset that may results from talking about your work as well as the time this exercise may take to complete. .

Benefits
You will not directly benefit from participating in this study. This study may benefit the microbicide trial investigators, current trial participants as well as future trial participants through the new knowledge that it will generate. We will provide you with feedback on these discussions as well as our findings during some meetings to be held at the end of the study.

Alternatives to Participation
Your participation in this study is entirely voluntary. You have the right to refuse or to withdraw from the study at any time. If you do not want to join the study, or if you withdraw from the study, this will not affect your work in the microbicide trial neither will it affect your relationship with the investigators. You may even choose to decline to respond to specific questions if you feel that you are not comfortable with them.

If you have not yet made a decision regarding your participation in this study, we request permission to contact you again tomorrow for a further discussion. We also request permission to contact you again in future for intervention activities if this study identifies some knowledge gaps that need to be filled.

Confidentiality

No reports will identify you in any way. You will be allocated a study number that will be used to identify you. This study number rather than your name will be used to label all study questionnaires. Our research staff will maintain a list linking all participants' names with their study numbers. The list will only enable us to contact you for follow-up activities and interviews. Your information will not be made available to any of the microbicide study staff.

Whom to Contact

For any questions you may have regarding this study, you are please advised to contact Paul Ndebele who is the person in charge of this study at 09619937. If for any reason you want to talk to anyone else about this study besides the person in charge, you can contact Mrs Thandizo Kamwendo, the administrator at the College of Medicine Ethics Committee on 01871911 Fax 01874700. Paul Ndebele's academic supervisor is Prof D Wassenaar who can be contacted at +27 33 2605373 or Wassenaar@ukzn.ac.za .

DECLARATION

PARTICIPATION IN INTERVIEW

I……(full names of participant) hereby confirm that I understand the contents of this document and the nature of the research project, and I consent to participating in the research project. I am willing to be re-contacted and to participate in future activities related to this study

I understand that I am at liberty to withdraw from the project at any time, should I so desire.

SIGNATURE OF PARTICIPANT DATE

……

DECLARATION

AUDIOTAPING OF INTERVIEW

I……(full names of participant) hereby confirm that I have given permission for the audiotaping of the interview. I understand that I have the liberty to refuse the audiotaping of the interview.

SIGNATURE OF PARTICIPANT DATE

……

NOTE TO THE INTERVIEWER:

Potential participants should be given time to read, understand and question the information given before giving consent. This should include time out of the presence of the investigator and time to consult friends and/or family. Please handover to the participant one copy of this information sheet.

Appendix 8: Focus Group Discussion Guide for Participants (English version)

UNIVERSITY OF KWAZULU-NATAL
SARETI
School of Psychology

A study of trial participants understanding and attitudes towards randomisation, double-blinding and placebo use – A pilot intervention in a microbicide trial in Malawi

Focus Group Discussion (Guide for the facilitator)

NOTES FOR FACILITATOR

Hello my name is (**FACILITATOR**). And this is my colleague **(NOTE TAKER).** Welcome to this discussion. As we have already mentioned to you individually, we are part of a team conducting a study to assess microbicide trial participants' understanding of trial procedures. The study will be part of a doctoral degree for Paul Ndebele at the University of KwaZulu-Natal. We are not members of staff at this clinic. Our study is a part of the training that is being offered by the University of KwaZulu-Natal aimed at promoting the ethical conduct of research in Africa. We would like to ask you to participate in this discussion. The purpose of our study is to assess microbicide trial participants' understanding and attitudes towards clinical trial procedures.

Today we would like to find out what you understand about these trial procedures as well as your opinions concerning these procedures. Please note that we are only interested in your views and there are no wrong or right answers; everything you say is important to us. Your name will not be written anywhere, which means that no one will know it was you who said something. The informed consent forms that you have all signed only serve to confirm that you have agreed to be a part of this discussion and you have also given permission for this discussion to be audiotaped for later transcription. We would also like everyone here to respect the opinion of others and not to discuss personal matters of others in this group either during or after the discussion.

If we happen to identify low levels of understanding of trial procedures, we intend to develop an intervention aimed at improving understanding. You have the freedom not to take part in this discussion and that will not affect your participation in the microbicide study or your use of health services at this clinic. We will provide you with feedback on these discussions as well as our findings during some meetings to be held at the end of the study. My colleague with me will also be taking notes just to make sure that we do not miss any important thing that we will disciss today. The discussion will take about one hour. Any one who is not willing to take part in this discussion may indicate that now. Do you have any questions at this point?

NOTES TO FACILITATOR & NOTE-TAKER - Please keep a list of issues to review at the end of the discussion. Leave to the end any questions that participants raise that may afect the discussion and ask for further questions then. Please immediately tell the researcher about any clear misunderstandings by participants about the study arising from the discussion)

ICE BREAKER
What do you think about the microbicide trial?

QUESTIONS ABOUT RESEARCH

1. What do you think when you hear the term research?
2. Can you please in your own words tell me what you understand to be the main purpose of the microbicide study?
3. What were you told in the beginning about the gel's effectiveness in reducing the transmission of HIV?
4. Think back to the beginning of the study, when information was being given to you about the study and you were given some papers with information about the study as well as the study products.
    a. What do you think about the amount of information in the informed consent form?
    b. What about the amount of information verbally given to you by study staff?
    c. Did you have the opportunity to ask questions? What kind of questions?
    d. Do you think the information was adequate? If not, what kind of information could have been added?
    e. What part of this study is hardest for you to understand?
5. What do you think is the most important thing a participant needs to understand about this research before they make their decision to enroll?
6. How would you explain the difference between enrolling in a research study/trial and coming to the clinic for routine care?
7. Do you think most participants understand the difference?
8. What do you think are some of the benefits of enrolling in this research trial for the participants?
9. What do you think are some of the disadvantages or burdens of enrolment in this research trial?
10. I know that sometimes people enroll in research studies/trials to get access to medical care. Do you think some participants ever enroll in medical research studies to get access to care?
11. Do you think there are participants who hesitate/refuse to participate in this trial? Why do you think they hesitate or refuse?
12. What were your main reasons for deciding to participate in the study?
13. What factors should participants consider before they decide to enroll in the study?
14. When you were told about the study when you first joined, do you think you were clearly told what would happen?

Questions on randomisation, placebos, and blinding

15. Can you please describe the different groups that participants in this study have been allocated to?
16. Describe the way participants are assigned into the groups.
17. Do you think that staff adequately explained the process of allocation to the different study groups to you? If not, what do you think you should have been told?
18. Did you expect that you would be in the group you were allocated to? How do you feel about being in the group you were placed in?
19. How are different products assigned in this study?
20. Does the doctor or clinic staff know which product a participant will receive?
21. What is a placebo?
22. To whom is the placebo given?
23. What are some of the advantages of participating in a microbicide trial?
24. What are some of the disadvantages of participating in this trial?

25. If at the end of the trial, you are informed that you were on the placebo, how would you feel?
26. Do you think that there is a chance of you becoming HIV positive while in this study?
27. Have you been told that this is a possibility?
28. If at the end of the study you were told that you are HIV positive how would you feel?

Let's talk about the various study procedures in the microbicide trial:

29. Can you please explain how participants are randomised into the various study arms?
30. Does the research participant as well as the researcher know which study product an individual has been allocated to?
31. Why do you think placebo is used in this study?
32. Why were participants randomised in this study
33. Why did the researchers employ the double blinding procedure for the study?
34. What do the following terms mean?
35. Placebo use?
36. Randomisation?
37. Double blinding?
38. To the above procedures and concepts have any implications to the trial participants?
39. Do people consider these procedures in deciding to participate in a microbicide trial?
40. Do you think participants understand enough about the purpose and procedures of this research?
41. What, if anything, would you change to improve understanding of the trial purpose and procedures?
42. Do you have any questions or comments about this discussion or the microbicide study?

We have come to the end of our discussion. Thank you very much for your time and for your comments. What did you think about this discussion? The information you have given us will be used in ensuring that participants' understanding of trial procedures is improved. Thank you for taking your time to answer these questions. The information you have provided is very useful.

End time……

Appendix 9: Informed Consent Script for FGDs
(English Version)

UNIVERSITY OF KWAZULU-NATAL
SARETI
SCHOOL OF PSYCHOLOGY

FOCUS GROUP DISCUSSION
INFORMED CONSENT FOR PARTICIPATION AND AUDIOTAPING OF FOCUS GROUP DISCUSSION

Title of Study: A study of trial participants' understanding and attitudes towards randomisation, double blinding and placebo use – A pilot intervention in a microbicide trial in Malawi

---

Explanation of the research project
Welcome to this discussion. We are part of a team conducting a study to assess microbicide trial participants' understanding of trial procedures. The study will be part of a doctoral degree for Paul Ndebele at the University of KwaZulu-Natal. We are not members of staff at this clinic. Our study is a part of the training that is being offered by the University of KwaZulu-Natal aimed at promoting the ethical conduct of research in Africa. We invite you to participate in this discussion. The purpose of our study is to assess microbicide trial participants' understanding and attitudes towards clinical trial procedures. Today we would like to explore what you understand about these trial procedures as well as your opinions concerning these procedures.

Please note that we are only interested in your views and there are no wrong or right answers; everything you say is important to us. Your name will not be written anywhere, which means that no one will know it was you who said something. We would also like everyone here to respect the opinion of others and not to discuss personal matters of others in this group either during or after the discussion. The answers that you provide will be recorded as we will be talking for analysis later on. Since this discussion is very important to us, we would like to record it, with your permission (ask for permission). You have the freedom not to take part in this discussion and that will not affect your participation in the microbicide study or your use of health services at this clinic. We will provide you with feedback on the findings through posters we will place in the clinic as well as a newsletter that will be made available to all study participants. My colleague with me will also be taking notes just to make sure that we do not miss any important thing that we will disciss today. The discussion will take about one hour.

Procedures
We plan to enrol a total of 20 microbicide trial participants for two focus group discussions. If you agree to participate in the discussions, you will be asked several questions relating to your microbicide trial participation. The discussion will last at least one hour. Since this discussion is very important to us, we would like to record it, with your permission. We are therefore requesting your permission to have the discussion audio-taped so that the contents of the tape may be transcribed and analysed later. The tapes will be destroyed after the data has been captured on computer.

Risks and Discomforts
There are no physical risks to you for participating in this study. The only risks we can foresee include a minor invasion of your privacy since we are going to ask you questions about your participation in the microbicide trial. The other risk is that of anxiety or upset that may result from talking about your participation. If you feel distressed please tell me and I will make sure that you are referred to appropriate trial support services. You will also receive MK500 to cover your travel, time and inconvenience.

Benefits
You will not directly benefit from participating in the discussions. This study may benefit the microbicide trial investigators as well as future trial participants through the new knowledge that it will generate. If we identify some needs for addional knowledge, we will develop an intervention which will be aimed at improving understanding of trial procedures. We will provide you with feedback on these discussions as well as our findings during some meetings to be held at the end of the study.

Alternatives to Participation
Your participation in this discussion is entirely voluntary. You have the right to refuse or to withdraw from the discussion at any time. If you do not want to join the discussion, or if you withdraw from the discussion, this will not affect your participation in the microbicide trial neither will it affect the quality of care you receive at this health institution.

Confidentiality
No reports will identify you in any way. We will not ask for your name and you will be allocated with a study number that will be used to identify your responses and comments.

Whom to Contact
For any questions you may have regarding this study, you are please advised to contact Paul Ndebele who is the person in charge of this study at 09619937. If for any reason you want to talk to anyone else about this study besides the person in charge, you can contact Mrs Thandizo Kamwendo, the administrator at the College of Medicine Ethics Committee on 01871911 Fax 01874700. Paul Ndebele's academic supervisor is Prof D Wassenaar who can be contacted at +27 33 2606162 or Wassenaar@ukzn.ac.za .

DECLARATION

PARTICIPATION IN FOCUS GROUP DISCUSSION AND PERMISSION TO AUDIOTAPE FOCUS GROUP DISCUSSION

I……(full names of participant) hereby confirm that I understand the contents of this document and the nature of the research project, and I consent to participating in the focus group discussion. I am willing for my responses and answers to be audiotaped during the discussions for later transcription.

I understand that I am at liberty to refuse to join the focus group discussion and also to withdraw from the discussion at any time, should I so desire.

SIGNATURE OF PARTICIPANT DATE

……

NOTE TO THE INTERVIEWER:

Potential participants should be given time to read, understand and question the information given before giving consent. This should include time out of the presence of the investigator and time to consult friends and/or family. Please hand to the participant one copy of this information sheet.

Appendix 10 Focus Group Discussion Guide for participants (ChiChewa Version)

University of KwaZulu-Natal
SARETI
School of Psychology

Kafukufuku ofuna kudziwa mamvetsedwe ndi maganizidwe a anthu amene akutenga mbali mu kafukufuku wa maikulobaiosaidi pa za kasankhidwe ka patalipatali (randomaizeshoni), kubisa kwa kawiri (dabo bulaindi) ndi kugwiritsa ntchito zinthu zomwe zimaoneka ndikumveka ngati zenizeni zimene zikuunikidwa mukafukufuku koma zisali izo (pulasibo).

Focus Group Discussion (Guide for the facilitator)

NOTES FOR FACILITATOR

Zikomo, ine dzina langa ndi ……..otsogolera zokambiranazi ndipo uyu ndi mzanga dzina lake ndi……. amene ali otolankhani. Muli olandiridwa kuzokambiranazi. Khalani omasuka. Monga takulongosolerani kale payekha payekha, ndife amodzi a gulu la anthu a kafukufuku ofuna kudziwa m'mene otenga mbali mukafukufuku wa maikulobaiosaidi amvetsera za ndondomeko ya kafukufukuyo. Kafukufukuyu ndi mbali imozi ya maphunziro apamwamba aukachenjede waung'anga wa a Paul Ndebele pa sukulu yaukachenjede ya KwaZulu-Natal. Ife sindife wogwira ntchito pachipatala pano ayi. Kafukufukuyu ndi mbali ya maphunziro amene akuperekedwa pa sukulu ya ukachenjede ya KwaZulu-Natal omwe cholinga chake ndi kulimbikitsa umunthu mukapangidwe ka kafukufuku mu Africa muno. Mukupemphedwa kuti mutengeko mbali muzokambirana zathu. Cholinga chenicheni cha kafukufuku wathuyu ndi kufufuza m'mene anthu otenga mbali mukafukufuku wa mankhwala ovalira amvetsera za ndondomeko ya kafukufuku.

Lero tikungofuna kudziwa m'mene mukumvetsera za ndondomeko ya kafukufuku amene inu mukutenga nawo mbali komanso maganizo anu pa ndondomekoyo. Chonde dziwani kuti palibe yankho lolondola kapena losalondola popeza ife tikungofuna kudziwa maganizo anu ndipo chirichonse chimene inu munganene ndichofunika kwa ife. Dzina lanu silizalembedwa paliponse kotero kuti palibe amene azadziwe kuti inu ndi inu amene mwapereka maganizo amenewo. Zikalata zachilolezo mutatha kudziwisidwa bwino zakafukufuku zimene nonse mwasaina aliyense payekha payekha zija ndizongoonesa kuti inu mwavomera kuti mutenga nawo mbali muzokambiranazi ndipo mwavomera kuti titha kujambula zokambiranazi pa chojambulira mawu. Tikukupemphaninso kuti tilemekeze maganizo a anzathu ndiponso tisakambirane zinthu zokhuza moyo wa anzathu mgululi pakadali pano komanso zokambiranazi zikatha. Tikapezakupelewera mukudziwa kwanu tizachitapokanthu pakuyambisa machitochito mtsogolo muno amene azakuthandizani inu kudziwa.

Dziwani kuti muli ndi ufulu osatenga mbali muzokambiranazi ndipo izi sizikukhuzana munjira iliyonse ndikutenga kwanu mbali mukafukufuku wa maikulobaiosaidi kapena chithandizo chimene mumalandira pachipatala pano. Tizakudziwitsani zotsatira za zokambirana zathuzi komanso kafukufukuyu kudzera mu misonkhano imene izakhaleko komalizira kwa kafukufukuyu. Mnzangayu adzilemba zina ndi zina zimene tizikambirana

pofuna kuonesetsa kuti sitinaphonye chinthu chirichonse pa zokambirana zathuzi lero. Zokambiranazi zitenga pafupifupi ola limodzi. Aliyense amene safuna kutenga mbali anene tsopano. Muli ndi funso lirilonse pamene tafikapa?

KWA OTSOGOLERA ZOLAMBIRANA NDI OTOLANKHANI

Chonde ikani komalizira zinthu zofunikira kuti zikambiranidwe komalizira kwa zokambirana. Ikani komalizira mafunso ali wonse amene otenga mbali afunsa amene angakhuze zokambirana ndipo mukatero mufunse ngati ali ndi mafunso ena. Chonde uzani eni kafukufuku za kusamvesetsa kulikonse kumene mwakuona pakati pa otenga mbali mukafukufuku pozera mu zokambirana zanu zokhuza kafukufukuyu msanga.

KALAMBULA BWALO

Kodi inu mukuganiza bwanji za kafukufuku wa mankhwala ovalira?

MAFUNSO OKHUZA KAFUKUFUKU

1. Kodi inu mumaganiza chiyani mukamva mau oti kafukufuku?

2. Tandiuzani mChichewa chanu mmene mukumvesera kuti cholinga chake chenicheni cha kafukufuku wa maikulobayasaidi nchiyani?

3. Kodi anakuuzani chiyani poyambilira penipeni zokhuza kagwiridwe ntchito kapena mphamvu zake za mankhwala ovalira pochepetsa kufalikira kwa kachirombo ka HIV?

4. Takumbukirani pamene poyamba penipeni pa kafukufuku pamene amakufotokozerani za kafukufukuyu ndipo anakupatsani zikalata zofotokoza za kafukufukuyu komanso zinthu zimene zikuunikidwa mukafukufukuyu;

   a. Mukuganiza bwanji za kuchuluka kwa chidziwitso chimene chinali mu chikalata chopempha chilolezo chanu mutatha kudziwitsidwa bwino lomwe za kafukufuku?

   b. Nanga mukuona bwanji zakuchuluka kwa chidziwitso chimene munalandira cha pakamwa kuchokera kwa opangitsa kafukufuku?

   c. Munali nawo mwayi ofunsa mafunso? Nanga munafunsa mafunso oti chiyani?

   d. Mukuganiza kuti chiziwitso chimene munalandira chinali chokwanira? Ngati ayi, nchiyani chimene mumafuna kuti chitaonjezeredwa pa chidziwitso chimene munalandira?

   e. Kodi ndi mbali iti yakafukufukuyu imene inakuvutani inu kwambiri kuimvetsetsa?

5. Kodi mukuganiza kuti chofunika kwambiri nchiyani mukafukufukuyu chimene munthu amene akutenga nawo mbali mukafukufukuyu akuyenera kumvetsetsa bwinoasanapange chisankho chotenga nawo mbali?

6. Mungafotokoze bwanji kusiyana pakati pa kulowa mkafukufuku ndi kubwera

kuchipatala kuzalandira mankhwala monga mwanthawi zonse?

7. Mukuganiza kuti anthu ambiri otenga mbali mukafukufuku amamvetsetsa kusiyana kwake?

8. Mukuganiza kuti pali phindu lanji kwa otenga mbali mukafukufukuyu?

9. Kodi inu mukuganiza kuti pali kuipa kapena kulemela kotani kwa kulowa mkafukufukuyu?

10. Tikudziwa kuti anthu ena amalowa mkafukufuku kuti apeza chithandizo chamankhwala. Inu mukuganiza kuti anthu ena amalowa mukafukufuku wa zachipatala kuti azipeza chithandizo chamankhwala?

11. Mukuganiza kuti pali anthu ena amene anakana/kukaika kutenganawo mbali mukafukufukuyu? Inu mukuganiza kuti anakana/kukaika chifukwa chiyani?

12. Kodi inu munalowa mkafukufukuyu chifukwa chiyani?

13. Kodi ndi zinthu ziti zimene otenga mbali mukafukufuku ayenera kuganizira asanavomere kutenga mbali mukafukufuku?

14. Pamene inu munauzidwa za kafukufukuyu nthawi imene mumalowa kumene kafukufukuyu mukuganiza kuti munafotokozeredwa bwinobwino zimene zizachitike?

MAFUNZO PA ZA KASANKHIDWE KAPATALIPATALI(RANDOMAIZESHONI) ZINTHU ZOWONEKANGATI ZENIZENI KOMA ZISALI IZO(PULASIBO) NDI KUBISA (BULAINDING'I)

15. Mungafotokozeko magulu osiyana siyana amene otenga mbali mukafukufukuyu aikidwa?

16. Tafotokozani njira imene amagwiritsa ntchito powagawa anthuwa mmagulu mmenemu?

17. Mukuganiza kuti opangisa kafukufuku anakufotokozerani inu bwinobwino ndondomeko yogawa anthu mmagulu osiyanasiyana akafukufukuyu? Ngati ndi ayi mukuganiza kuti akanakufotokozerani bwanji?

18. Kodi inu mumayembekezera kuti mukhala mugulu limene munayikidwalo? Mukumva bwanji kukhala mugulu limene mulilo?

19. Kodi zinthu zimene zikuperekedwa mukafukufukumu zikumaperekedwa bwanji kwa anthu otenga mbali?

20. Kodi adokotala kapena ogwira ntchito kuchipatala kuno amadziwa chimene munthu otenga mbali akulandira?

21. Kodi pulasibo ndi chiyani?

22. Pulasibo amapatsidwa kwa yani?

23. Kodi ubwino wina ndiwotani okhala munthu otenga mbali mu kafukufuku wa

mankhwala ovalira?

24. Kodi kuipa kwake ndikotani kotenga mbali mu kafukufuku wa mankhwala ovalira?

25. Ngati komalizira kwa kafukufukuyu mudzauzidwa kuti mumalandira pulasibo muzamva bwanji?

26. Mukuganiza kuti nzotheka kuti inu mutenga kachirombo ka HIV muli mukafukufukuyu?

27. Munauzidwako kuti izi ndizotheka?

28. Ngati komalizira mutazauzidwa kuti muli ndi HIV muzamva bwanji?

Tiyeni tikambe za ndondomeko zosiyanasiyana za mukafukufuku wa mankhwala ovalira

29. Mungafotokoze mmene anthu amagawidwira mwapatali patali mmagulu osiyanasiyana akafukufukuyu

30. Kodi anthu otenga mbali mukafukufuku ndi opangitsa kafukufuku amadziwa kuti otenga mbali akulandira chiyani?

31. Mukuganiza kuti pulasibo ikugwirisidwa ntchito mukafukufukuyu chifukwa chiyani?

32. Kodi otenga mbali mukafukufukuyu amasankhidwa mwapatali patali chifukwa chiyani?

33. Kodi ofufuza anasankha njira yobisa kawiri (dabo bulaibdi) chifukwa chiyani

34. Kodi mau otsatirawa akutanthauza chiyani?

35. Kugwiritsa ntchito pulasibo

36. Kusankha mwapatali patali (randomaizeshoni)

37. Kubisa kwakawiri (dabo bulaindi)

38. Kodi ndondomeko zachulidwazi zikutanthauza kalikonse kwa otenga mbali mukafukufuku?

39. Kodi anthu amaganizira izi pofuna kupanga chisankho chofuna kutenga mbali mukafukufuku wa mankhwala ovalira?

40. Mukuganiza kuti anthu amene akutenga mbali mukafukufuku ameneyu akumvetsetsa bwino za cholinga ndi ndondomeko ya kafukufukuyu?

41. Inu mukuganiza kuti mutakhala ndimwayi woti nkusintha mungasinthe chiyani kuti muthandize anthu otenga mbali kumvetsetsa za cholinga?
ndi ndondomeko ya kafukufuku?

42. Muli ndi mafunso kapena ndemanga pa zokambirana zathuzi kapena kafukufuku

wa mankhwala ovalira?

Apa tafika kumapeto kwa zokambirana zathu. Zikomo kwambiri chifukwa cha nthawi yanu komanso ndemanga zanu. Zinthu zimene mwatiuzazi tizigwiritsa ntchito poonesetsa kuti otenga mbali mukafukufuku akumvesetsa ndondomeko ya kafukufuku. Zikomo potenga nthawi yanu kuyankha mafunsowa. Uthenga mwatipatsawu ndiwofunikira kwambiri.

Nthawi yomalizira…….

Appendix 11 Informed Consent Script for FGDs (Chichewa)

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KUKAMBIRANA KWA PAGULU

CHILOLEZEZO CHOPEREKEDWA NDI WOTENGA MBALI ATALANDIRA CHIDZIWITSO NDIKUTI ZOKAMBIRANAZO ZIKHOZA KUJAMBULIDWA PA CHOJAMBULIRA MAWU

MUTU WAKAFUKUFUKU

Kafukufuku ofuna kudziwa za kamvetsedwe ndi kaonedwe ka otenga mbali pa za kusankha otenga mbali mwa patalipatali (randomaizeshoni), kubisa kwa mbali ziwiri (dabo bulaindi) ndi kugwiritsa ntchiito zinthu zooneka ndikumveka ngati zinthu zenizeni zimene zikuunikidwa mukafukufuku koma zisali izo (pulasibo).

---

kufotokoza mvemvemve weniweni wa kafukufuku

Muli olandiridwa kuzokambiranazi. Khalani omasuka. Ndife amodzi a gulu la anthu akafukufuku ofuna kudziwa m'mene otenga mbali mukafukufuku wa maikulobaiosaidi akumvetsera za ndondomeko ya kafukufukuyo. Kafukufukuyu ndi mbali imodzi ya maphunziro apamwamba aukachenjede waung'anga wa a Paul Ndebele pa sukulu yaukachenjede ya KwaZulu-Natal. Ife sindife ogwira ntchito pachipatala pano. Kafukufukuyu ndi mbali ya maphunziro amene akuperekedwa pa sukulu ya ukachenjede ya KwaZulu-Natal omwe cholinga chake ndi kulimbikitsa umunthu pakapangidwe ka kafukufuku mu Africa muno. Mukupemphedwa kuti mutengeko mbali muzokambirana zathu. Cholinga chenicheni cha kafukufukuyu ndi kufufuza m'mene anthu otenga mbali mukafukufuku wa mankhwala ovalira akumvetsera za ndondomeko ya kafukufuku.

Lerotikungofuna kudziwa mmene mukumvetsera za ndondomeko ya kafukufuku amene inu mukutenga nawo mbali komanso maganizo anu pa ndondomekoyo. Chonde dziwani kuti palibe yankho lolondola kapena lasalondola. Ife tikungofuna kudziwa maganizo anu ndipo chirichonse chimene inu munganene ndichofunika kwaife. Dzina lanu silizalembedwa paliponse kotero kuti palibe amene azadziwe kuti inu ndi inu amene mwapereka maganizo amenewo. Tikukupemphaninso kuti tilemekeze maganizo a anzathu ndiponso tisakambirane zinthu zokhuza moyo wa anzathu mgululi pakadali pano komanso zokambiranazi zikatha. Mayankho anu azajambulidwa pa kaseti pamene tili kukambirana kuti ikatithandize pamene tikaunika zotsatira za kafukufukuyu. Poti zokambiranazi ndizofunika kwambiri kwaife tifuna kuzijambula pa kaseti ngati mungatilole. Ndiye mukuvomera kuti zokambiranazi zijambulidwe? Dziwani kuti muli ndi ufulu osatenga mbali muzokambiranazi ndipo izi sizikukhuzana munjira iliyonse ndikutenga mbali kwanu

mukafukufuku wa maikolobaiosaidi kapena chithandizo chimene mumalandira pachipatala pano. Tizakudziwitsani zotsatira zakafukufukuyu kudzera mu mapepala amene adzakhomedwe muchipatala muno komanso zikalata zimene zidzaperekedwa kwa munthu aliyense otenga mbali mukafukufukuyu. Mnzangayu azilemba zinandizina zimene tizikambirana pofuna kuonesetsa kuti sitinaphonye chinthu chirichonse pa zokambirana zathuzi lero. Zokambiranazi zitenga pafupifupi ola limodzi.

Ndondomeko yake.

Takonza kuti tilembe anthu 20 omwe atenge mbali muzokambirana zathuzi m'magulu awiri. Ngati muli olola kutenga mbali mzokambiranazi muzafunsidwa mafunso ambiri okhuzana ndikutenga mbali kwanu mu kafukufuku wa maikulobaiosidi. Kukambirana kwathu kuzitha pafupifupi ola limodzi. Popeza kuti zokambirana zathuzi ndi zofunika kwambiri kwaife tifuna kuti tijambule ndi chimjambula mawu ndiye tikupempha chilolezo chanu kuti tijambule pa chinjambula mawu zokambirana zathu kuti tikathe kuziunika bwino lomwe. Titatha kulowetsa zokambirana zathuzo pa makina a kompyutala makasetiwo tizawaononga.

.

Cholowa chanu mkafukufukuyu

Palibe cholowa cheni cheni chimene mungapeze pamene mukutenga nawo mbali mukafukufukuyu kupatula kuti mwina tilowako pang'ono mkati mwa moyo wanu wachinsinsi pamene tikukufunsani za kutenga mbali mukafukufuku wa maikulobaiosaidi. China nchakuti mwina mukhoza kukhala osasangalala kapena wokhumudwa pamene tikambirana za kutenga mbali kwanu mu kafukufuku wa maikulobaiosaidi. Pamene zokambirana zili mkati ngati penapake muona kuti simukumva bwino muli ndi ufulu kundiuza ine ndipo ndidzayesetsa kuti mwalondoleredwa kwa anthu oyenera amkafukufukumu omwe azakusamalirani. Mudzalandira K500 imene izakuthandizani inu m'mayendedwe ndi zina zotero.

Phindu lanu

Palibe phindu lenileni lowoneka limene inu muzapeza pakutenga mbali mukafukufukuyu. Kafukufukuyu azapindulira omwe akupanga kafukufuku wa maikolobaiosaidi ndi otenga mbali mukafukufuku wa maikulobaiosaidi a mtsogolo kupyolera mu chidziwitso chatsopano chimene chipezeke kuzera mu kafukufukuyu. Ngati tipeza kuti pakusoweka chidziwitso chowonjezera, tidzayambitsa zichitochito zomwe zizakuthandizani inu kumvetsetsa ndi kudzindikira ndondomeko ya kafukufukuyu ndipo tidzakupemphani inu kuti mutengeko mbali ndipo tidzakudziwitsani zazotsatira za zokambirana zathuzi ndinso zotsatira zakafukufuku wathuyu mumisonkhano imene izakhala komalizira kwa kafukufukuyu.

Ngati muli osasangalasidwa kutenga nawo mbali

Dziwani kuti kutenga mbali kwanu muzokambiranazi ndimwakufunakwanu simuli okakamizidwa ayi. Inu muli ndi ufulu okana kutenga mbali kapena kusiya zokambiranazi nthawi ina iliyonse imene inu mufuna. Ngati simukufuna kutenga mbali muzokambiranazi kapena musiila panjira zokambiranazi, izi sizizakhuzana munjira iliyonse ndikutenga mbali kwanu mukafukufuku wa maikolobaiosaidi kapena chithandizo chimene mumalandira pachipatala pano.

Chinsinsi

Simuzadziwika munjira iliyonse ndi maganizo anu chifukwa sitizafuna dzina lanu koma mmalo mwake muzapatsidwa nambala imene izagwiritsidwa ntchito poyimirira mayankho ndi ndemanga zanu.

Amene mungampeze

Ngati pali zofunsa zina zokhuzana ndi kafukufukuyu, mukhoza kuwapeza a Paul Ndebele amene ali oyang'anila zakafukufukuyu panambala iyi 09619937. ngati pazifukwa zina mufuna kuyankhula ndi munthu wina osati A Ndebele zokhuza kafukufukuyu mukhoza kuyankhula ndi Mrs Thandizo Kamwendo amene ndi wamkulu wa komiti ya ethics pa sukulu ya ukachenjede ya College of Medicine pa nambala iyi 01871911 kapena pangani fax pa nambala iyi 01874700. Amene akuwayang'anira kapena kuti kuwathandiza a Ndebele pa maphunziro awo a ukachenjede ndi Prof D. Wassenaar amene akupezeka pa nambala iyi +27 33 2605373 kapena email iyi wassenaan@ukzn.ac.za

Chigamulo

KUTENGA MBALI MUKUKAMBIRANA KWA PAGULU NDI CHILOLEZO CHOTI ZOKAMBIRANA ZIJAMBULIDWE NDI CHOJAMBULIRA MAWU

Ine……(maina onse a otenga mbali)

ndili pano kutsimikiza kuti ndamvetsetsa zomwe zili muchikalata ichi ndi tsatanetsatane wa kafukufuku uyu ndipo ndikuvomera kutenga mbali muzokambirana zimenezi. Kuonjezera apo ndikuvomera kuti mayankho anga akhoza kujambulidwa ndi chojambulira mawu pamene tikukambirana kuti azathe kugwiritsa ntchito pamene azaunikira zotsatira zakafukufuku ameneyu.

Ndamvetsetsa kuti ndili ndi ufulu okana kutenganawo mbali pazokambirana zimenezi kapena kusiya zokambiranazi nthawi ina iliyonse imene ine ndikufuna.

Saini ya otenga mbali **Tsiku**

…… **……**

Kwa ofunsa mafunso

Chonde dzindikirani kuti munthu amene akufuna kutenga mbali ayenera kupatsidwa nthawi yoti awerenge ndi kumvetsa zonse za kafukufukuyu. Ngati angakhale ndi mafunso pa ndondomeko ya kafukufukuyu ayenera kufunsa asanavomere kutenga mbali. Izi zikuyenera kuchitika nthawi zonse kuphatikizapo ndi pa nthawi imene opangitsa kafukufuku palibe komanso nthawi yoti akhoza kukafunsa abale.. Chonde mpatseni otengambali aliyense chikalatachi.

Appendix 12 Post Intervention assessment Questionnaire (English Version)

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POST-INTERVENTION QUESTIONNAIRE

105 QUESTIONNAIRE NUMBER	
106 INTERVIEWER	
107 PARTICIPANT IDENTIFIER	
108 SITE CODE	
109 DATE	

General questions concerning the microbicide research

110 Tell me a bit about the programme you were participating in here.
1. Study to test microbicides
2. Programme to protect women against HIV infection
3. Other (specify)……..
4. Don't know

111 What was the main purpose of the study?
1. To test new microbicides
2. To protect women from HIV infection
3.. Other (specify)……..
4. Don't know

112. What do you know now about the microbicides that you were using?
1. Microbicide not effective
2. microbicide effective
3. nothing
4. Other ……

TABLE 1 - QUESTIONS ON RANDOMISATION,

113. Describe the groups that participants in this study were allocated to. ……	4 correct arms 3 arms (2 gels + placebo) 2 arms (gel + placebo) 1arm /DK	3 2 1 0
114. Describe the way participants were assigned into the groups. ……	1 Describes the process of randomisation 2 Other/DK	1 0
115. Why do you think that participants were randomly allocated to these groups? ……	1 similar samples 2 DK/other wrong answer	1 0
116. TOTAL SCORE FOR THIS TABLE (OUT OF 5)		

117. Which group were you in?
1. Active product arm (buffergel/pro2000)
2. Placebo
3. Don't know

118. How did you feel when you were told about the group you were in?

1 Cheated/ Betrayed
2 Indifferent/Nothing
3 Ok because its part of the study
4 Other (specify)……

119. (If felt cheated/betrayed) Why did you feel that way?

1. Though I was getting microbicide
2. Other specify…….
3. N/A

TABLE 2 - QUESTIONS ON PLACEBO USE

120. Describe the products that were being used in this study …….	4. Two gels plus 1 placebo gel 5. Microbicide + placebo 6. Microbicide only	2 1 0
121.Are you aware that some participants in this study were being given something that looked and feels like the product under study? ……	1 yes 2 No	1 0
122. Why do you think some participants were being given such a product as part of this study? ……..	1 comparison easy 2 wrong answer	1 0
123. How were different products assigned to study participants in this study? …….	1. randomly 2. By need or any wrong answer	1 0
124. What do you think were some of the implications of the use of the placebo to you as a participant? ……..	4. Aware 5. Not aware	1 0
125. TOTAL SCORE FOR THIS TABLE (OUT OF 6)		

126. When you were told that the microbicide that what you were using did not protect you against HIV infection, how did you feel?

1 Cheated/betrayed
2 Indifferent/Nothing
3 Ok because its part of the study
4 Other (specify)……

127. If you felt cheated/betrayed, why did you feel that way?

1 Thought I was being protected from HIV
2 Other (specify)……
3. N/A

128. How did you feel when the research staff requested for the gels that you were using?

1 Cheated/ Betrayed
2 Indifferent/Nothing
3 Ok because its part of the study
4 Other (specify)……

129. If felt cheated/betrayed why?

1. liked the product
2. partner liked product
3. product protected participant
4. Other specify……

5. N/A

TABLE 3 - QUESTIONS ON BLINDING

130. Are you aware that participants, staff and nurses were not supposed to know which product a participant was getting?	1 yes 2 No	1 0
131. Why do you think that neither you, the doctors nor the research staff did not know during the trial about whether you are being given the trial microbicide or placebo? …….	1.Avoid researcher bias 2 Other/DK	1 0
132. What does this mean to a research participant. …….	1 aware 2 not aware	1 0
133. TOTAL SCORE FOR THIS TABLE (OUT OF 3)		

TABLE 4: PLEASE INDICATE WHETHER THESE STATEMENTS ARE TRUE OR FALSE

134. The microbicide that you were given was supposed to prevent you against HIV infection.	**T** **F**	0 1
135. Everybody who participated in the study received the microbicide under study.	**T** **F**	0 1
136. In order to protect themselves against HIV, microbicide trial participants could have used condoms.	**T** **F**	1 0
137. People who joined the microbicide trial were not supposed to worry about HIV infection, no matter what they did.	**T** **F**	0 1
138. People in the microbicide trial were supposed to worry less than people not in this study about catching HIV if they forget to use a condom with a new sex partner.	**T** **F**	0 1
139. People who joined this study could catch HIV anyway.	**T** **F**	1 0
140. The microbicide that was being provided was 100% effective in preventing HIV infection.	**T** **F**	0 1
141. Trial participants needed to continue taking precautions against risky behaviour.	**T** **F**	1 0
142. It was not possible to catch HIV whilst you were using the microbicide.	**T** **F**	0 1
143. TOTAL SCORE FOR THIS TABLE (out of 9)		

TABLE 5 - PLEASE INDICATE YES OR NO

144. In this trial, some women were given the study microbicide and others were given a product which looked like the study microbicide.	**Yes** **No**	1 0
145. You had a one in three chance of receiving a placebo.	**Yes** **No**	1 0
146. The staff were not aware whether they were giving you the real microbicide or the one that looked like the real microbicide.	**Yes** **No**	1 0
147. You could not make a choice whether you received the real microbicide or the other product that looked like the real one.	**Yes** **No**	1 0
148. TOTAL SCORE FOR THIS TABLE (OUT OF 4)		

TABLE 6 - PLEASE INDICATE WHETHER YOU AGREE OR DISAGREE WITH THE FOLLOWING STATEMENTS

149. Researchers should advise participants whether they are on the placebo or actual study product	Disagree Agree	1 0
150. Participants should be allowed to choose which study group they want to join.	Disagree Agree	1 0
151. Doctors and nurses should know which product each participant is receiving.	Disagree Agree	1 0

152. Can you share with us any comments that you have about the microbicide study?
……..

……
……
153. Can you share with us any comments about this study.

…….
…….
Thank you for taking your time to speak to me. The information you have given me will be very useful.

TABLE 7: COMPOSITE SCORE CALCULATION AND CATEGORY CLASSIFICATION

TABLE	POSSIBLE SCORE	SCORE	%	CATEGORY
154 Table 1 Randomisation	5			
155. Table 2 Placebo use	6			
156. Table 3 Blinding	3			
157. Table 4 Knowledge about trial	9			
158. Table 5 Knowledge about procedures	4			
159. COMPOSITE SCORE	27			
160. **CATEGORY**				

CATEGORY CLASSIFICATION

0%-50% = CATEGORY 1
51%-74% =CATEGORY 2
75% + = CATEGORY 3

NOTES:...……

……

……

……

……

Appendix 13: Informed consent form for Intervention Phase (English Version)

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INFORMED CONSENT SCRIPT FOR PARTICIPATION IN THE INTERVENTION AIMED AT IMPROVING UNDERSTANDING

Title of Study: A study of trial participants' understanding and attitudes towards randomisation, double blinding and placebo use – A pilot intervention in a microbicide trial in Malawi

---

Explanation of the intervention ACTIVITIES
I am sure you all remember meeting one of our partners who was asking some questions relating to the microbicide trial that you were participating in. We have invited you all because you participated in that earlier activity. In the questions that were being asked, we noted some areas that needed strengthening. As mentioned in the earlier discussions, we are part of a team conducting a study to assess microbicide trial participants' understanding of trial procedures. The study will be part of a doctoral degree for Paul Ndebele at the University of KwaZulu-Natal. We are not members of staff at this clinic. Our study is a part of the training that is being offered by the University of KwaZulu-Natal aimed at promoting the ethical conduct of research in Africa. We now invite you once again to participate in this additional activity. The purpose of this activity is to find out if we can assist in improving your understanding of the microbicide trial procedures.

Procedures
If you are willing to participate in this activity, we will randomly assign you into two groups using small pieces that you will pick from a box. Each group will go through a different discussion session on research. After the sessions, you will be asked to come one by one for a few questions that will be asked by our colleagues about the session you will have gone through. The two sessions will each take about one hour. The questions to each one after the sessions will take about 10 minutes for each person. We will provide refreshments whilst you wait for your turn.

Risks and Discomforts
There are no physical risks to you for participating in this study. The only risks we can foresee include a minor invasion of your privacy since we are going to ask you questions about your participation in the microbicide trial. The other risk is that of anxiety or upset that may result from talking about your participation. If you feel distressed please tell us we will make sure that you are referred to appropriate trial support services. You will also receive MK500 to cover your travel.

Benefits
You will not directly benefit from participating in the discussions. This study may benefit the microbicide trial investigators as well as future trial participants through the new knowledge that it will generate. If we identify the sessions to be important in improving understanding, we will recommend the sessions for use in this and future trials. We will

provide you with feedback on these discussions as well as our findings during some meetings to be held at the end of the study. We will also provide feedback to the microbicide trial staff.

Alternatives to Participation
Your participation in these activities is entirely voluntary. You have the right to refuse or to withdraw from the activities at any time. If you do not want to join the activities, or if you withdraw from the activities, this will not affect your participation in the microbicide trial neither will it affect the quality of care you receive at this health institution.

Confidentiality
No reports will identify you in any way. We will not ask for your name and you will be allocated with a study number that will be used to identify your responses and comments.

Whom to Contact
For any questions you may have regarding this study, you are please advised to contact Paul Ndebele who is the person in charge of this study at 09619937. If for any reason you want to talk to anyone else about this study besides the person in charge, you can contact Mrs Thandizo Kamwendo, the administrator at the College of Medicine Ethics Committee on 01871911 Fax 01874700. Paul Ndebele's academic supervisor is Prof D Wassenaar who can be contacted at +27 33 2606162 or Wassenaar@ukzn.ac.za .

DECLARATION

PARTICIPATION IN INTERVENTION ACTIVITIES

Those who are not willing to participate in the sessions and the individual discussions afterwards can indicate now. Your participating in these sessions and the individual discussions afterwards, is confirmation that the activities have been clearly explained to you, you understand the nature of this study and the current activities, that have been provided with an opportunity to ask any questions, that the questions have been answered to your satisfaction and that you have voluntarily chosen to participate in these activities after having considered the information provided to you. By agreeing to participate you are also confirming that you understand that you are at liberty to refuse to join these activities and also to withdraw from the discussion at any time, should I so desire.

Appendix 14: Post Intervention Assessment Questionnaire (ChiChewa Version)

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SARETI
SCHOOL OF PSYCHOLOGY

MAFUNSO KWA WOTENGA NAWO MBALI MKAFUKUFUKU

105 QUESTIONNAIRE NUMBER	
106 INTERVIEWER	
107 PARTICIPANT IDENTIFIER	
108 SITE CODE	
109 DATE	

MAFUNSO WOYAMBILIRA WOKHUZA KAFUKUFUKU WA MANKHWALA WOVALIRA

110 Mungandiuze mwachidule za kafukufuku amene munatenga nawo mbali kuno ku chipatala.

1. Kafukufuku woyesera mankhwala ovalira
2. Health intervention/chilinganizo choteteza azimai ku kachirombo ka HIV
3. Ngati pali zina (tchulani)……
4. Sindikudziwa

111 Kodi cholinga chenicheni cha kafukufukuyo chinali chotani?

1. Kuyesera mankhwala ovalira
2. Kuteteza azimai ku kachirombo ka HIV
3.. Zina (tchulani)……..
4. Sindikudziwa

112. Mukudziwapo chiyani za mankhwala ovalira amene m'magwiritsa ntchito?

5. Mankhwalawa analibe mphamvu
6. Mankhwalawa anali ndi mphamvu
7. Palibe
8. Zina (tchulani ……

TABLE 1 - MAFUNSO OKHUZA ZA KASANKHIDWE KA ANTHU M'MAGULU MOPANDA NDONDOMEKO (RANDOMISATION)

113. Fotokozani magulu amene wotenga mbali mukafukufukuyu anagawidwa. . …….	4 correct arms 3 arms (2 gels + placebo) 2 arms (gel + placebo) 1arm /DK	3 2 1 0
114. Fotokozani mmene anthu amagawidwira m'magulu mmenemu. . ……	1 Describes the process of randomisation 2 Other/DK	1 0
115. Mukuganiza kuti nchifukwa chiyani wotenga mbali mukafukufukuyu anagawidwa mmagulu munjira yotere (randomization) ……	1 similar samples 2 DK/other wrong answer	1 0
116. Malikisi onse kuonkhesera pamodzi (pa 5)		

117. Inu munali mgulu lanji?

1. Active product arm (buffergel/pro2000)
2. Placebo
3. Sindikuziwa

118. Munamva bwanji atakuwuzani za gulu limene munali?

1 Cheated/betrayed
2 Indifferent/Nothing
3 Ok because its part of the study
4 Other (specify)……

119. (If felt betrayed/cheated ask) Nchifukwa chiyani munamva choncho?

1. Thought I was getting protection
2. Other (specify…….
3. N/A

TABLE 2 - MAFUNSO OKHUZA KUGWIRITSA NTCHITO PULASIBO (PLACEBO USE)

120. Tafotokozani mankhwala amene amagwiritsidwa ntchito mkafukufukuyu …….	7. Two gels plus 1 placebo gel 8. Microbicide + placebo 9. Microbicide only	2 1 0
121. Mukudziwa kuti anthu ena amalandira Zinthu zowoneka chimodzimodzi ngati zimene zikuyesedwa mukafukufukuyu koma zisali izo? ……	1 yes 2 No	1 0
122. Inu mukuganiza kuti nchifukwa chiyani anthu ena amapatsidwa zinthu zimenezo ngati mbali imodzi yakafukufukuyu? ……..	1 To make comparison easy 2 Don't know /wrong answer	1 0
123. Kodi zinthuzi zimaperekedwa bwanji kwa anthu wotenga mbali mkafukufukuyu? …….	1. randomly 2. By need or any wrong answer	1 0
124. Kodi inu mukuganiza kuti kugwiritsa ntchito zinthu zowoneka ngati mankhwala koma zisali choncho (pulasibo) kukutanthauzanji kwa inu monga otenga mbali mukafukufukuyu? ……..	6. Aware 7. Not aware	1 0
125. Malikisi onse kuonkhesera pamodzi (pa 6)		

126. Kodi pamene anakuwuzani kuti mankhwala ovalira amene m'magwiritsa ntchito samakutetezani ku kachirombo ka HIV munamva bwanji?

1 Cheated/ Betrayed
2 Indifferent/Nothing
3 Ok because its part of the study
4 Other (specify)……

127. (If felt cheated/betrayed) Nchifukwa chiyani munamnva choncho?

1 Thought I was being protected from HIV
2 Other (specify)……
3 N/A

128. Munamva bwanji pamene wopanga kafukufuku anaitanisa mankhwala amene m'magwiritsa ntchito?

1 Cheated/ Betrayed
2 Indifferent/Nothing
3 Ok because its part of the study
4 Other (specify)……

129. (If felt cheated/betrayed) Nchifukwa chiyani munawona ngati anakunamizani?

5. liked the product
6. partner liked product
7. product protected participant
8. Other specify……
5. N/A

TABLE 3 - MAFUNSO OKHUZA KABISIDWE (BLINDING)

130. Mukudziwa kuti inu, adokotala komanso ofufuza samayenera kudziwa za mankhwala amene wina aliyense amalandira	3 yes 4 No	1 2
131. Mukuganiza kuti nchifukwa chiyani inu adokotala komanso ofufuza samadziwa pamene kafukufku amachitika kuti inu mumalandira pulasibo kapena mankhwala enieni amene akuunikidwawo? …….	1.Avoid researcher bias 2 Other/DK	1 0
132. Izi zikutanthauza chiyani kwa anthu wolowa mkafukufuku? …….	1 aware 2 not aware	1 0
133. MALIKISI ONSE KUWONKHESERA PAMODZI (PA 3)		

TABLE 4: CHONDE NENANI NGATI ZIGANIZOZI ZILI ZOWONA KAPENA ZABODZA

134. Mankhwala ovalira amene akuunikidwa mukafukufukuyu amayenera kukutetezani ku kachirombo ka HIV.	**T** **F**	0 1
135. Aliyense amene anatenga mbali mukafukufukuyu analandira mankhwala ovalira amene amaunikidwawo.	**T** **F**	0 1
136. Pofuna kuziteteza okha kukachirombo ka HIV wotenga mbali mukafukufuku anakakhoza kugwiritsa ntchito ma kondomu.	**T** **F**	1 0
137. Anthu wotenga mbali mukafukufuku wa mankhwala ovalira sayenera kudandaula za HIV posayang'anira chirichonse chimene angachite.	**T** **F**	0 1
138. Anthu wotenga mbali mukafukufukuyu samayenera kudandaula kwambiri zotenga HIV ngati sadagwiritse ntchito kondomu pamene amagonana ndi bwenzi la tsopano poyerekeza ndi anthu amene sanali mukafukufukuyu.	**T** **F**	0 1
139. Anthu amene analowa mkafukufukuyu ndi woti akhozabe kutenga HIV	**T** **F**	1 0
140. Mankhwala ovalira ndi amphamvu kwambiri (ali 100/100 mphamvu zake) poteteza kukachirombo ka HIV.	**T** **F**	0 1
141. Wotenga mbali mkafukufuku anayenera kusamala pochita zinthu zoti asatenge HIV.	**T** **F**	1 0
142. Nzosatheka kutenga kachirombo ka HIV pamene munthu amagwiritsa ntchito mankhwala ovalira.	**T** **F**	0 1
143. MALIKISI ONSE KUWONKHESERA PAMODZI (PA 9)		

TABLE 5 - CHONDE NENANI NGATI ZIGANIZOZI ZILI ZOWONA KAPENA ZABODZA

144. Mukafukufukuyu azimayi ena analandira mankhwala ovalira akuunikidwawo ndipo ena analandira zinthu zooneka ngati mankhwala ovalirawo koma zisali mankhwala akuwunikidwawo	**Yes** **No**	1 0
145. Munali ndi mwayi umodzi pa katatu kalikonse kuti mukhoza kulandira polasibo	**Yes** **No**	1 0
146. Ogwira ntchito samadziwa ngati amakupatsani mankhwala ovalira enieni kapena zinthu zonga mankhwala ovalira.	**Yes** **No**	1 0
147. Sim'matha kusankha kuti mulandira mankhwala ovalira enieni kapena zinthu zooneka ngati mankhwala ovalira koma zisali izo.	**Yes** **No**	1 0
148. MALIKISI ONSE KUWONKHESERA PAMODZI (PA 4)		

TABLE 6 - CHONDE NENANI NGATI MUKUGWIRIZANA NDI ZIGANIZO ZILI MMUSIZI KAPENA AYI

149. Wopanga kafukufuku aziwauza anthu otenga mbali ngati akulandira pulasibo kapena zinthu zenizeni zimene zikuunikidwazo	Disagree Agree	1 0
150. Wotenga mbali aziloledwa kusankha gulu limene akufuna kukhala.	Disagree Agree	1 0
151. Madokotala ndi anamwino akuyenera kudziwa chinthu chimene munthu aliyense wotenga mbali mukafukufuku akulandira.	Disagree Agree	1 0

152. Mungandiuze ndemanga zimene muli nazo zokhuzana ndi kafukufuku wa mankhwala ovalira?

……..

……

……

153. Mungandiuzeko ndemanga ina iliyonse imene muli nawo yokhuzana ndi kafukufukuyu..

……

……

Zikomo kwambiri chifukwa choyankha mafunso athu. Mayankho amene mwandipatsa akhale wothandiza kwambiri.

TABLE 7 - KUONKHEZERA MALIKISI ONSE PAMODZI NDI KUWAIKA/KUWAGAWA MMAGULU

TABLE	MALIKISI ONSE	MALIKISI AMENE APEZA	MALIKISI PA 100	GULU
154 Table 1 Randomisation	5			
155. Table 2 Placebo use	6			
156. Table 3 Blinding	3			
157. Table 4 Knowledge about trial	9			
158. Table 5 Knowledge about procedures	4			
159. COMPOSITE SCORE	27			
160. **CATEGORY**				

CATEGORY CLASSIFICATION

0%-50% = CATEGORY 1
51%-74% =CATEGORY 2
75% + = CATEGORY 3

Mawu owonjezera……

……

……

……

Appendix 15: Informed Consent form for Intervention Phase (Chichewa Version)

UNIVERSITY OF KWAZULU-NATAL
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KALATA YA CHILOLEZO CHA ANTHU AMENE AKUTENGA NAWO MBALI MKAFUKUFUKU AMENE CHOLINGA CHAKE NDI KUPITITSA PATSOGOLO KAMVETSEDWE KA NDONDOMEKO ZA MKAFUKUFUKU

MUTU WAKAFUKUFUKU: *Kafukufuku ofuna kudziwa za momwe anthu otenga mbali mu kafukufuku wa mankhwala ovalira (maikurobisaidi) amvetsera ndi umo amaonera zokhuza kasankhidwe ka patali patali ka otenga mbali (randomaizeshoni), kubisa kwa mbali ziwiri (otenga mbali kapena ofufuza sadziwa zimene otenga mbali akulandira) ndi kugwiritsa ntchito mankhwala owoneka ngati ndi enieni amene akuwunikidwa mukafukufuku koma zisali choncho (pulasibo).*

Kufotokoza mvemvemve weniweni wa kafukufukuyu.

Ndikukhulupirira kuti mukukumbukira kuti m'modzi wa ife anazakufunsani mafunso wokhuza kafukufuku wa mankhwala ovalira yemwe mumatenga nawo mbali. Takuitanani nonse chifukwa munazayankha mafunso amene timafunsa pa nthawi imeneyo. Kuchokera ku mafunso amene timafunsa tinazindikira kuti pali mbali zingapo zimene zikusowa kuzikonza kapena kuzilimbikitsa. Monga momwe tinakuuzani mzokambirana zathu, ife tiri mgulu la anthu akufukufuku amene akufuna kudziwa m'mene anthu amene akutenga mbali mkafukufuku wa mankhwala ovalira akumvetsera za ndondomeko ya kafukufukuyo.

Kafukufukuyu ndi mbali imozi ya maphunziro apamwamba aukachenjede waung'anga wa a Paul Ndebele pa sukulu yaukachenjede ya KwaZulu-Natal. Ife sindife wogwira ntchito pachipatala pano. Kafukufukuyu ndi mbali imodzi ya maphunziro amene akuperekedwa pa sukulu ya ukachenjede ya KwaZulu-Natal omwe cholinga chake ndi kulimbikitsa umunthu pakapangidwe ka kafukufuku. Choncho, tikukupemphani kuti mutengeko mbali mukafukufukuyu. Mukupemphedwa kutenga nawo mbali pokhalanso inu otenga mbali mukafukufuku wa mankhwala ovalira. Kafukufukuyu akufuna kufufuza za mamvetsedwe ndi m'mene otenga mbali mu kafukufuku wa mankhwala ovalira akuwonera za njira ineme ikugwiritsidwa ntchito mu kafukufukuyu.

Tikungofuna kudziwa mmene mukumvetsera za ndondomeko ya kafukufuku amene inu mukutenga mbali komanso maganizo anu pa ndondomekoyo. Palibe yankho lolondola kapena losalondola. Ngati mulola kutenga nawo mbali tidzatenga mayankho anuwo ndipo akatithandiza pamene tikaunika zotsatira za kafukufuku ameneyu. Tikapeza kupelewera

mukudziwa kwanu tizachitapo kanthu pakuyambisa machitochito mtsogolo muno amene azakuthandizani inu kudziwa. Anthu onse amene analowa kafukufuku miyezi itatu yapitayo kupita m'mbuyomu ndiwo ali woyenera kutenga nawo mbali mukafukufukuyu.

Ndondomeko ya momwe tipangire kafukufukuyu.

Ngati muli wokonzeka kutenga nawo mbali mkafukufukuyu, tikugawani m'magulu awiri pochita mayere. Tigwiritsa ntchito mapepala ang'ono ang'ono amene mutenge kuchokera mkabokosi. Gulu lirilonse lizakambirana mosiyana ndi gulu linzake zokhuza kafukufukuyu. Mukamaliza zokambirana za m'magulu anu, tidzapempha wina aliyense mwa inu kuti adzayankhe mafunso angapo wokhuzana ndi zokambirana za magulu onse awiri zidzatenga ola limodzi. Mafunso kwa wina aliyense adzatenga maminisi khumi. Tidzakupatsani zoziziritsa kukhosi pamene muzidikirira mafunso a payekha payekha.

Zolowa za mkafukufukuyu.

Palibe cholowa chenicheni chimene muchipeze chifukwa cha kutenga nawo mbali pakafukufukuyu. Komano chovuta chimene tikuchiwona nchakuti mwina tilowako pang'ono mkati mwa moyo wanu wachinsinsi pamene tizikufunsani za kutenga kwanu mbali mukafukufuku wa mankhwala ovalira. China nchakuti mwina mukhoza kukhala osasangalala kapena kukhumudwa pamene tikambirana za kutenga mbali kwanu mu kafukufuku wa mankhwala ovalira. Pamene zokambirana zili mkati ngati penapake muona kuti simukumva bwino, chonde tiuzeni ndipo tidzayesetsa kuti mwalondoleredwa kwa anthu oyenera omwe azakusamalirani.

Pomaliza pa zokambirana zathuzi aliyense adzalandira K500 yoyendera.

Phindu lanu

Palibe phindu lenileni limene muzapeza pakutenga nawo mbali mukafukufukuyu. Kafukufukuyu adzapindulira omwe akupanga kafukufuku wa mankhwala ovalira ndi wotenga mbali mukafukufukuyu a mtsogolo muno kupyolera mu chidziwitso chatsopano chimene chipezeke kuzera mu kafukufukuyu. Ngati tipeza kuti pakusoweka chidziwitso chowonjezera, tizayambitsa zichitochito zomwe zizakuthandizani inu kumvetsetsa ndi kudzindikira ndondomeko ya kafukufukuyu ndipo tidzakupemphani inu kuti mutengeko mbali. Tizakudziwitsani inu za zotsatira za zokambiranazi komanso zotsatira za kafukufukuyu kupyolera mu misonkhano imene izachitike kumapeto kwa kafukufukuyu

Ngati muli osasangalatsidwa kutenga mbali

Dziwani kuti kutenga mbali mukafukufukuyu ndimwakufuna kwanu. Simukuumirizidwa kutenga nawo mbali ayi. Muli ndi ufulu wosankha kutenga mbali kapena ayi ndipo pamene mwasankha kutenga mbali ndipo pazifukwa zina mwaganiza zosintha maganizo anu wotenga nawo mbali mkafukufukuyu, muli ndi ufulu woturuka nthawi ina iliyonse. Ngati simukufuna kulowa mkafukufukuyu, kapena ngati mulowa koma nthawi ina muganiza zosiya kutenga mbali mukafukufukuyu muli womasuka ndipo izi sizikukhuzana munjira iliyonse ndikutenga kwanu mbali mukafukufuku wa mankhwala wovalira kapena chithandizo cha mankhwala chimene mumalandira pachipatala pano. Muzapitiriza kutenga mbali mukafukufuku wa mankhwala ovalira monga kale komanso mudzapitiriza kulandira chithandizo pachipatala pano ngati kale.

Chinsinsi

Simuzadziwika munjira iliyonse ndi maganizo anu chifukwa sitizafuna dzina lanu koma m'malo mwake mudzapatsidwa nambala imene muzadzindikiridwa nayo kotero kuzakhala kovuta kuti aliyense adziwe kuti maganizo amenewo ndi anu. Mayankho ndi ndemanga zonse zimene mupereke zizaimiridwa ndi nambalayo.

Amene mungampeze

Ngati pali zofunsa zina zokhuzana ndi kafukufukuyu, mukhoza kuwapeza a Paul Ndebele amene ali oyang'anira zakafukufukuyu panambala iyi 09619937. Ngati pazifukwa zina mukufuna kuyankhula ndi munthu wina osati a Ndebele zokhuza kafukufukuyu mukhoza kuyankhula ndi Mrs Thandizo Kamwendo amene amagwira ntchito ku Ofesi yowona za kafukufuku pa sukulu ya ukachenjede ya College of Medicine pa nambala iyi 01871911 kapena pangani fax pa nambala iyi 01874700. Amene akuwayang'anira kapena kuti kuwathandiza a Ndebele pa maphunziro awo ndi Prof D. Wassenaar amene akupezeka pa nambala iyi +27 33 2605373 kapena pa email iyi wassenaan@ukzn.ac.za

Chigamulo (verbal consent for all)

Anthu amene Sali wokonzeka kutenga nawo mbali mzokambirana kapena mukuyankha mafunso akhonza kunena panopa. Kutenga kwanu mbali mzokambirana ndi mukuyankha mafunso zikutsimikizira kuti mwamvetsetsa zomwe ziri muchikalatachi komanso mwamvetsetsa tsatanetsatane wa kafukufukuyu ndipo mukuvomera kutenga nawo mbali mkafukufukuyu. Kuonjezera apo zikutsimikizira kuti anakupatsani mwayi wofunsa mafunso ndipo mafunso anu anayankhidwa momveka bwino ndipo mukupanga chisankhochi mwa ufulu wanu. Kuvomera kutenga nawo mbali kukutanthauza kuti mwamvetsa kuti muli ndi ufulu kukana kapena kuturuka mkafukufukuyu nthawi ina iliyonse ngati mungafune kutero.

Appendix 16: PowerPoint Presentation of intervention (English version)

What you need to know about clinical trials

About this session

- This message was developed after realising that some research participants have problems understanding clinical trial procedures.
- It seeks to improve understanding about research using everyday language
- To empower people to make informed decisions about participating in research
- Uses every day examples in explaining the clinical trial procedures and their implications

Aim

- To make participants aware about the procedures that are used in clinical trials
  - The purpose of those procedures
  - Justification for the procedures
  - Implications of the procedures to research participants

How are medicines developed

- For drugs to end up being sold in a pharmacy and being used in a hospital, it means that some research has been done to establish that they are effective and safe.
- There are some people who have participated in some research which looked into the effectiveness and safety of all the medicines we are using today.
- We will use an illustration to show you why we conduct research and how it is done.

Some modern drugs came from traditional medicine

- Some of these medicines we use today have been in use for several hundreds of years.
- Some medicines were developed from the traditional medicines that were used by traditional healers, herbalists and our ancestors.

Medicines in a hospital

1

Illustrating how medicines come about through research

- To illustrate how research on medicines is conducted, we will use an example of people from Nseula Village in Ncheu.
- They grow potatoes every year without using any fertilizers.
- After some years, their soils get tired and they produce very small potatoes.
- The yiels per acre is very small.

Growing small potatoes in Nseula Villages

Stunted potato plants
Small potatoes
Low yield per acre

Zakwatu Company

- Zakwatu Company in Blantyre realises this problem and tries to come up with a new fertiliser that they believe can improve the yields for the farmers in Nseula Village.
- The company cannot sell the fertiliser at this moment because no one is sure if the fertiliser works in improving potato yields.
- The company needs to conduct a research using the fertiliser so that they are sure that the fertiliser works.
- The company needs to test the fertiliser against another known fertilizer which is used for potatoes.
- How do they conduct the research.

Meeting with the farmers from Nseula

- The company asks the Agriculture extension Officers (Alangilizi) in Ncheu to do the Research.
- Alangilizi invite farmers from Nseula village to a meeting where they talk to them about the new fertiliser that has been developed.
- They invite those who are willing to join a programme which will test the fertiliser.

During the meeting

- Alangilizi tell the farmers that they are looking for One hundred a farmers who are willing to grow potatoes on a one acre plot as part of the study and to use the fertilizer to be provided and to adhere to other study conditions such as not harvesting any potatoes from the plot until instructed to do so.
- About 123 farmers volunteer and they pick the first 100 farmers.
- They remind the farmers that this is not a programme aimed at improving yields but a study to test the effectiveness of a new fertilizer.
- They also inform the farmers that they have done some initial research in a small garden in Blantyre and that they have found some promising results and remind them that since this new fertilizer has not yet been tested, it is possible they may find it is not effective at all.

How can the alangilizi test the fertiliser

- The people of Nseula have not been using any fertilizers before.
- So in testing the new fertilizer, the Alanlizi can just compare the effectiveness of the new fertiliser without using any other fertilizer as a comparator.
- They may compare results obtained after using the new fertilizer this year to results obtained last year when there was no new fertilizers.
- This comparison may not be the best due to differences in rainfall and pests each year.
- If Alangilizi give all the farmers this new fertiliser they may not be able to ascertain the effectiveness of the new fertiliser since the yield may be affected by the differences in rainfall between last year and this year.
- Alangilizi therefore decides to test the new fertiliser against some sugar which looks exactly like the new fertiliser.

100 bags of fertiliser

- Zakwatu Company has delivered 100 bags of fertiliser which consist of 50bags of the new fertliser and 50 with the sugar which looks exactly like the new fertiliser.
- It is well known that if you apply sugar to your potato crop, nothing will happen.
- The 100 bags are labeled randomly from number 1 to 100 by someone from the company and he is the only one who knows which bag contains what.

Allocating the bags of fertilisers

- During the meeting farmers are asked to pick out some small papers labeled from 1-100.
- These numbers correspond to the numbers labeled on the 100 bags.
- Based on the numbers they pick, each farmer is now allocated a 50kg bag whose number corresponds with the number they picked from the hat.

One 50kg bag per farmer

- The 50kg bag is the one each farmer is supposed to use on their one acre plot of potatoes.
- For each farmer, name and bag number are recorded in a book so that at the end they can tell which bag went to which farmer.
- Both Alangilizi and the farmers do not both know what is in each of the bags assigned.
- In this study, they are testing the new fertiliser against the sugar which looks exactly like fertiliser.
- The study will indicate whether the new fertilizer is effective or not.
- It is possible that the study may reveal that the new fertilizer is not effective at all in improving yields.

Why did they give 50 farmers some bags with something which looked like the new fertiliser?

- So that they can clearly test the effects of the new fertilizer against the sugar which does not in any way work like a fertilizer.
- If they were going to give nothing to the 50 farmers who got the sugar, perhaps they would give little attention to their plots knowing well that they have not been given any fertilizer.
- If the two groups are given something which look similar, they will all give similar attention to their plots.
- What does this mean to the 100 farmers – it means that each of the 100 farmers has a one in two chance of receiving the fake fertilizer.
- The farmers should therefore not believe that they are all receiving the a fertilizer.

Why did the company ensure that both the agricultural extension workers and the farmers would not know what was in each bag?

- To ensure that Alangilizi would not be biased in favour of those who would have received the true fertiliser.
- All the 100 farmers would not be aware what they had been given so they will all give similar attention to their plots.
- The farmers and Alangilizi both do not know what farmer so-and –so received.
- When Alangilizi are advising the 100 farmers, they are assuming that each one got the "new fertilizer"

Randomising: ***Why did the Agric extension workers ask the 100 farmers to pick some small papers from the hat? Why did they not just assign the 100 farmers into the 2 groups?***

- They did not want to group them according to their abilities, friendship, kinship or villages.
- They wanted to ensure that each of the two groups is made up of a variety of farmers in terms of skills, soil quality, irrigation facilities, land slope, pest problems etc so as to truly tell the effects of the new fertliser.
- At least 50 farmers have been selected by chance to receive the new fertilizer which is being tested and 50 to receive the fake fertilizer.

3

Instructions to the farmers

- All 100 farmers are given same instructions on how to use the fertilizer.
- They are to grow potatoes on one acre.
- They are to use 1 teaspoon per potato plant at 3 and 6 weeks.
- They are not allowed to harvest any potatoes from the plot until they are instructed to do so.
- They are supposed to report any issues that they note with the crops on the research plot.
- They are not allowed to use any other type of fertilizer on the plot for this year's crop
- The Alangilizi would visit them every week to ascertain the size of plot, ensure that the farmers are not using any other fertilizers and that they are not harvesting from the research plots.

Alangilizi visiting the farmers

Measuring the effectiveness of the fertiliser

- When the time for harvesting came, Alangiliziasked all the 100 farmers to harvest their crop during the same week and pack them in 50kg bags.
- They went around weighing the produce harvested by each farmer from the 1acre plot.

How were they going to tell if the new fertliser works?

- The agriculture extension workers recorded the harvests for each farmer in the book in which they had recorded the farmers names and the bag numbers.
- Alangilizi observed that some farmers had bumper harvests as compared to others - but noone was sure what was in the bags they had used.
- Someone was then sent from Blantyre with a list which indicated the bag number and the contents for each bag.
- Alangilizi then went back to their book and added a column which stated whether the farmer had been given a bag of fertilizer or sugar.

Findings

- Alangilizi found out that indeed, the new fertilizer had doubled the yield for the 45 farmers who received the bags containing the new fertilizer.
- Those who got the bags containing what looked like the new fertilizer got yields which were not very different from the yields from the past year or other fields which had not had a fertiliser application.




4

Disseminating study findings

- Alangiliz i then sent a report to Zakwatu Company in Blantyre as well as all farmers organizations informing them about their findings.
- After a few months, the new fertilizer was available for everyone to buy through the shops.
- All farmers throughout the Country including those in Ncheu could now use the new fertilizer to improve their yields.
- Thanks to the 100 farmers who participated in the trial.

New Potato fertiliser on the market

- The new fertiliser had passed the testing
- The same applies to medicines.
- When you find medicines in shops, hospitals and phamarcy, they have been tested and passed.

Moving from the Ncheu Farmers to the present study.

- Now we can apply the story of the farmers from Ncheu to the testing of new medicines.
- New medicines cannot be used in patients or sold in pharmacies without going through testing.
- The new medicines developed from plants and other things have to be tested against something so that we are sure that they indeed work.
- Some people who include doctors and nurses are assigned to do the testing – just like the staff you see here.
- In this place, they are testing a new product that has been developed to find out if it can protect women against infection with HIV.
- Women just like you have been invited to participate in this study.

Research Vs Health programmes

- This study is not an HIV prevention programme in which people are given options that assist them in ensuring that they are protected from HIV.
- The purpose of HIV prevention programmes is to protect citizens against HIV infection and the purpose of this study is to identify an option that may be used in ensuring that women are better protected against HIV infection.
- Research differs from HIV prevention programmes in purposes and in the procedures that are followed.
- We will discuss about the various procedures that are used in research and not used in HIV prevention programmes.

In this study

- Products called buffergel and Pro2000 were being tested to find out if they can protect women against HIV infection.
- The 2 products were being tested against a substance which looks like the two products and yet does not contain any of the chemicals contained in the 2 products.
- Another group which only receive condoms without receiving any of the 3 gels has been added to the study so that at the end, they can compare the differences in levels of HIV infection among those ones who receive condoms only against those who received the 3 gels (buffergel, Pro2000 and placebo).

Important issues to note

- What you need to know at all times is that the 3 different products that are being given to women here are not aimed at protecting them against HIV infection.
- The purpose of the programme is to test the two products to find out if they work in protecting women against HIV infection and if they are safe for use in women.
- The tubes containing all 3 products look very similar but each one has got a unique number.
- You were assigned into 4 groups just like the farmers who were assigned into 2 group by picking an ill pieces of paper.
- In your case, you have been assigned a product by a computer which picks up your study number and randomly assigns you the number for the tubes you are going to receive.
- You need to realize that, neither the doctors nor the nurses who work here know what is contained in the specific tubes you have been assigned.
- You also cannot tell what is in the specific tube you have been assigned.
- This means that you may be using any of the two products or the third one which looks and feels like the two which are being tested.

Important things to note about the effectiveness of a product being tested

- At the end of the trial, that is only when we can tell what specific product you have been receiving.
- When this is known, that is when the researchers will determine whether the 2 products work.
- Findings from women who had been assigned to the 2 products will be compared to findings from women taking the product which looks and feels like Pro2000 or Buffergel and those who were given condoms only.
- At the end the study may establish that one of the two works or that they are all not effective in protecting women against HIV infection.
- You have been assigned to either Buffergel or Pro2000 or another product which only looks and feels like the two.
- The staff here did not have any part in the assignment of the product you are receiving.
- There is a one in three chances that you may be using pro2000, buffergel or the product that looks like these 2.

Important things to note about the gels

- At all times, you need to remember that you are not being given the gels so as to protect you against HIV infection.
- You are actually participating in a study to test the effectiveness and safety of these two products.
- The only proven methods that are known to protect you from HIV are condoms and abstinence.
- You yourself cannot tell which product has been assigned to you neither can staff tel.
- This is done in order to ensure that the behaviours of women in all the groups are the same and that staff treat all women in the same way.

The effectiveness of the gels provided through the study

- The gels you received as part of this study may not protect you from HIV infection.
- At the moment there is no evidence which shows how effective the product is.
- This information will only come out at the end of the study.
- This study may establish three things concerning the 2 microbicides:
  - Either buffergel or PR2000 or both are not effective at all in protecting women against HIV infection
  - Either Buffergel or Pro2000 or both are partially effective in protecting women against HIV infection
  - Either Buffergel or Pro2000 or both have been proven effective in protecting women against HIV infection

A word of caution

- Women participating in the programme should therefore not convince themselves that they are in any way protected by the gels as the effectiveness of these products is yet to be proven through this study.
- Women participating in this study should not increase their risky behaviours hoping that they will be protected by the products being tested through this study.
- Women participating in this study should always remember that they can still be infected even when using the gels.

Products that are found useful

- AT the end of the study if the researchers find any of the products to be safe and effective, they recommend them for use by all women and may be made available for sale through phamarcies and other outlets.

Safeguarding the safety of those who participate in research

- **The safety of research participants is assured through various ways including the following:**
- **Experienced research leaders and staff**
- Research involving human beings is only conducted by persons who are adequately trained and qualified. These leaders are assisted by teams of made of people with some specialised skills
- **Laboratory and animal studies** – Before research is conducted in humans, it is first conducted in laboratories using machines and then animals such as mice. Once it is determined that the research is not harmful in animals, the researchers may then consider moving to human beings. What is harmful to animals is usually also harmful to humans.
- **Phases of clinical trials** - Research involving humans is conducted in phases. In Phase one a few individuals from 10-30 are involved. This phase looks at the safety of the product, how the substance moves in the human body and how much of the product is human body can tolerate. Phase 2 looks at whether the drugs works against a specific condition and continues to gather data on safety and includes less than 100 people. Phase 3 looks at the effectiveness of the substance in a large population usually around 3000 persons.

Safeguarding the safety of those who participate in research (2)

- **Scientific and ethical review**- Before research can be conducted, a written plan of the study has to be reviewed by a committee made up of fellow scientists and then by another committee made up by people with various backgrounds including human rights experts. This is referred to as a Research Ethics Committee.
- **National Drug Regulatory authority** - Research is also reviewed by a Government agency responsible for the registration of medicines before it can be initiated.
- **Eligibility criteria** – persons who participate must meet certain criteria before they can join such as age, disease type and health status.
- **Monitoring by study staff**– During the study, study staff will try to identify any side effects as quickly as possible so that action can be taken to address them or even stop the trial. Ethics Committees and National Drug regulatory agencies are also involved in monitoring. Sponsors may also send some monitors to monitor research.
- **Reporting of adverse events**– study participants are required to report any untoward events that occur to them after taking the product being tested.
- **The right to withdraw** – study participants are free to withdraw from the study at any time.

Points to remember

- Research is a search for knowledge
- Research contributes to improvements in health and medicine
- Medicines can only be made available to the general population after being tested using other human beings and proven to be effective.
- You are participating in a research that is testing a product whose effectiveness is yet to be proven.
- It is the intention of this study to test the effectiveness of PRO2000 and Buffergel for protection against HIV infection.
- The study is testing PRO2000 and Buffergel against another substance which does not have any of the active ingredients of the 2 products and against another group which has not received any of the three.
- Condoms are provided to all participants in this study since they are the known best way to protect yourself against HIV infection.
- You may be infected with HIV whilst you are participating in this study and using the products being tested.

A study of trial participants' understanding and attitudes towards randomisation, double-blinding and placebo use: A pilot intervention in a microbicide trial in Malawi.

NOTES FOR PRESENTER

Please read these notes. They are aimed at ensuring that you become familiar with the presentation that you will make in PowerPoint.

1. After welcoming the participants and making them feel relaxed, give a description of the study as provided in the informed consent form for the intervention phase.
2. Proceeds to re-confirm the consent of all the participants.
3. Proceeds to give the presentation using the PowerPoint slides provided

This discussion is aimed at improving your understanding about research and the procedures that are used in research. Several studies have found out that some trial participants participate in trials without understanding the purpose of the trials as well as the implications of participation and trial procedures on themselves as individuals.

It has been found that in some cases researchers make assumptions which may contribute to problems of limited understanding. The following weaknesses have been identified in some interventions aimed at improving understanding:

- Some interventions assume that all people know what research is.
- Some interventions assume that all people are familiar with clinical trial procedures.
- Some interventions do not assist potential participants by making them aware of the trial procedures and their purposes.
- Most of the interventions that have been reviewed do not deal in adequate depth with the personal implications of research participation and the trial procedures.

The current intervention therefore seeks to improve understanding of research using everyday language. Today we are going to talk about how research on human medicines is done using the example of potato farmersfrom Ncheu. This session also seeks to achieve the following:

- To empower people to make informed decisions about participating in research.
- To make people aware that research may fail.
- It uses every day examples in explaining the clinical trial procedures and their implications.
- It does not make any assumptions about pre-existing knowledge.

How do medicines find their way onto shelves in the pharmacy?

As human beings, when we are sick, at times we need medicine. One question that we often do not asks ourselves is: How did these medicines end up in hospitals or pharmacies? For drugs to end up being sold in a pharmacy and being used in a hospital, it means that some research has been done to establish that they are effective and safe. Some of the medicines we use today have been in use for several hundreds of years. Some have been used by traditional healers and our elders for over centuries. In some cases when our children are sick, we may seek the service of a herbalist or we may go to the bush to dig for some herbs. The only difference between those herbs and the medicines is that the medicines have been tested and proven to work in a systematic way while the herbs are simply known to work from experience. It is the systematic way of testing that we will be looking at today. The testing involves other human beings just like us. There are some people who have participated in some research which looked into the effectiveness and safety of most of the medicines we use today. We will use an illustration of farmers from Ncheu to show you why we conduct research and how it is done.

Lets talk about people who live in Ncheu District. Ncheu is well known for potato growing and most of the potatoes we find at the market come from Ncheu. The people in Ncheu grow potatoes every year without using any fertilisers. After some years, their soils get tired and Zakwatu Company in Blantyre has come up with a new fertiliser that they believe can improve the yields for the farmers in Ncheu. Zakwatu Company cannot sell the fertiliser at this moment because noone knows for sure if the fertiliser works in improving potato yields. The Government cannot buy or promote the new fertiliser if they do not know how effective it is. The company therefore needs to conduct a research study using the fertiliser so that they are sure that the fertiliser works. **How do they conduct the research?**

Conducting research

First of all the company uses the fertiliser with a few potato plants in their offices. After finding some promising results, they then try the substance using two small gardens in their yard. After finding yet again some promising results, the company then decides to have the substance tested in the real farmers' settings. The company invites Alangilizi from Ncheu to a meeting in Blantyre where they talk to them about the new fertiliser they have developed and their plans to have the new fertiliser tested. The people from Zakwatu request the Alangilizi to assist by conducting the research activities in Ncheu and Alangilizi agree to the request. The people from Zakwatu inform Alangilizi that they would want them to conduct a study involving 100 farmers in Ncheu. Zakwatu people asked Alangilizi since Alangilizi were based in Ncheu and had knowledge and expertise about farming. If Zakwatu themselves were going to do the research in Ncheu, it is possible that the Government or other NGOs might not accept the results – as Zakwatu might cheat so as to come about with results that show that their new fertiliser works – even if it does not work.

Alangilizi return to Ncheu and immediately call for a meeting where they inform the community about the new study to test the new test the fertiliser. They inform the farmers that they are looking for 100 farmers who are willing to grow potatoes on a one acre plot as part of the study and to use the new fertiliser to be provided and to adhere to other study conditions such as not harvesting any potatoes from the plot until instructed to do so. About 123 farmers volunteer to participate in the study and Alangilizi confirm that all the 123 have 1 acre plots and that they are willing to grow the potatoes as part of the research programme and to abide by the instructions given by the Company. Three farmers show some hesitation and report that they currently do not have adequate labour necessary for the one acre plot. The three are dropped from the group. Since Alangilizi only required a group of 100 farmers, they ask all the 120 to pick small pieces of paper numbered from 100-120. They select those who picked numbers from 1-100 and inform all those that picked number 101 -120 that they were not to be included in the study.

Alangilizi remind the farmers that this is not a programme aimed at improving yields but a study to test if the substance was effective as a fertiliser or not. They also inform the farmers that Zakwatu Company had done some initial research in their offices as well as in two small gardens in Blantyre and that they have found some promising results and remind them that since this new fertiliser has not yet been tested under real conditions, it is possible they may find it is not effective at all.

The people of Ncheu have not been using any fertilisers before. So in testing the new fertiliser, Alangilizi can just compare the effectiveness of the new fertiliser without using any other fertiliser as a comparator. They may compare results obtained after using the new fertiliser this year to results obtained last year when there was no new fertilisers. This comparison may not be the best. If Alangilizi give all the farmers this new fertiliser they may not be able to ascertain the effectiveness of the new fertiliser since the yield

may be affected by the differences in rainfall between last year and this year. Also during the past year, farmers did not make precise measurements of the amount of potatoes they harvested.

The Alangilizi therefore decide to test the new fertiliser against some sugar which looks exactly like the new fertiliser. Zakwatu had provided 2 sets of 50kg bags, one set with the new fertiliser and the other set with the sugar which looks exactly like the new fertiliser. They have added some salt to the sugar so that it tests like real fertiliser (in case farmers tried to differentiate between the two by tasting). It is well known that if you apply sugar to your potato crop, nothing will happen. The 100 bags are labeled randomly from number 1 to 100 by someone from Zakwatu and he is the only one who knows which bag contains what.

The 100 farmers are allocated a bag with a number corresponding to the number they had picked initially. That is the bag they are going to use on their one acre plot of potatoes. For each farmer, name and bag number are recorded in a book so that at the end they can tell what was in each of the bags handed out to the farmers. The agriculture extension workers and the farmers both do not know what is in each of the bags assigned. The study will indicate whether the new fertiliser is effective or not. If the new fertiliser improves the yields significantly, then they can conclude that it is effective. It is possible that the study may reveal that the new fertiliser is not effective at all in improving yields. (Therefore the farmers cannot go and borrow against predicted yields from this plot as they do not know how much they will harvest from the plot after using the new fertiliser)

Why did they give 50 farmers some bags with something which looked like the new fertiliser?

- So that they can clearly test the effects of the new fertiliser against the other substance which does not in any way work like a fertiliser. If they were going to give nothing to the other 50 farmers, perhaps the farmers would give little attention to their plots knowing fully well that they had not been given any fertiliser. If the two groups are given something which looks similar, they will all give similar attention to their plots.
- What does this mean to the 100 farmers – It means that each of the 100 farmers has a one in two chances of receiving the fake fertiliser. The farmers should therefore not trick themselves into believing that they are all receiving the new fertiliser.

Why did the company ensure that both the agricultural extension workers and the farmers would not know what was in each bag?

- To ensure that the agriculture extension workers would not be biased in favour of those who would have received the true fertiliser during their scheduled visits to the farmers to provide advice and to check on progress.
- All the 100 farmers would not be aware what they had been given so they will all give similar attention to their plots.
- The farmers and the extension workers both do not know what farmer so-and –so received.

Why did the Agric extension workers ask the 100 farmers to pick some small papers from the hat? Why did they not just assign the 100 farmers into the 2 groups?

- They did not want to group them according to their abilities, friendship, kinship, area or villages.

- They wanted to ensure that each of the two groups is made up of a variety of farmers across village, ability, kinship and friendship lines so as to truly tell the effects of the new fertliser.
- They wanted to ensure that farmers had been selected by chance to receive either the new fertiliser which is being tested or the fake fertiliser.

The farmers go back to their villages to use the fertiliser

All 100 farmers are given same instructions on how to use the fertiliser. The instructions included the following:

- They are not allowed to harvest any potatoes from the plot until they are instructed to do so.
- They are supposed to report any issues that they note with the crops on the research plot.
- They are not allowed to use any other type of fertiliser on the plot for this year's crop.
- The Alangilizi would visit them every week to ascertain the size of plot, ensure that the farmers are not using any other fertilisers and that they are not harvesting from the research plots.
- The Alangilizi would also receive some reports from the farmers on how their crops were performing and the challenges they were facing, the pests that were destroying the crops if any and any other issues relating to the growth of the plants.

How were they going to measure the effectiveness of the new fertiliser?

When the time for harvesting came, Alangilizi asked all the 100 farmers to harvest their crop during the same week and pack them in 50kg bags. They went around weighing the produce harvested by each farmer from the 1 acre plot. The agriculture extension workers

recorded the harvests for each farmer in the book in which they had recorded the farmers names and the bag numbers. They also collected some potatoes from each farmer for further analysis.

How were they going to tell if the new fertiliser works?

Some farmers had bumper harvests as compared to others - but no-one was sure what was in the bags they had used. Someone was then sent from Blantyre with a list which indicated the farmer's number, bag number as well as the weight of the potatoes harvested. The Alangilizi then went back to their book and added a column which stated whether the farmer had been given a bag of fertiliser or sugar. They found out that indeed, the new fertiliser had doubled the yield for 45 farmers who had received the bags containing the new fertiliser. Those who got the bags containing what looked like the new fertiliser got yields which were not very different from the other people from Ncheu who did not participate in the testing of the new fertiliser. Alangilizi then spoke to the 5 farmers who had been given the new fertiliser to find out what had happened. They found out that 3 of them had not used the new fertiliser and 2 had sold it to their relatives. From these findings, it was obvious that the new fertiliser was effective in improving potato yields.

Alangilizi then sent a report to Zakwatu Company in Blantyre as well as all farmers organizations informing them about the findings. After a few months, the new fertiliser was available for everyone to buy through the shops. All farmers throughout the Country including those in Ncheu could now use the new fertiliser to improve their yields. The Government even bought the new fertiliser for distribution to potato farmers in various Districts. Thanks to the 100 farmers from Ncheu who had participated in the trial. It is important to remember that in this case the study was successful. It could also have proven that the substance from Zakwatu was not effective at all as a potato fertiliser.

Moving from the Ncheu Farmers to the present study.

Now we can apply the story of the farmers from Ncheu to the testing of new medicines. New medicines cannot be used on patients or sold in pharmacies without going through testing. The new medicines developed from plants and other things have to be tested against something so that we are sure that they indeed work. Some people who include doctors and nurses are assigned to do the testing – just like the staff you see here.

In this place, they are testing a new product that has been developed, to find out if it can protect women against infection with HIV. Women just like you have been invited to participate in this study. This study is not an HIV prevention programme in which people are given options that assist them in ensuring that they are protected from HIV. The purpose of HIV prevention programmes is to protect citizens against HIV infection and the purpose of this study is to identify an option that may be used in ensuring that women are better protected against HIV infection. Research differs from HIV prevention programmes in purposes and in the procedures that are followed. We will discuss the various procedures that are used in research and not used in HIV prevention programmes.

In the study, products called Pro-2000 and Buffergel are being tested to find out if they can protect women against HIV infection. The two products area being tested against a substance which looks like the two products and yet does not contain any of the active ingredients contained in the two products. Another group which only receives condoms without receiving any of the gels has been added to the study so that at the end, they can compare the differences in levels of HIV infection among those ones who receive condoms only against those who received the two products (Pro-2000 and Buffergel) and those who received a third product which looks like the two products being tested. What you need to know at all times is that the three different products that are being given to

women here are not aimed at protecting them against HIV infection. The purpose of the programme is to test the two products to find out if they work in protecting women against HIV infection and if they are safe for use in women.

The tubes containing all three products look very similar but each one has got a unique number. You have been assigned into four groups just like the farmers who were assigned into two groups by picking small pieces of paper. In your case, you have been assigned a product by a computer which picks up your study number and randomly assigns you the number on the tubes you are going to receive. You need to realise that neither the doctors nor the nurses who work here know what is contained in the specific tubes you have been assigned. You also cannot tell what is in the specific tube you have been assigned. This means that you may be using any of the two products or the third one which looks and feels like the two which are being tested.

At the end of the trial, that is only when it can be known what specific product you have been receiving. When this is known, that is when the researchers will determine whether the 2 products work. Findings from women who had been assigned to the 2 products will be compared to findings from women taking the product which looks and feels like Pro-2000 and Buffergel and those who were given condoms only. At the end the study may establish that one of the two works or that they are all not effective in protecting women against HIV infection.

You have been assigned to either Pro-2000 and Buffergel or another product which only looks and feels like the two. The staff here did not have any part in the assignment of the product you are receiving. There is a one in three chances that you may be using Pro-2000 and Buffergel or the product that looks like these 2.

At all times, you need to remember that you are not being given Pro-2000 and Buffergel so as to protect you against HIV infection. You are actually participating in a study to test the effectiveness and safety of these two products.

The only proven methods that are known to protect you from HIV are condoms and abstinence.

You yourself cannot tell which product has been assigned to you neither can staff tell. This is done in order to ensure that the behaviours of women in all the groups are the same and that staff treat all women in the same way.

The product you received as part of this study may not protect you against HIV infection. At the moment there is no evidence which shows how effective the product is. This information will only come out at the end of the study. This study may establish three things concerning the two products being tested:

- Either Pro-2000 or Buffergel or both are not effective at all in protecting women against HIV infection
- Either Pro-2000 or Buffergel or both are partially effective in protecting women against HIV infection
- Either Pro-2000 or Buffergel or both have been proven effective in protecting women against HIV infection

Women participating in the programme should therefore not convince themselves that they are in any way protected by the Pro-2000 or Buffergel as the effectiveness of these products is yet to be proven through this study. Women participating in this study should not reduce their safe sex practices hoping that they will be protected by the products being tested through this study. Women participating in this study should always remember that they can still be infected even when using Pro-2000 or Buffergel. If the researchers find any of the 2 products to be safe, they will then be recommended for use

by women and may be made available for sale and distribution through pharmacies, hospitals, NGOs and other outlets.

How is safety of those who participate in research safeguarded?

Experienced research leaders and staff: Research involving human beings is only conducted by persons who are adequately trained and qualified. These leaders are assisted by teams of made of people with some specialized skills

Laboratory and animal studies – Before research is conducted in humans, it is first conducted in laboratories using machines and then animals such as mice. Once it is determined that the research is not harmful in animals, the researchers may then consider moving to human beings. What is harmful to animals is usually also harmful to humans.

Picture of laboratory and animals

Phases of clinical trials - Research involving humans is conducted in phases. In Phase one a few individuals from 10-30 are involved. This phase looks at the safety of the product, how the substance moves in the human body and how much of the product a human body can tolerate. Phase 2 looks at whether the drug works against a specific condition and continues to gather data on safety and includes less than 100 people. Phase 3 looks at the effectiveness of the substance in a large population usually around 3000 persons.

Scientific and ethical review- Before research can be conducted, a written plan of the study has to be reviewed by a committee made up of fellow scientists and then by anther committee made up by people with various backgrounds including human rights experts. This is referred to as a Research Ethics Committee.

National Drug Regulatory Authority - Research is also reviewed by a Government Authority responsible for the registration of medicines before it can be initiated. In Malawi this Authority is called Pharmacy Medicines and Poisons Board.

Eligibility criteria – persons who participate must meet certain criteria before they can join such as age, disease type and health status.

Monitoring of the study by various groups – During the study, study staff will try to identify any side effects as quickly as possible so that action can be taken to address them or even stop the trial. Ethics Committees and National Drug Regulatory Authorities are also involved in monitoring. Sponsors may also send some monitors to monitor research. A data safety monitoring Committees are also set up to monitor the findings from the study as and when they become available.

Reporting of adverse events – study participants are required to report any untoward events that occur to them after taking the product being tested.

The right to withdraw – study participants are free to withdraw from the study at any time.

Points to remember

- Research is a search for knowledge
- Research contributes to improvements in health and medicine
- Medicines can only be made available to the general population after being tested using other human beings and are proven to be effective.
- You are participating in a study that is aimed at testing a product whose effectiveness is not yet known.
- If it was known that the two product worked, then there would be no need to conduct the microbicide study.
- It is the intention of this study to test the effectiveness of Pro-2000 and Buffergel for protection against HIV infection.
- The study is testing Pro-2000 and Buffergel against another substance which does not have any of the active ingredients of the 2 products and against another group which has not received any of the three.

- Condoms are provided to all participants in this study since they are the known best way to protect yourself against HIV infection.
- You may be infected with HIV while you are participating in this study and using the products being tested if you have unprotected sex. This implies that you have to take precautionary measures to protect yourselves at all times. Condoms are a well known methods that can protect you from HIV infection besides abstinence.
- You are being recruited into this study because you are HIV negative. Take steps as an individual to guard against HIV infection and ensure you stay negative.
- If you do not understand anything about the study, fee free to ask the research staff or the Research Ethics Committee.

Appendix 17 Powerpoint Presentation of intervention
(ChiChewa version)

ZIMENE MUKUYENERA KUDZIWA ZA AKAFUKUFUKU A MANKHWALA

ZA PHUNZIROLI

- Tinaganiza zokonza phunziroli titazindikira kuti pali anthu ena amene samvetsa bwino za m'mene akufukufuku a mankhwala amayendera.
- Cholinga cha phunziroli ndi kufuna kuti anthu azimvetsesa za kafukufuku pogwiritsa ntchito chiyankhulo chomveka.
- Kuwathandiza anthu kuti aziganga zisankho zawo mozindikira pamene akufuna kutenga nawo mbali mkafukufuku.
- Tikugwiritsa ntchito zitsanzo za tsiku ndi tsiku polongosola m'mene kafukufuku wa mankhwala amayendera ndi zomwe amatanthauza.

Cholinga chathu

- Tikufuna kuwonesesa kuti anthu amene amatenga mbali mu akafukufuku akuzindikira za ndondomeko zimene zimagwiritsidwa ntchito mu akafukufukuwo komanso
- - Chilonga cha kafukufuku
  - –Zifukwa zimene akutsatira ndondomeko zosiyanasiyanaJustification for the procedures
  - – Ndi tanthauza la ndondomekozi kwa anthu wotenga mbali

M'mene amakonzera mankhwala

Akankhwala

•Kuti mankhwala apezeke mzipatala, m'mashopu kapena m'mafamasi amayenera kuyesedwa kaye nkuwona ngati angathe kuchiza matenda komanso kusawononga moyo wa munthu.

•Pali anthu ena amene anatenga nawo mbali mu akafukufuku a mankhwala amene tikugwiritsa ntchito leroli.

•Tigwiritsa ntchito chitsanzo chimodzi kuti tikuwonetseni chifukwa chimene timapangira kafukufuku ndi m'mene kafukufuku amachitikira.

Mankhwala ena amene tikugwiritsa ntchito masiku ano anachokera ku mankhwala a chikuda

- Ena mwa mankhwala amene timagwiritsa ntchito anachokera ku mankhwala achikuda ndipo akhala akugwiritsidwa ntchito kwa nthawi yaitali. Ena mwa mankhwalawa amagwiritsidwa ntchito ndi asing'anga ndi makolo athu.

Mankhwala mzipatala

Anthu wodwala mzipatala

M'mene mankhwala amayeseredwa mkafukufuku

- Kuti tilongosole m'mene mankhwala amayeseredwa mkafukufuku, tigwiritsa ntchito chitsanzo cha anthu a m'mudzi wa Nseula ku Ntcheu.
- Anthu a m'mudzi wa Nseula amazala mbatatesi chaka chirichonse ndipo sathira feteleza.
- Patapita zaka zingapo, nthaka yawo inaguga ndipo amapeza mbatatesi yochepa kwambiri pa ekala imodzi.

Kuzala mbatata ya kachewere m/mudzi wa Nseula

•Mbatatesi imene siyinakule bwino
•Mbatatesi ing'ocing'ono
•Kukolola mbatatesi yochepa pa ekala

Kampani ya Zakwathu

- Kampani ya Zakwathu ya ku Blantyre inazindikira za vuto limene alimi a ku Ntcheu anali nawo ndipo anaganiza zobweretsa feteleza watsopano amene amaganiza kuti angathandize kuchulukitsa mbewu ya mbatatesi kwa alimi a kwa Nseula.
- Komano Kampaniyi siyingayambe kugulitsa feteleza yu panopa chifukwa palibe amene akudziwadi kuti feteleza atha kuchulukitsa mbewu ya mbatatesi.
- Choncho Kampaniyi yaganiza zopanga kafukufuku wa feteleza kuti awone ngati angathe kuchulukitsa mbewu ya mbatatesi.
- Kampaniyi yaganiza zoyesera feteleza watsopanoyu ndi feteleza amene wakhala akugwiritsidwa ntchito ku mbatatesi mbuyomu.
- Kuti apange kafukufukuyi anatani?

Msonkhano wa alimi a m'mudzi mwa Nseula

- Kampani inapempha Alangizi aku Ntcheu kuti apange kafukufuku.
- Alangizi anaitana alimi a kwa Nseula ndikuwalongosolela za feteleza watsopano amene wapangidwa kumene.
- Anawapempha ena mwa alimiwo kuti atenge nawo mbali mupologalamu yoyetsera feteleza wa tsopanoyo.

Pa nthawi ya msonkhano

- Alangizi anawauza alimi kuti iwo akufuna alimi 100 amene ali wokonzeka kuzyala mbatatesi pa ekala imodzi ya kafukufukuyu ndipo kuti agwiritse ntchito feteleza ndi kutsatira ndondomeko yonse ya kafukufuku mpaka pomwe adzauzidwa kukolola mbatatesiyi.
- Alimi 123 anawonetsa chidwi chotenga nawo mbali mkafukufukuyu koma alimi 100 woyambirira ndi imene anasankhidwa kutenga nawo mbali.
- Alimi wonse anauzidwa kuti cholinga cha pologalamuyi sichinali kuchulukitsa mbewu ayi, koma kuyesera ngati feteleza wa tsopanoyu angagwiri ntchito yochulukitsa mbewu.
- Anawauzanso alimiwo kuti kafukufuku woyambirira wa feteleyu anachitikira ku munda wa ung'ono m'boma la Blantyre ndipo zotsalira zake zinali zochititsa chidwi.

M'mene alangizi anayetsera feteleza uja

- Anthu a kwa Nseula sanagwiritsopo ntchito feteleza chiyambire.
- Choncho poyetsera feteleyu, alangizi aja anataniza mbewu za m'minda m'mene munatsiridwa feteliza uja ndi minda imene siyinatsiridwe feteleza.
- Anafaniza zotsatira za mbewu za m'minda imene inatsiridwa feteleza ija ndi mbewu z a m'minda imene siyinatsiridwe feteleza chaka chatha.
- Kufaniza kuliero kukhoza kukhala kosathandiza kwambiri chifukwa cha kusiyana kwa nyula ndi fizirombo towononga mbewu m'chaka chirichonse.
- Ngati Alangizi aja apereka feteleza watsopano uja kwa alimi wonse, sangathe kudziwa ngati feteleza uja angagwire ntchito yochulukitsa mabwu chifukwa cha kusiyana kwa nyula pakati pa chaka chino ndi chaka chatha.
- Choncho Alangizi aja anaganiza zoyetsera feteleza watsopano uja ndi shuga amene ahaweroleka ngati wofanana ndi feteleza uja.

Matumba 100 a feteleza

- Kampani ya Zakwatu inapereka matumba 100 ndipo pa matumbawa panali matumba 50 a feteleza watsopano uja ndi matumba 50 a shuga amene anawoneka ngati feteleza wa tsopano uja.
- Aliyense amadziwa kuti ngati munthu wabisira shuga m'munda mwake, palibe chimene chimachitika.
- Matumba 100 aja analembedwa manambala 1 mpaka 100 ndi n'modzi wogwira ntchito ku kampaniyi ndipo ndi yekhayo amene amadziwa za chimene chiri mthumba lirilonse.

Kaperekedwe ka matumba a feteleza aja

- Pa msonkhano paja mlimi aliyense anapemphedwa kusankha pepala imodzi imene inali ndi nambala kuchokera mchipewa m'mene munali mapepala. Mapepala aja analembedwa kuyambira 1 mpaka 100.
- Manambala aja amagwirizana ndi manambala amene analembedwa pa matumba 100 aja.
- Mlimi aliyense anatenga thumba limene linali ndi nambala yofanana ndi nambala ya papepala yomwe anatola.

Thumba limodzi la makilogalamu 50 kwa mlimi aliyense

- Mlimi aliyense anauzidwa kuti agwiritse ntchito thumba limodzi la makilogalamu 50 pa puloti yake.
- Dzina ndi nambala ya mlimi aliyense zinalembedwa m'bukhu ndi cholinga choti kumapeto kwa kafukufukuyu adzadziwe kuti mlimi aliyense anatenga thumba lanji.
- Alangilizi ndi alimi wonse samadziwa chimene chinali m'matumba amene analandira.
- Kafukufukuyu adzawonetsa ngati feteleza watsopanoyu ali ndi mphamvu.
- Nzothekanso kuti mwina feteleza watsopanoyu sakugwira ntchito yochulukitsa mbewu.

Nchifukwa chiyani anapereka matumba 50 m'mene munali zinthu zofanana chabe ndi feteleza watsopano uja?

- Amafuna kudziwa ngati feteleza watsopano uja analidi wamphamvu.
- Akanakhala kuti sanapereke chirichonse kwa alimi 50 ena aja, ndiye kuti sakanasamalira minda yawo mokwanira chifukwa akanakhala akudziwa kuti sanalandire feteleza.
- Koma pamene alimi onse analandira matumba wofanana, aliyense anayesesa kusamalira munda wake.
- Izi zikutanthauza chiyani kwa alimi 100 aja? Izi zikutanthauza kuti mlimi aliyense anali ndi mwayi wolandira feteleza weniweni kapena shuga.
- Choncho mlimi aliyense amakhulupirira kuti walandira feteleza weniweni.

Nchifukwa chiyani kampani ija sinafune kuti alangizi ndi alimi adziwe za chimene chinali mthumba lirilonse?

- Amafuna kuwonetsesa kuti Alangizi aja asakondere anthu amene analandira feteleza weni weni uja.
- Amafuna kuti alimi 100 wonse aja asadziwe za chomwe analandira kuti asamalire mbewu zawo mofanana.
- Amafuna kuti alimi ndi alangizi asadziwe chimene mlimi aliyense analandira.
- Polangiza alimi 100 aja, Alangizi amapereka malangizo wofanana poganizira kuti aliyense analandira feteleza watsopano uja.

Kuchita mayeso:Nchifukwa chiyani alangizi aja anapempha alimi 100 aja kuti asankhe mapepala mchipewa muja? Nchifukwa chiyani sanagawe alimi 100 aja m'magulu awiri?

- Sanafune kuwayika m'magulu potengera ubwenzi, mtundu kapena mudzi umene amachokera.
- Amafuna kuti gulu lina lirilonse likhale ndi alimi a nzeru ndi maluso wosiyanasiyana ncholinga choti atha kudziwa ngati feteleza watsopano uja amagwira ntchito.
- Choncho alimi 50 anasankhidwa mwa mayere kuti alandire feteleza watsopano uja ndipo ena 50 analandire shuga/feteleza wa feki uja.

Malangizo kwa alimi

- Alimi wonse 100 apatsidwa malangizo olanana wokhuza kagwiritsidwe ntchito ka feteleza
- Akuyenera kuzala mbatata yawo pa ekala imodzi.
- Akuyenera kugwiritsa ntchito supuni ya tea imodzi pa phanda la mbatata imodzi pa mwezi wa chitatu ndi wa chisanu ndi chimodzi.
- Sakuloledwa kukolola mbatata yawo mpaka atawuzidwa kutero.
- Akuyenera kuwuza alangizi ngati angawone china chirichonse pa puloti yawo ya kafukufuku.
- Sakuloledwa kugwiritsa ntchito ntundu wina uliwonse wa feteleza pa puloti yanwi kwa chaka chonse.
- Alangizi akhala akumawayendera wiki iliyonse kuwona kukula kwa puloti ndi kuwonetsetsa kuti alimi onse sakugwiritsa ntchito mafeteleza ena ndipo kuti sakukolora m'mapuloti a kafukufuku.

Alangizi akuyendera alimi

- Alimi akuyendera alimi

Kuyesa ngati feteleza watsopano uja akugwira ntchito

- Pamene nthawi yokolola inafika, Alangizi aja anapempha alimi 100 aja kuti akolole mbewu zawo zija pa wiki imodzi ndi kuti aziike m'matumba a 50 kg.
- Atatero anayeza mbewu zimene mlimi aliyense anakolola kuchokera pa puloti yake.

Nanga anadziwa bwanji ngati feteleza watsopano uja akugwira ntchito?

- Alangizi aja analemba makilogalamu a mbewu zimene mlimi aliyense anakolola pa puloti yake m'bukhu limene analemba dzina ndi nambala ya thumba limene analandira.
- Alangizi aja anazindikira kuti alimi ena anakulola zochuluka kusiyana ndi anzawo – koma aliyense samadziwa chimene chinali mthumba lake.
- Kenako m'modzi wa wogwira ntchito ku Kampani ya Feteleza ija anabweretsa ndondomeko ya nambala ya thumba lirilonse ndi chomwe chinali mthumbamo.
- Tsiteo Alangizi aja anapita mbukhu lawo lija ndikuwonjezera mbali imodzi imene inawonesa chimene mlimi aliyense analandira, khaya analandira thumba la feteleza watsopano uja kapena shuga.

Zotsatira za kafukufuku

- Alangizi aja anapeza kuti alimi amene analandira feteleza weniweni aja ndi amene anakolola zochuluka. Feteleza uja anachulukitsa mbewu za alimi 45 amene analandira feteleza uja.
- Alimi amene analandira shuga anakolola mbewu zofanana ndi mbewu zimene amakolola m'zaka zambuyomo pamene samatsira feteleza.

Minda ya alimi ndi mbewu zomwe anakolola

Kuwulusa zotsatira za kafukufuku

- Alangizi anatumiza ripoti ya zotsatira za kafukufuku ku Kampani ya za Zakwathu ku Blantyre ndi ku mabungwe alimi.
- Patapita miyezi ingapo, feteleza watsopanoyo anayamba kugulitsidwa kwa aliyense m'mashopu wosiyasiyana.
- Alimi wonse m'dziko muno kuphatikizirapo aku Ntcheu anayamba kugwiritsa ntchito feteleza watsopanoyu pochulukitsa mbewu zawo.
- Tithokoze alimi 100 aja amene anatenga nawo mbali mkafukufukuyu.

Feteleza watsopano wa mbatata afika pa msika

- Feteleza watsopano uja adachita bwino pakafukufuku wake
- Ndi m'mene zimayenderanso ndi mankhwala amene tikugwiritsa ntchito.
- Mukapeza mankhwala m'mashopu, mzipatala ndi m'mafamase, amakhala kuti kafukufuku wake wachitika kale ndipo adayenda bwino.

Kugwirizana kwa alimi a ku Ntcheu ndi kafukufuku amene munalowa inu

- Nkhani ya kafukufuku wa feteleza ikutanana ndi m'mene mankhwala atsopano amayesedwa.
- Mankhwala atsopano sangagwiritsidwe ntchito kwa wodwala kapena kugulitsidwa m'mashopu popanda kuyesedwa.
- Amayenera kuyesedwa kuti awone ngati angagwiredi ntchito. work.
- Anthu wopanga kafukufuku monga madotolo ndi anamwino ndi amene amapangitsa akafukufuku woyesera mankhwala monga momwe akupangira wogwira ntchito kuno ku chipatala.
- Mwachitsanzo, mkafukufuku amene munalowa amayesera mankhwala atsopano amene awapeza kuwona ngati angateteze azimai ku kachirombo ka HIV.
- Azimainu anakupemphani kuti mutenge nawo mbali mkafukufuku amenayu.

Kafukufuku ndi chilinganizo cha chitetezo cha matenda

- Kafukufuku ndi wosiyana ndi chitetezo cha mankhwala chimene timalandira ku chipatala
- Mwachitsanzo cholinga cha mapologalamu a HIV ndi kuteteza mtundu wa a Malawi ku matenda a HIV/AIDS pamene cholinga cha kafukufukuyu ndi kupeza njira ina imene ingathandize azimayi kupewa kutenga kachirombo ka HIV.
- Kafukufuku amasiyana ndi ma pologalamu woteteza anthu ku kachirombo ka HIV pa zolinga zake ndi ndondomeko zimene zimatsatiridwa.
- Tikhala tikukamba za ndondomeko zimene zimagwiritsidwa ntchito mu akafukufuku osati m'mapologalamu woteteza anthu ku kachirombo ka HIV.

Mkafukufukuyu

- Mankhwala ovalira amayetsedwa kuti awone ngati angatetezе azimayi kukachirombo ka HIV.
- Mankhwalawa amayetsedwa pamodzi ndi zinthu ziwir zowonaka ngati mankhwalawa kapena zomwe zinalibe mankhwala amene anali m'mankhwala ovalira.
- Gulu lina lomwe linalandira mipira ya abambo linawonjezeredwa mkafukufukuyu ncholinga choti azathe kufananiza kumapeto kwa kafukufukuyu magulu amene akanakhala wotetezedwa ku kachirombo ka HIV.

Zinthu zofunikira kudziwa

- Mukayesera kudziwa kuti ntisudu itatuya nzakhwala imene ikuperekedwa mkafukufukuya cholinga chake sikuteteza azimayi ku kachirombo ka HIV.
- Cholinga cha kafukufukuyu sdi kuyesera ngati ntundu iwiriya mankhwalawa ingateteze azimayi ku kachirombo ka HIV ndipo ngati ali woyenera kuwagulitsa ntchito kwa azimayi.
- Mochuluka amene mufi nzakhwalawa sdi woteteza kuno chubu chirichonse chiri ndi nambala yakeyake.
- Inuyo munayikidwa ni'magulu asayi ngati alimi aja amene anagawidwa mugagulu awiri pochita mliyero pamene anasankha mapapala'nchipewa chija.
- Kumbali yanu, ndi nzakina a Kompyuta amene anapangka nzapambala kwa wina aliyense wa inu amene amagwirizana ndi nambala ya chubu chimene munalandira.
- Mukayesera kudziwa kuti pdokotala kapena anagwiritsa ntchito kuno sakudziwa chimene aliyense mwa inu analandira.
- Simungatheneo kudziwa chimene aliyense mwa inu analandira.
- Kizikutsatheyza kuti nyamlandira amodzi mwa nzakhwala angene akuyesedwa kapena chinthu chimene chikuwonaka ngati mankhwalawo.

Zofunikira kudziwa zokhuzana ndi mphamvu za mankhwala amene akuyesedwa

- Kumapeto kwa kafukufukuyu ndi pamene tidzadziwe za mankhwala amene mwakhala mukugwiritsa ntchito.
- Pamene izi zidziwika ndi pamene akafukufuku anagadziwe ngati mankhwala awiriwa akugwira ntchito.
- Zotsatira za azimayi amene akulandira mankhwala awiri oni oni zidzafananitsidwa ndi zotsatira za azimayi amene akugwiritsa ntchito zinthu zonga ngati Buffergel kapena Pro2000 kapenanso amene akugwiritsa ntchito mpira ya abambo.
- Kumapeto kwa kafukufukuyu, zidzadziwika ngati amodzi mwa mankhwalawa akugwira ntchito kapena ngati mankhwala wonse sakugwira ntchito.
- Chonchi aliyense ali ndi mwayi umodzi wogwiritsa ntchito Pro2000 , buffergel kapena chinthu chokonseka ngati mankhwala awiriwa.

Zinthu zofunikira kudziwa zokhuzana ndi mankhwala ovalira

- Nthawi zonse muzizindikira kuti mankhwala ovalira saperekedwa kwa inu kuti akutetezeni ku kachirombo ka HIV.
- Mukutenga nawo mbali mkafukufuku amene akuyesera mankhwalawa nkuwona ngati angagwiritsidwe ntchito kwa azimayi.
- Njira zokhazo zimene zingakutetezeni ku kachirombo ka HIV ndi makondomu ndi kuzisunga.
- Inu mwa inu nokha simungadziwe mankhwala amene mukulandira ndipo wopanga kafukufukuyu sakudziwanso.

Mphamvu za mankhwala ovalira amene akuperekedwa mkafukufukuyu

- Mankhwala ovalira amene mwalandira akhonza kusakuteteza ani ku kachirombo ka HIV.
- Panopa palibe umboni uliwonse woti mankhwalawa ali ndi mphamvu.
- Izi zidzadziwika kumapeto kwa kafukufukuyu
- Kafukufukuyu adzasonyeza zinthu zitatu zokhuza mankhwala ovalira awiriwa:
  - Mankhwala ovalira a buffergel kapena Pro 2000 sakugwira ntchito yoteteza azimayi ku kachirombo ka HIV
  - Mankhwala ovalira a buffergel kapena Pro 2000 akugwira ntchito pang'ono poteteza azimayi ku kachirombo ka HIV
  - Mankhwala ovalira a buffergel kapena Pro 2000 akugwira ntchito yoteteza azimayi ku kachirombo ka HIV

Uthenga wochenjeza

- Azimayi wonse adziwe kuti mankhwala mkafukufukuyu sakuwateteza ku kachirormbo ka HIV.
- Azimayi a mkafukufukuyu asatayirira m'makhalidwe awo poganizira kuti mankhwalawa akuwateteza ku ka chirombo ka HIV.
- Azimayi a mkafukufukuyu adziwe kuti akhonza kutenga kachirombo ka HIV pa nthawi imene akugwiritsa ntchito mankhwala ovalira.

Mankhwala amene akhale ndi mphamvu

- Ngati mankhwalawa apezeka kuti ali ndi mphamvu kumapeto kwa kafukufukuyu, wopanga kafukufukuyu adzapempha kuti mankhwalawa azigwiritsidwa ntchito pakati pa azimayi wonse ndipo adzakhala akumapezeka m'misika ya mankhwala.

Kuyang'anira umoyo wa anthu amene akutenga mbali mkafukufuku

- **Umoyo wa anthu amene akutenga mbali mkafukufuku umatetezedwa mu(ku zosiyanasiyana kuphatikizapo zimene zili pansi:**
- **Atsogoleri ndi wogwira ntchito woyang'anira bwino za mkafukufuku**
- Kafukufukuyu yamwe amachitika pakati pa anthu amagwirizana ndi anthu amene ali wopfunira bwino za ntchito yakafukufuku. Atsogoleriwa amakhazikitsa ndi gulu la anthu amene ali ndi luso lapadera lopenga akafukufuku.
- **Akafukufuku woshitika pakati pa nyansa odi m'nsolo woyezera (lab)** – Kafukufuku aa nachitika pakati pa anthu, amakhala akapanga kale kafukufukuyu m'mabina amene amapezeka m'mjelo woyezera ndi pa amapezangaraso nmyama, monga mbewa. Akafukufukuyu akawonjeza kotero ka moyo ka nyama ndi pamene amamuyesera kwa anthu. Nthawi zambiri, chinthu chimene chiri chopnya ku moyo wa nyama chimakhalanso chowopnya ku moyo wa anthu.
- **Magawo a pkafukufuku a nasitiwala** – Kafukufuku yamwe amachitika pakati pa anthu amachitika m'magawo wosiyanasiyana. Mgawo oyamba, anthu wochepa a pakati pa 10 ndi 20 amalenga nawo mbali mkafukufukuyu. Mchigawochi amafukufuza ngati mankhwala amene ali oyesa nawo ndi abwino ku moyo wa munthu komanso m'mene akugwirira ntchito m'moyo wa munthu. Mchigawo chachiwiri amafukufuza m'mene mankhwalawo akugwirira ntchito pochiza matenda imene munthu akudwala. Amakhala akufukuzanso za ubwino wa mankhwalawa ku moyo wa munthu ndipo anthu ochepera 100 amalenga nawo mbali mgawoli. Mgawo lachitatu amafukuza ngati mankhwalawagwira kachiza matenda yomwe anthu akudwala ndipo anthu wokwana pakati 200 amene nawo mbali mkafukufukuyu.

Kuyang'anira umoyo wa anthu amene akutenga mbali mkafukufuku (2)

- [illegible]
- [illegible]
- [illegible]
- [illegible]
- [illegible]
- [illegible]

Mfundo zoti muzikumbukira

- Kafukufuku amachitika pofuna kudziwa m'mene zinthu zilili.
- Kafukufuku amathandiza kupititsa patsogolo umoyo wa anthu ndi mankhwala.
- Mankhwala amaperekedwa kwa anthu atayesedwa kaye kwa anthu ena pofuna kudziwa ngati ali wothandiza kapena akugwiri ntchito.
- Mukutenga nawo mbali mkafukufuku amene akufuna kudziwa ngati mankhwala amene akuyeserawo ali ndi mphamvu.
- Ndi cholinga cha kafukufukuyu kuyesera ngati mankhwala ovalira a PRO2000 ndi Buffergel angakutetezeni ku kachirombo ka HIV.
- Mkafukufukuyu akuyesera PRO2000 ndi Buffergel ndi zinthu zina zimene zili bé mankhwala. Makondomu akuperekedwa kwa wina aliyense amene akutenga nawo mbali mkafukufukuyu chifukwa njira yokhayo imene ili yodziwika kuti imateteza anthu ku kachirombo ka HIV.
- Dziwani kuti mutha kutenga kachirombo pamene mukutenga nawo mbali mkafukufukuyu ndi pamene mukugwiritsa ntchito mankhwala ovalira.

Appendix 18: Letter of approval from UKZN Research Ethics Committee

RESEARCH OFFICE (GOVAN MBEKI CENTRE)
WESTVILLE CAMPUS
TELEPHONE NO.: 031 – 2603587
EMAIL : ximbap@ukzn.ac.za

UNIVERSITY OF
KWAZULU-NATAL

12 NOVEMBER 2007

MR. PM NDEBELE (203520379)
PSYCHOLOGY

Dear Mr. Ndebele

ETHICAL CLEARANCE APPROVAL NUMBER: HSS/0679/07D

I wish to confirm that ethical clearance has been granted for the following project:

"A study of trial participants' understanding and attitudes towards randomization, double blinding and placebo use – A pilot intervention in a microbicide trial in Malawi"

PLEASE NOTE: Research data should be securely stored in the school/department for a period of 5 years

Yours faithfully

MS. PHUMELELE XIMBA
RESEARCH OFFICE

cc. Post-Graduate Office (Beulah Jacobsen)
cc. Supervisor (Prof. D Wassenaar)

UNIVERSITY OF
KWAZULU-NATAL

University of KwaZulu-Natal
Research Office, Govan Mbeki Centre
Westville Campus
Private Bag x54001
DURBAN
4000
Tel No: +27 31 260 3587
Fax No: +27 31 260 4609
xlmbap@ukzn.ac.za

29 October 2010

Mr. PM Ndebele [203520379]
School of Psychology

Dear Mr. Ndebele

PROTOCOL REFERENCE NUMBER: HSS/0679/07D
PROJECT TITLE: A study of trial participants' understanding and attitudes towards randomisation, double blinding and placebo use – A pilot intervention in a microbicide trial in Malawi

In response to your application dated 2007, the Humanities & Social Sciences Ethics Committee has considered the abovementioned application and the protocol has been given **FULL APPROVAL**.

Any alteration/s to the approved research protocol i.e. Questionnaire/Interview Schedule, Informed Consent Form, Title of the Project, Location of the Study, Research Approach and Methods must be reviewed and approved through the amendment /modification prior to its implementation. In case you have further queries, please quote the above reference number.
PLEASE NOTE: Research data should be securely stored in the school/department for a period of 5 years.

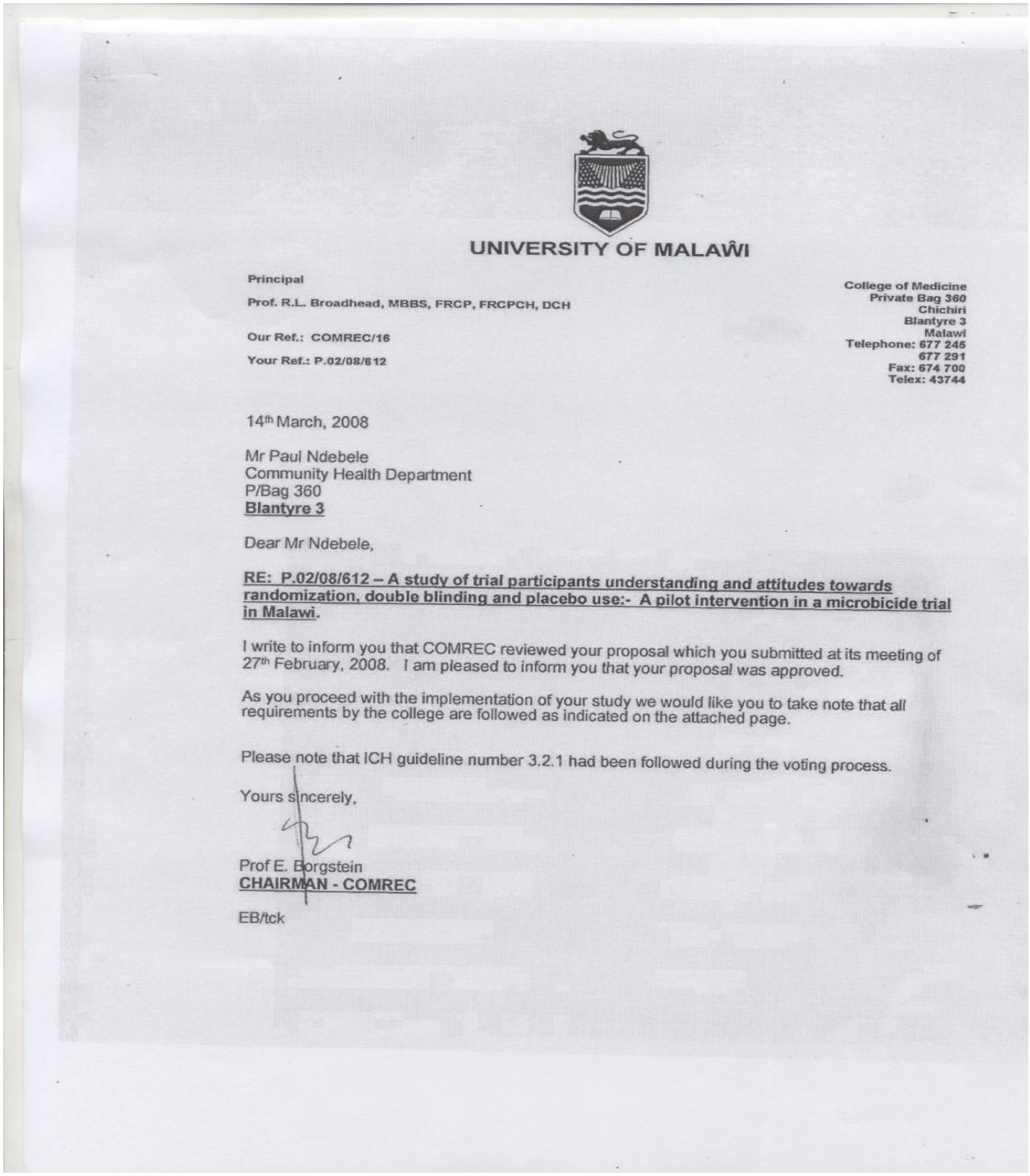
I take this opportunity of wishing you everything of the best with your study.

Yours faithfully

Professor Steven Collings (Chair)
HUMANITIES & SOCIAL SCIENCES RESEARCH ETHICS COMMITTEE

cc Supervisor – Prof. D Wassenaar
cc Mrs B Jacobsen

Appendix 19: Letter of Approval from Malawi Research Ethics Committee (COMREC)



UNIVERSITY OF MALAWI

Principal

Prof. R.L. Broadhead, MBBS, FRCP, FRCPCH, DCH

College of Medicine
Private Bag 360
Chichiri
Blantyre 3
Malawi
Telephone: 677 245
677 291
Fax: 674 700
Telex: 43744

Our Ref.: COMREC/16

Your Ref.: P.02/08/612

14th March, 2008

Mr Paul Ndebele
Community Health Department
P/Bag 360
Blantyre 3

Dear Mr Ndebele,

RE: P.02/08/612 – A study of trial participants understanding and attitudes towards randomization, double blinding and placebo use:- A pilot intervention in a microbicide trial in Malawi.

I write to inform you that COMREC reviewed your proposal which you submitted at its meeting of 27th February, 2008. I am pleased to inform you that your proposal was approved.

As you proceed with the implementation of your study we would like you to take note that all requirements by the college are followed as indicated on the attached page.

Please note that ICH guideline number 3.2.1 had been followed during the voting process.

Yours sincerely,

Prof E. Borgstein
CHAIRMAN - COMREC

EB/tck

Appendix 20: Letter to Director of UNC Requesting for permission

UNIVERSITY OF MALAWI

COLLEGE OF MEDICINE

Principal : Prof. R.L. Broadhead, MBBS, FRCP, FRCPCH, DCH

Centre for Bioethics in Eastern and Southern Africa (CEBESA)
Private Bag 360
Chichiri, Blantyre 3
Malawi
Telephone : +265 9 619937
Fax : +265 1 674 700
E-mail: pndebele@medcol.mw

October 10th, 2006

Dr F. Martinson
Director
UNC Project Lilongwe
Private Bag A104
Lilongwe

Dear Dr Martinson

PROPOSED BIOETHICS STUDY: A STUDY OF TRIAL PARTICIPANTS UNDERSTANDING OF RANDOMISATION, PLACEBO USE AND DOUBLE BLINDING - APILOT INTERVENTION IN MALAWI

My name is Paul Ndebele and I am the Deputy Director in the Centre for Bioethics at the College of Medicine. I am currently studying towards a PhD in Bioethics at the University of KwaZulu Natal (South Africa). As part of this degree, I intend to conduct the above titled study as a sub-study within a study which has a randomized, placebo controlled and double blinded design. I specifically intend to assess trial participants understanding of research participation and clinical trial procedures namely randomisation, double blinding and placebo use.

Several studies that have been conducted elsewhere have shown that trial participants have problems understanding these trial procedures and also that researchers have problems in explaining these to trial participants. The proposed study will involve structured questionnaires to be administered to research participants and staff involved in obtaining informed consent. For the trial participants, the questionnaire will seek information on understanding of the procedures in question whilst the questionnaire for trial staff would seek information on how they explain the procedures to trial participants. Depending on the findings, I intend to develop an intervention aimed at improving understanding.

I note that your HPTN035 Microbicide study includes all the important procedures that I am interested in and hence I am kindly requesting for your permission to conduct my PhD study as a sub-study using participants from your Microbicide study. I would like

to assure you that results of any concern will be made known to you as soon as any concerns become apparent. Furthermore, I offer to run and evaluate a remedial intervention if it appears necessary. The intervention itself will be designed with reference to current literature on improving participant understanding retention etc (cf. Flory J, & Emanuel E. Interventions to improve research participants' understanding in informed consent for research: A systematic review. JAMA 2004;292:1593-1601). My intention is to identify and address generic problems with understanding in a way that is helpful to you as PI and your team. If you feel that there may be need for a supporting letter from my supervisor or a formal signed agreement, I will be more than happy to do so.

Below is an abstract of the proposed study. The proposal has already been accepted by the School of Psychology and I now intend to submit it to COMREC including the Ethics Committee and Postgraduate Committee at UKZN. The Ethics Committees as well as the Postgraduate Committees will require a letter from the PI of the main study indicating his agreement. I intend to submit the proposal to the committees as soon as I get your letter of agreement since I intend to start collecting data from January onwards. I am quite confident that the proposed study will add value to your study as well as other studies by ensuring that informed consent is truly informed and do trust that you will find it worthy to support my efforts which are aimed at promoting the ethical conduct of research in Malawi and Africa.

For any additional information, please feel free to contact me on mobile **09 619 937**. I look forward to hearing from you and thank you for your support.

Sincerely

Paul Ndebele
Centre for Bioethics in Eastern and Southern Africa (CEBESA)
COLLEGE OF MEDICINE, UNIVERSITY OF MALAWI

Appendix 21: Letter to Director of Johns Hopkins Research project

UNIVERSITY OF MALAWI

COLLEGE OF MEDICINE

Principal : Prof. R.L. Broadhead, MBBS, FRCP, FRCPCH, DCH

Centre for Bioethics in Eastern and Southern Africa (CEBESA)
Private Bag 360
Chichiri, Blantyre 3
Malawi
Telephone : +265 9 619937
Fax : +265 1 674 700
E-mail: pndebele@medcol.mw

July 3rd, 2008

Dr J. Kumwenda
Director
Johns Hopkins Research Centre
BLANTYRE

Dear Dr Kumwenda

PROPOSED BIOETHICS STUDY: A STUDY OF TRIAL PARTICIPANTS UNDERSTANDING OF RANDOMISATION, PLACEBO USE AND DOUBLE BLINDING - APILOT INTERVENTION IN MALAWI

My name is Paul Ndebele and I am the Deputy Director in the Centre for Bioethics at the College of Medicine. I am currently studying towards a PhD in Bioethics at the University of KwaZulu Natal (South Africa). As part of this degree, I intend to conduct the above titled study as a sub-study within a study which has a randomized, placebo controlled and double blinded design. I specifically intend to assess trial participants understanding of research participation and clinical trial procedures namely randomisation, double blinding and placebo use.

Several studies that have been conducted elsewhere have shown that trial participants have problems understanding these trial procedures and also that researchers have problems in explaining these to trial participants. The proposed study will involve structured questionnaires to be administered to research participants and staff involved in obtaining informed consent. For the trial participants, the questionnaire will seek information on understanding of the procedures in question whilst the questionnaire for trial staff would seek information on how they explain the procedures to trial participants. Depending on the findings, I intend to develop an intervention aimed at improving understanding.

I note that your HPTN035 Microbicide study includes all the important procedures that I am interested in and hence I am kindly requesting for your permission to conduct my PhD study as a sub-study using participants from your Microbicide study. I would like to assure you that results of any concern will be made known to you as soon as any

concerns become apparent. Furthermore, I offer to run and evaluate a remedial intervention if it appears necessary. The intervention itself will be designed with reference to current literature on improving participant understanding retention etc (cf. Flory J, & Emanuel E. Interventions to improve research participants' understanding in informed consent for research: A systematic review. JAMA 2004;292:1593-1601). My intention is to identify and address generic problems with understanding in a way that is helpful to you as PI and your team. If you feel that there may be need for a supporting letter from my supervisor or a formal signed agreement, I will be more than happy to do so.

Below is an abstract of the proposed study. The proposal has already been accepted by the School of Psychology and I now intend to submit it to COMREC including the Ethics Committee and Postgraduate Committee at UKZN. The Ethics Committees as well as the Postgraduate Committees will require a letter from the PI of the main study indicating his agreement. I intend to submit the proposal to the committees as soon as I get your letter of agreement since I intend to start collecting data from January onwards. I am quite confident that the proposed study will add value to your study as well as other studies by ensuring that informed consent is truly informed and do trust that you will find it worthy to support my efforts which are aimed at promoting the ethical conduct of research in Malawi and Africa.

For any additional information, please feel free to contact me on mobile **09 619 937**. I look forward to hearing from you and thank you for your support.

Sincerely

Paul Ndebele
Centre for Bioethics in Eastern and Southern Africa (CEBESA)
COLLEGE OF MEDICINE, UNIVERSITY OF MALAWI

Appendix 22: Letter granting permission from UNC

UNC
PROJECT
Lilongwe, Malawi

www.unc.edu/malawi

29 November 2006

Paul Ndebele
Centre for Bioethics
College of Medicine
P Bag 360
Blantyre 3

Dear Mr Ndebele

RE: A STUDY OF TRIAL PARTICIPANTS' UNDERSTANDING OF RANDOMISATION, PLACEBO USE AND DOUBLE BLINDING – A PILOT INTERVENTION IN MALAWI.

Thank you for your communication regarding the above titled proposed study which you intend to conduct as part of your PhD degree with the University of Kwa?ulu Natal.

I am very glad to advise that we do not have any objections to your request to conduct the above titled study using trial participants from our Microbicide Study. We note that the study that you propose to undertake will in several ways strengthen the Microbicide trial as well as the other trials that we are currently conducting as it seeks to improve informed consent. Please ensure that you apprise the Manager about your plans so that our research team as well as trial participants are appropriately notified about your study. We will do all that we can to ensure that you successfully complete your study. We will be very glad if will present your findings to our team so that if there are any areas of need, appropriate steps may be taken to address them.

We look forward to working with you as you conduct your study and wish you success in your studies.

Sincerely

P A Martinson
COUNTRY DIRECTOR

Malawi Office
Postal address
UNC Project
Private Bag A-104
Lilongwe, Malawi

Physical address
Tidziwe Centre
Kamuzu Central Hospital
Lilongwe, Malawi
Phone: 265 (0) 1 755 356
265 (0) 1 750 613
265 (0) 1 582 274
Fax: 265 (0) 1 756 956
Email:

USA Office
The University of North Carolina
At Chapel Hill
School of Medicine
CB# 7435, 130 Airport Road
Chapel Hill, NC 27599-7435
Phone: (919) 509 9324
Fax: (919) 966 9538
Email:

Communications should be addressed to:
The Country Director
Attn: "Responsible Officer"

Appendix 23: Letter granting permission from Johns Hopkins Centre

UNIVERSITY OF MALAWI

COLLEGE OF MEDICINE

Johns Hopkins Research Centre
College of Medicine
Queen Elizabeth Central Hospital
P.O. Box 1131,
Blantyre,
MALAWI.
Tel (+265) 1 875 132
Fax (+265)1 870 132
Email: jhopkins@sndp.org.mw

12th July, 2008.

Centre for Bioethics in Eastern and Southern Africa (CEBESA),
College of Medicine,
Private Bag 360,
Chichiri
BLANTYRE 3.

Dear Mr. Ndebele,

RE: A STUDY OF TRIAL PARTICIPANTS' UNDERSTANDING OF RANDOMIZATION, PLACEBO USE AND DOUBLE BLINDING – A PILOT INTERVENTION IN MALAWI.

Thank you for your letter dated 3rd July 2008 regarding the above titled study.
I am pleased to inform you that I do not have any objections to your request to conduct the above titled study using our trial participants from the HPTN035 Microbicide Study. I have noted that the proposed study seeks to improve the quality of informed consent in our setting and this is a very welcome idea. As the PI of the Microbicide Trial at our site, I will do all I can to support your study. It will be my great pleasure if you disseminate the results of your study to our research team and trial participants after you complete the study. If you need any assistance, please feel free to contact Ms Linley Seyama, the study coordinator.

I look forward to working with you as you implement your study and I wish you every success in your study.

Yours sincerely,

Dr. Newton Kumwenda,
Field Director, Johns Hopkins Research Project.

JOHNS HOPKINS BLOOMBERG SCHOOL of PUBLIC HEALTH

Appendix 24: Transcript of FGD held at Lilongwe site

TRANSCRIPT OF A FOCUS GROUP DISCUSSION HELD WITH HPTN 035 TRIAL PARTICIPANTS AT THE UNC PROJECT IN LILONGWE

FGD ID Number: **FM_FGD 01**
Geographic Location of FGD: **Tidziwe UNC Centre – Kamuzu Central Hospital LILONGWE**
Type of FGD: **Adult Females participating in HPTN 035 Trial**
Date of FGD: **Sunday June 8, 2008**
No of Participants: **8 Adult females**
Facilitator/Moderator: **Francis Masiye**
Transcriber and Translator: **Francis Masiye**
Time interview began: **9:10 a.m.**
Time interview ended: **11:55 a.m.**

Participants' personal details

Participant	Gender (M/F)	Age	Education (years)
1. P1	Female	57	3
2. P2	Female	22	6
3. P3	Female	22	10
4. P4	Female	30	6
5. P5	Female	26	13
6. P6	Female	32	8
7. P7	Female	32	7
8. P8	Female	24	16

SUMMARY:
Number of participants: 8
Gender: All females
Average education attainment: 8.6

Average age distribution: 30.6

ENGLISH TRANSCRIPT

F (Ice breaker): What do you know about the microbicide trial?

P6: It is a study that is testing some gels to find out if they can prevent the spread of HIV/AIDS.

F: Hmm, what do others say?

P4: I think what she has said is true, but I just want to add that the researchers would also like to find out if the use of the gels can cause some side effects to the woman or her partner. They are also interested in finding out if husbands enjoy sex when a woman is using the gels (**OTHERS:** Laugh)

P8: chips in and says yes my husband enjoys it and wants me to continue using the gel (further laughter from the other participants).

F: And do you enjoy it too?

SOME: say yes

OTHERS: say no.

F: For those who like it, how do you feel?

P6: When you use it, you feel like your husband has already deposited semen into your vagina which increases your sexual pleasure and when he penetrates you and ejaculates, you get more satisfaction (**OTHERS** laugh).

F: Alright, now let's discuss something else. I would like to know what comes to your mind when you hear the word "research".

P6: Can you repeat the question?

F: Well, my question is "what is research" according to you?

P4: Research is about finding out what one does not know.

F: Can you give an example?

P4: Yes, for example, if you hear that there is a new drug which can cure TB, you try to find out what that drug is and you come to know it.

F: So, according to you, that is research.

P4: Yes, that is a research because you are trying to find out what you don't know and you eventually know it.

F: Ok, and you my friend, what do you understand by the term clinical research?

P2: Clinical research means trying to find out how people are taking care of themselves healthwise. If they get health care when sick, how they travel to the hospital; how far it is to the hospital and how are they taken care of at the hospital.

F: Alright. Is there any other view on the meaning of research?

P3: They do research on a person with the aim of examining his/her body to see how it is functioning; if he/she has malaria, they will know and the person will be informed and given treatment.

F: Hmm, is there any other view on this? *(Silence)*

F: Let's be talking, eh, ladies? When you hear the word research, how do you understand it?

P6: It is like when we are pregnant and go to the hospital, they take your blood to test and see if you are alright and they tell you the results e.g. if you have malaria, they pick you by car to your home.

F: How do the rest of you understand the meaning of research?

P3: It means the person should be given treatment so that she is completely cured of the malaria.

F: Are there any other views on the meaning of research? How do you understand the meaning of research?

P8: Research can also mean looking around for something so that you know what problems are there in the area; therefore, the word research stands for looking around here and there in order to find out what goes on in a village or community.

P5: Thank you. My understanding is that a research involves investigation into a disease; to find out how and why the disease has come about, how to prevent it incase it has no cure as well as how to find a cure for the disease. So, in the course of their investigation, people say they *(the researchers)* are conducting a research. For instance, there is cancer as a disease **(F:** Hmm). And they conduct a research on cancer to find out its causes and how to combat it.

F: Alright, what do the others say? What does the term research mean according to you?

P1: We always hear that there is a research going on at the clinic. [Baby's noise] And we are sometimes called to the clinic to participate in such research. When we go there, they explain what the research is all about and get our permission to participate. (**F:** Hmm).

F: Ok, what do the rest of you say? [No reply] didn't you say you are all participating in the Microbicide trial? (**ALL:** Yes) So, what does research mean to you? Give me your views as they come to your mind. [A child calls from outside, mum (*mayi)]* Don't you have any other idea?

P5: When they say research they mean when they want to assist on a specific part of our welfare such as wells to see if there is enough hygiene i.e. how we are
taking care of them……. That is what I can say, anybody can continue if there are other views.

F: Alright, what do you think it means when you hear the term research? Are there any other views?

P2: The views that I have are that research is where we hear a lot about the diseases that attack us and do not seem to get treated. The main thing is to have our blood tested in order to see how things are and what can be done about it.

F: What do you have in mind when you say to have your blood tested to see how things are; what things are you talking about?

P2: I can say that sometimes we hear of diseases like……. ***(F: Hmm)*** Yes.

F: Do you mean that you should know about the condition of your body? ***(P2: Yes)*** Alright; what about the rest of you, what do you think research means?

P1: For me I think is it one aspect of trying to find out the origins of some issues concerning our health, like diseases; they can do a research to find out what caused the disease.

F: Hmm, can you please make sure you raise your voices as you are speaking because of this *(points to the recorder)*. So what do the rest of you think on the meaning of research?

P6: Research also aims at finding out how people are behaving like if they are following the advice given by health workers in terms of sanitation in the households. They look at things like availability of toilets, bathrooms and the like; and if they are not available, they make sure that they visit those households to ensure that the facility is constructed in order to reduce the burden of diseases.

F: Let's now talk about the objectives of this study; can you tell what the objectives of the microbicide study are?

P2: We were told that in this study they are trying to find out the efficacy of different types of gels in preventing HIV transmission from a man to a woman.

F: Hmm, how many gels are they trying?

P1: They are trying three different types of gels (**P2** chips in and says; no, there are two gels they are testing).

F: So, which is which? Are they testing two or three gels?

P4 + P5: We don't know.

F: No, you should know – I am sure the Research Staff explained to you the objectives of this study and they must have explained to you the gels they are testing.

P8: What I can remember is that they informed us that we would be allocated to different groups and in one group they would receive one type of gel, in the second group they would receive a different type and in the third group, they would also get a different type of gel. So, basically, there should be three different types of gels.

P4: In my case, I understood it differently. What I understood was that we would receive two different kinds of gels and another group would get a placebo, not a real gel.

F: Hmm, it seems you understood it differently, anyway, what I would like to know are the objectives of the study. So, let's continue talking about the objectives of the study.

P5: Apart from the efficacy of the gels, they were also trying to find out if the gels are safe to be used in the vagina, whether they would cause any irritation or itching when applied to the vagina.

F: Ok, so they were also looking at the safety of the gels.

P5: Yes.

F: Alright, any other objectives?

P7: The main objective is to find out if the different gels can protect women from contracting HIV from a man, that's all!

F: Yes, I get that, but sometimes a study can have several objectives apart from the main objective. So, I would like you to mention all the objectives that you know.

P8: Since you have said a study can have different objectives, then one of the objectives of this study could be to encourage people to use condoms as one way of fighting HIV/AIDS.

F: Was that one of the objectives of this study?

P8: Yes, it was because we were being encouraged to use condoms to prevent the spread of HIV/AIDS.

P4: The distribution of condoms was not one of the objectives of the study. It was just part of the services that were being provided in the study.

F: Do you all agree that the distribution of condoms was not an objective of the study?

ALL: Yes.

F: Ok, then what are the other objectives of the study?

ALL: Silence.

F: Ok, at the beginning of the study, what did the study staff say about how the gels work and how they could prevent the spread of HIV/AIDS from a man to a woman?

P3: We were told that the gels had the potential to kill the virus in the vagina, in this case, if one sleeps with a man who is HIV positive and the virus is deposited into the vagina during intercourse, the gel could kill the virus before it circulates into the blood system.

P7: For those who received a placebo, they were advised to use condoms whenever they had intercourse.

F: So, what was the relationship between the use of condoms and the placebo gels?

P7: They wanted to compare whether the use of condoms and the use of gels could prevent the spread of HIV/AIDS.

F: Alright, how do the gels work?

P2: We were advised to apply the gels in the vagina some minutes before sexual intercourse and have sexual intercourse whilst the vagina was awash with the gels. In this way, we would be protected from becoming infected with the virus.

F: Alright, can you remember when the study staff distributed to you the study information sheets; was the information on the sheets about the study sufficient? Did you understand what the study was all about by going through the information sheet?

P3: In my view, the information was readable and clear. I think for all of us who can read, we understood what the study was all about.

F: Hmm, what about those who can not read and the information sheet had to be read for them by others, did you understand what the study was all about by listening to the information on the sheet?

P1: Their message on the leaflets was enough. They wrote in simple Chichewa and we could understand it.

F: Alright, what about the explanation that was given to you by the study staff, was it enough for you to understand what the study was all about?

ALL: Yes.

F: How did they explain the study to you?

P6: The nurse who consented me explained what the study was all about in her own words and after explaining she asked me some questions about the study and after that she asked me if I had some questions or I needed any clarification on the study.

F: Ok, so between the written information on the sheets and the oral information given by the nurses, which information did you understand best?

P7: The oral information was the best because we could ask questions where we didn't understand and it was interactive.

F: Ok, did you ask any questions about the study?

P4: Yes some of us asked questions because we used to hear a lot of stories about the gels.

F: Hmm, what kind of stories did you hear about the gels?

ALL: Laugh.

F: Can you explain to me some of the stories you used to hear about the gels?

P2: There were stories that people who used the gels would become HIV infected.

P5: Some were also saying that people who use the gels become infertile.

F: Hmm, so what did the nurse say about all these stories?

P2: She said they were lies and that the gels were meant to prevent the transmission of HIV/AIDS from a man to a woman.

F: Ok, were you satisfied with her response?

P6: Yes, we were satisfied because the study staff know better than our fellow friends who tell such lies (**P7:** chips in and says; some have never come to *Tidziwe* and know nothing about the gels. They just spread these rumors without facts).

F: Alright, which part of the study was difficult for you to understand?

P4: When you say a part of the study, are you referring to the procedures or what?

F: I mean when the nurse was explaining the study to you, what did you find difficult to understand?

P4: Ooh, I did not like the part which talked about giving placebos to us. I would have loved it if they were giving gels to all of us so that we would benefit.

F: But did you understand the concept of a placebo?

P4: Yes, I understood that some people would be given a placebo?

F: So, what is a placebo according to your understanding?

P5: Let me help her – the nurse explained that a placebo is something that looks like a gel but it is not the real gel. It would be like receiving nothing.

F: Hmm, apart from the placebo, what else did you find difficult to understand?

ALL: Silence.

F: Ok, what do you think is the most important thing one needs to understand before making a decision to join the study?

P2: I think one has to understand the objectives of the study, the procedures and what one is required to do in the study.

P6: It is also important to understand that the researchers were testing the gels and that they have not yet found them to be effective because some people think that the gels work and this can make them accept to participate in the study.

F: Hmm, what else should one understand about the study before deciding to participate in the study?

P8: I would like to remind people that it is also important to note that the nurses would not know to which group one would belong. I think we were all informed that we would be randomized into the groups and that this would be done by a computer otherwise some people might think that the nurses are biased in giving the gels to participants.

F: Yes, you have brought up a very important concept in this research. Do you all understand the concept of randomization?

SOME: say yes.
OTHERS: No.

F: For those who understand what all is about, can you explain to the others what randomization means?

P7: The nurse explained that randomization is the process of putting people in different groups.

F: So who does the randomization?

P6: She said it was done by a computer.

F: How does the computer do it? Is it programmed by anybody to allocate numbers to individuals?

P3: We don't know how the computer does it. We were just told that we were assigned those numbers by a computer and not anybody.

F: Ok, can somebody else also explain what randomization means?

P1: Why do you want us to repeat the meaning? I think my colleague has already given you the meaning!

F: No, I am not asking you to repeat what she has said. I want you to explain in your own words what you understand by randomization.

P7: Another thing she said about randomization is that it is like a game of chance whereby you do not know who will get this or that – it is by chance that some people received the real gels and others did not get any gel.

F: Ok, I think you are coming up now. Is there anybody else who wants to add on that?

ALL: Silence.

F: Alright, let's talk about a different topic now. You seem to be bored with the subject of randomization! Well, if I may ask you, does health research or clinical research differ from

the medical attention that you receive at the Kamuzu Central or any other Health Centre when you are sick?

P4: Yes, there is a difference.

F: Mmm. What can the difference be?

P4: The difference is that at the hospital they can diagnose us with malaria or diarrhea and give us medicine. While in clinical research, they take blood samples and screen them and eventually inform us about the disease we are suffering from before giving us medicine. For example, in this study, our blood samples were taken and tested for HIV but we did not receive any medication.

F: After testing you, did they tell you that you have the virus?

P4: No, I was told that I am negative.

F: So, did you expect them to give you treatment?

P4: No, what I am trying to say is that in clinical research they do not treat you but they test your blood for a particular disease.

P6: Sometimes, they take your blood, screen it well and give the right diagnosis. In some cases, they can also treat you if you have a treatable disease.

F: So, are you suggesting that in both clinical research and clinical care, there is treatment?

P5: Yes to some extent there is treatment in both cases. But as my friend has said, researchers approach you to participate in research – you don't go to them. And if they screen you and find that you are sick, they may treat you before you enroll in their research or even in the course of your participation in the research.

P4: And in clinical research, they give you better drugs than at the hospital!

F: Hmm, I would like you to clarify. Do you mean that at the hospital they don't give you good medicine unlike in research?

P4: Well, the medicine can be helpful. I can give an example. When you are sick at the hospital they can screen you and if they see that you are coughing, they may give you medicine for a cough while it is TB. While in clinical research, they take your blood, screen it and find the TB quite quickly. They then tell you that you have TB and give you the right medicine. The difference is not necessarily that they may give you drugs that are not powerful. Rather, the difference is in the screening process. In research, they screen in a way that they find the results quickly and rightly, yes.

F: Alright. Do you have any other views on the difference clinical research from normal medical attention you receive from the hospital?

P7: Let me answer like my friend. It is true; you may go to the hospital and tell them you are suffering from headache or you have fever. They just prescribe the medicine for you for fever. They do not screen you. While when you go into a health research, they screen you first to find out exactly what the problem is. Soon after the diagnosis, you are given medicine.

F: What are the views of the rest of you who have not spoken?

P8: it is the same as they have said.

F: Hmm, are they different according to you?

P8: Yes, they are.

F: So, can you explain the difference according to you?

P8: In research, they may tell you to have your urine or stool screened. They find the diseases fast. While at the hospital they just tell you that you are suffering from this and prescribe medication without proper diagnosis.

P7: They just see how you are breathing.

P4: Yes, may be you have pneumonia, may be you have TB, you see, that is where the difference is.

F: Alright, any other views? Ladies, feel free to express yourselves! What is the difference between clinical research and the health care you access from the clinic every day? [No reply]

F: Alright, do you think that those who take part in research understand the difference?

P1: I think many people know the difference between the two. As we have said the two are different and everybody knows this.

F: Hmm, do you any other views on this? Do you think people who participate in research understand the difference clinical research and clinical care?

P7: Yes, they understand the difference as she has said. We all know that we go to the hospital to receive treatment when we are sick while we are normally asked by health workers to participate in research.

F: Well, according to what you remember, what did the nurse say are the benefits of this study to research participants?

P3: One of the benefits is that we will have access to the use of the gels if they are proven to be effective and safe.

F: Hmm, that is a future benefit, not so?

ALL: Yes.

P3: But that is what we were told and I feel it is still a benefit.

F: Yes, it is a potential benefit but I am talking about the benefits of the study to you at the moment.

P8: Another benefit is that we are allowed to come for treatment here at Tidziwe whenever we fall sick – this is for us and our families.

F: Ok, what are the risks of participating in this study to you?

P1: I don't think there are any risks in taking part in this study because every time we come for a visit, we are screened and if there is any problem we are advised what to do.

F: Hmm, that's your opinion, let's hear from others!

P6: I think one of the risks is that when we apply the gels to the vagina, sometimes we feel itching and this can discourage some people. They may decide to stop using the gels as advised by the nurse.

F: Hmm, do you all feel itching when you apply the gels?

P2: No, not everybody feels itching. It all depends on how your body reacts to the gels and it also depends on the type of gel one has received.

F: Ok, let's continue talking about the risks in this study – what are the other risks?

P7: Another risk is the smell – the gel I am using smells badly and I don't like it when I use it.

F: Hmm, is there anything else? [No reply]

F: Ok, when we were talking about the difference between clinical research and clinical care, some of you said in clinical research they provide better treatment than at the hospital or health centre, now do you think that there are some people who accept to participate in clinical research because they would like to better treatment?

P7: Not really because treatment is not provided in every research. In some research, they don't provide treatment. For example, there are some students from KCN who come to do some research in our homes and they don't provide any treatment. So, one can not participate in such research in order to access better treatment.

F: Hmm, but do you think such a thing can happen if people learn that they are providing treatment in a particular research?

P5: Yah it can happen.

P8: The problem we have in our hospitals is that they don't have sufficient drugs and every time we go to the hospital, they provide the same drugs. While in research they have enough drugs and they provide drugs that cure the disease you are suffering from.

F: Are there people who refused to participate in this research and if you do, why did they refuse to participate in this?

P8: Some people did not refuse but they were told that they were not eligible to participate.

F: Do you mean you don't know anybody who refused to participate after being approached?

P4: Well, what's happening in this study is that some people withdraw from the study at their own will and some of them don't explain why they withdraw.

P7: But I know a friend of mine withdrew because her husband did not know that she was participating in research and when he knew it, he forced her to withdraw from the study.
F: Hmm, did she explain to you why the husband forced her to withdraw?

P7: No.

P4: The rumors we talked about could also discourage people from participating.

F: Which rumors?

P4: You remember we talked about rumors concerning the gels that they cause HIV/aids.

F: Ok, I remember now. Now for you what really motivated you to accept to participate in this study?

P6: I think most of us were just convinced by what the nurse explained.

F: What convinced you?

P6: The fact that the gels could prevent the transmission of HIV from a man to a woman.

F: Hmm, what are the other reasons why you decided to take part in this study?

P3: Some of us are used to taking part here at Tidziwe. So, when the nurse approached us, we couldn't refuse.

F: What if you were approached by somebody else whom you didn't know and not the nurse, would you still accept to participate and why?

P3: Yes, I would still participate because all these research projects that are conducted for our benefits and the benefit of our own children.

F: Ok, what do the rest of you say?

P8: In my case, I just wanted to see for myself what the gels look like and how they work because I heard a lot about them from people. So, when the nurse asked me to participate, I had to accept.

F: Alright, is there anything else?

ALL: No.

F: Well, before you decided to take part in this study, do you think the nurse explained adequately about your role and the procedures in the study?

ALL: Yes.

P3: All of us went through the consent process in which the nurse explained in detail about the study before we joined.

F: So, do you think the information disclosed by the nurse was adequate for you to make an informed decision about the study?

ALL: Yes.

F: Alright, earlier on you said that you were assigned to different groups, do you know how many groups there were in this study?

P7: We were assigned to four groups according to what the nurse said. Three groups would receive gels and the fourth group would receive nothing.

F: Hmm, for the groups that received the gels, what type of gels did they receive?

P5: My understanding was that there were testing two gels and other two groups would not receive anything. However, the names of the gels are difficult to say.

F: So, are you trying to say that two groups received gels and the other two groups received nothing?

P4: No, I think she is mixing up things – the nurse said two groups would receive the real gels, another group would receive a placebo gel and the fourth group would get nothing.

F: Ok, in your own opinion, did the nurses know what each one of you received?

P1: In my view, they didn't.

F: Why do you think they didn't know?

P1: Because the nurse explained that neither the researchers nor ourselves would know in advance what we were getting.

P5: We were just given numbers and we received the gels according to the numbers.

F: So, did you understand why both the researchers and you did not know what you were getting?

P8: I think that's how they planned it.

F: What if you had known in advance that you were receiving a placebo gel, would you have accepted it?

P6: It's difficult to accept something which is not what you are looking for.
F: What about those who received nothing, how did you feel about it?

P5: No one here received nothing.

F: Is that so?

P2: Yes, but in my case I was in the group of those who received a placebo gel?

F: How did you feel about it?

P2: It was ok because it was part of the study.

F: Hmm, what do the rest of you say about the placebo gels?

P8: You know it was difficult to know that one was getting a placebo gel. We all thought we were getting the real gels.

F: So, for you (pointing at P2) how did you know that you were getting a placebo gel?

P2: At first I didn't know but later I learned that it was a placebo gel.

F: How did you know it?

P2: It looked different from the rest of the gels.

F: Hmm, that's strange! What if they told you that you were getting placebo gels at the end of the study, how would you feel?

P5: As my colleague has already, it would be fine because it was how the study was designed.

F: And you my friend, how would you feel?

P2: Since it would not be the wish of the researchers, I would accept it.

F: OK, do you have additional views on placebo gels?

ALL: No.

F: Ok, why are the researchers using a placebo in this Microbicide study?

P8: It was part of the design of the study

F: Yah, but why did they choose to use placebo gels?

P6: The researchers themselves know.
F: Of course they may know but I would like you to tell me what you think about it; why you think they used the placebo gels!

P8: That is a difficult question because we were not there when the researchers thought of including placebo gels in this study.

F: Well, is there anybody else who has an idea as to why placebo gels were used? [No reply]

F: Anyway, if you have nothing else to say about the placebo gels, then this marks the end of the questions I had. I don't know if you have any questions or comments on what we have discussed.

P7: On behalf of my friends, I am grateful to you for your coming. To be frank we have learnt a lot from this discussion about the Microbicide study. Your questions made us think about what we went through during our participation in this study and it will help us to remember this study forever. So, we don't take our participation in the discussion for granted- we thank you so much!

F: You are welcome.

P3: We also appreciate what the researchers at Tidziwe are doing. A lot of us are benefiting from their work. Please, encourage them to continue conducting these studies.

F: Ok, I will convey your message to them. Hmm, do you have any more comments or questions?

ALL: No.

F: Ok, then I thank you most sincerely for taking your time to participate in this study. I know most of you are busy working either in the field or doing business and you have left all those duties and have come to participate in this discussion – thank you very much. Please, maintain this good spirit!

ALL: It's our pleasure.

F: Thank you for that. I hope I will see you again next time.

ALL: Thanks.

END

Appendix 25: Transcript of FGD held at Blantyre site

TRANSCRIPT OF A FOCUS GROUP DISCUSSION WITH HPTN 035 TRIAL PARTICIPANTS HELD AT QUECH (JOHNS HOPKINS RESEARCH CLINIC) IN BLANTYRE

FGD ID Number: **FM_FGD 02**
Geographic Location of FGD: **Queen Elizabeth Central Hospital Blantyre**
Type of FGD: **Adult Females participating in a Microbicide Trial (HPTN 035)**
Date of FGD: **Friday 26th September, 2008**
No of Participants: **10 Adult females**
Facilitator/Moderator: **Francis Masiye**
Transcriber and Translator: **Francis Masiye**
Time interview began: **15:10 p.m.**
Time interview ended: **16:55 p.m.**

Participants' personal details [recorded at end]

Participant	Gender (M/F)	Age	Education (years)
9. P1	Female	44	9
10. P2	Female	23	14
11. P3	Female	26	14
12. P4	Female	20	3
13. P5	Female	20	13
14. P6	Female	22	13
15. P7	Female	25	8
16. P8	Female	20	6
9. P9	Female	21	9
10. P10	Female	21	8

SUMMARY:
Number of participants: **10**
Gender: **All females**
Average education attainment: **9.7**

Average age distribution: **24.2**

NOTES IN FOCUS GROUP DISCUSSION

I arrived in Queens at 14:56 p.m. and I found all the participants at the venue waiting for me. The responsible Research Nurse was well organized and she had identified the right people for the FGD.

The FGD started at 15:10 and it was held in the Consultation Room of the Johns Hopkins Research Clinic. Before the beginning of the FGD, I distributed the information sheets to all the participants. I then gave a brief explanation of the study and for those who participated in the individual interviews; they knew what the study was all about. I also asked for oral consent from each of the participants and all of them accepted to take part in the discussion.

Reading from the responses given by the participants, they were all aware of the objectives of the Microbicide study. They were able to give the procedures they were required to follow from recruitment up to the final visit. Finally, the discussion flowed very well.

The discussion ended at 16:55 p.m.

Key:
F: Facilitator/Moderator
P: Participant

ENGLISH TRANSCRIPT OF THE DISCUSSION

F: Ice breaker – What do you know about the Microbicide Study?

P7: It is a study about the use of a special gel to find out if the gel is effective in preventing transmission of HIV/AIDS.

F: Hmm, so, they are trying to find out the efficacy of the gel in preventing HIV/AIDS

P7, P9 & P10: Yes (together)

P5: Can I also say something?

F: Yes, you can.

P5: Yah in the study, they are also trying to find out if men can accept the use of the gel by their wives. You know there are some men who do not want to see anything in the vagina when they are having intercourse (OTHERS: Laugh). Yes, this is true. So, the researchers want to know if men can allow their women to use the gel.

F: Hmm, is there anything else someone would like to add.

P2: Yes, I would like to add that this gel is very good.

F: Can you explain how it is very good?

P2: I am saying it is very good because most men like it. They say they enjoy sex when a woman uses the gel.

F: Ooh, really! Do you all have the same comments from men?

ALL: Yes (they like it).

P5: But my husband does not like it. He does not want to see anything in the vagina when we are having intercourse. He doesn't even want to use a condom nor does he allow me to use it. So, it varies. We can say some like it and others don't. (**P3** chips in and says; however, most men enjoy it).

F: Ok, let's talk about a different subject. What comes to your mind when you hear the word "research"? I am sure you have all participated in research. Now, I would like to know your understanding of the term research; when you hear the term research, what concept comes to your mind?

P3: Research means investigation into people's everyday lives (F: Hmm). For example, in the research I am participating, they are investigating into the health of women and how they can prevent the transmission of HIV/AIDS. So, if you ask me the meaning of the term research, in short, it means investigating into a person's health. This is done if the person has accepted to be investigated.

F: Ok, Madam over there, what do you say?

P9: They *(researchers)* conduct a research in order to find out if a person is HIV positive or not. Sometimes they also conduct it to investigate into other diseases such as Candidiasis (*mauka*), gonorrhea (*chizonono*) or even malaria. [**F:** Hmm] yes.

F: Alright, what do others say? What does the term research mean? [Silence] When you decided to participate in the Microbicide Study, what did you want to participate in?

P3: Anyway, when we were asked to take part in the Microbicide Trial, we did not know what the trial was all about until the researchers explained to us what the research was all about (F: Hmm). What they said was that in the research they were trying to investigate into the efficacy of using the gel in the prevention of HIV/AIDS. One of the requirements was that one had to be tested for HIV/Aids if one accepted it. So, this is what we were told during the research.

F: Ok, what you are saying is correct, however, I would like to know your understanding of the term research [Silence].When you hear the word research, what comes to your mind? We are not only talking about the Microbicide Trial but we are talking about your general understanding of the word research.

P1: In most research, they take blood from the arm in the ward and test it for sexually transmitted infections.

F: **Sexually transmitted infections?**

P1: **Yes, for example, HIV/AIDS, gonorrhea [*chizonono*] (F: Ok) and they give medication every month if you test positive.**

F: **Alright, do you have any other view? Ladies over there, what is the meaning of the term research?**

P8: **Research means … (speaks faintly)**

F: **Can you speak up please so that it may be recorded (points to recorder)?**

P8: **In research** (F: **Hmm) they investigate into the health of people, whether diseases such as HIV/Aids affect them or not. If you are HIV positive** (F: **Hmm), they give you antiretroviral drugs to boost your immune system.**

F: **Alright, now can you explain to me in your own words, what the objectives of the Microbicide Trial are according to your understanding?**

P6: **As we have explained above, the study is about the use of a gel to prevent the transmission of HIV/AIDS from a man to a woman. It is the woman who uses it.**

F: **Hmm, what's the objective in that case?**

P6: **It is to find out if the gel can help prevent transmission of the virus from a man to a woman.**

F: **Alright, what are the other objectives of the trial?**

P2: **I think the main aim is to prevent the spread of HIV/AIDS. If the gel is effective, it means it will help in the prevention of the spread of HIV/AIDS.**

P6: **Yah but the objective you have given is not different from mine because I said the aim of the trial is to help prevent HIV transmission from a man to a woman.**

P2: **Of course, it is not very different but I have stressed the fact that it is the main aim of the trial.**

F: **Anyway, let's hear from others. What are the objectives of the Microbicide Trial?**

P10: **Another objective is to provide counseling, HIV testing and support to those who test positive.**

F: **Hmm, were you all counseled before being tested?**

ALL: **Yes.**

F: **Hmm, what happened to those who tested positive? You have said they provide support to those who test positive, what type of support do they provide?**

P10: **They refer them to the ART Clinic for treatment.**

P8: **They also do CD4 Count of all whose results are positive before they send them to the ART Clinic to receive ARVs.**

F: **How did you know all this? Did researchers explain this to you?**

P9: **Yes, during counseling and the consenting process, they explained to us that people who test positive will be sent to the ART Clinic for treatment. We also have friends who tested positive and were referred to the ART Clinic.**

F: **How did you know that your friends tested positive?**

P9: **We would know if one was tested and did not join us.**

P8: **After some days, you would see her going to the ART Clinic and we would say "sorry" for our friend.**

P2: **It is not a secret at all when one tests positive because we know each other.**

F: Hmm, does this mean there is no confidentiality on the part of those people who test positive?

P6: Confidentiality is there because each one is told privately. However, when one goes for counseling and testing and does not join us in the study, we automatically know that that person has not met the requirements (eligibility criteria), one of which is her HIV status.

So, it's very easy for us to know that one is HIV positive and if one attempts to join the trial.

F: Ok, let continue with the objectives. Are there other objectives apart from the ones you have mentioned?

P4: I think another objective is to know the number of people with HIV/AIDS.

F: Hmm, did they explain to you that this was one of the objectives of the study?

P8: No, they didn't say they wanted to find out the number of people with HIV/AIDS. However, from the HIV tests, they were able to know the number of people with HIV/AIDS from our group. And it's possible that one of the objectives of the study was to find out the prevalence of HIV/AIDS among women.

F: Ok, is there any other objective? [Silence]

F: Alright, during your recruitment into the trial, what did the nurse say about how the microbicide works and the potentiality of the microbicide in preventing the transmission of a virus from a man to a woman?

P5: The nurse who consented me explained that there was a possibility that the gel could reduce the male to female transmission of HIV. However, she insisted that they were only testing the gels and that they have not yet found them to be effective in preventing the transmission of HIV/AIDS from a man to a woman. I think this is what she also explained to the others.

OTHERS: Nod their heads to show agreement.

F: Ok, what did she say about how the microbicide works?

P3: We were told that we had to apply the gel before any sexual contact and they used to check us every time we came for a visit.

P8: She also said that if the gel worked, we would not become infected by the virus from an infected person.

F: Hmm, how did you explain it to your partners?

P8: It wasn't easy.

P1: Some of us didn't inform our partners that we were using the gels.

P3: But one could not hide it because it was applied on the vagina and he could feel it whenever he penetrated into the vagina.

P5: You are right, but you know that when some men are hot (when their penises erect), they don't care about what's on the vagina – what they care about is just penetration and ejaculation – they would have no time to check what's around the vagina.[OTHERS: Laugh]

F: Ok, can you recall when the nurse explained the study to you and gave you information sheets about the study, was the information you received about the study enough? Was it sufficient for you to make an informed decision/choice?

P4: Yes, the information was enough, that's why we were able to say yes or no. If it was not enough, we would not have accepted to participate in the trial.

F: Hmm, that's your view. What are the views of the rest of you?

P8: I think the information was very enough. In fact, the nurse who approached us explained the study to us and again when we came to the Clinic, they also explained to us clearly and requested us to ask questions where we didn't understand. We also had leaflets given to us so that we could read at home. So, we can't blame the researchers about information about the study (P5 chips in and says)

P5: Their message was very clear and it was up to us to decide. Nobody can cheat you that the researchers did not explain the study to us.

F: Alright, it seems you had both oral information and written information about the study, now between the two, what did you understand clearly?

P8: Both were clear. However, the oral information was the best because we could ask questions where we didn't understand.

F: What type of questions did you ask?

P8: In my case, I asked the sister (Research Nurse) to explain further on the negative effects of using the gel.

F: Hmm, and what did she say were the negative effects of the gel?

P8: She explained that the gel could cause itchiness in the genital area and one could feel irritated.

F: Who else asked questions about the study and what type of questions did you ask?

ALL: Silence.

F: Alright, what do you think is the most important thing for one to know before deciding to take part in the microbicide study?

P2: I think is important for one to know that the gels have not yet been proven that they can prevent the HIV transmission but that they are in the process of testing them. I think this is important because some people might think by using the gels; they are protected from contracting the virus, which is not the case.

F: Yes, that's a good point. Is there anything one ought to know?

P7: Yes, one has to know that participation in the trial is voluntary - nobody is forced to participate in this trial.

F: Hmm, it's an important point as well. Is there anything else one should know?

P5: The procedures for using the gel are also important because they help you to use the gels correctly and this can affect the outcome of the trial.

F: Ok, is there anything else one ought to know?

P4: I think the objectives and procedures of the trial are very important – In fact, the information sheet contains all this information and it is necessary for each potential participant to understand what is in the information sheet before deciding to take part in the trial.

F: What else should one know?

ALL: Silence.

F: Alright, what is the difference between clinical research and clinical care (medical treatment) at a hospital?

P6: Firstly, there is need for a person to do something or hear it before one knows it.

F: What do you mean by that? [**P6:** Laughs]

P4: The difference is that in clinical research we visit villages to see how people live and their health (**F:** Hmm) while we go to the clinic to get medical attention when we are sick (**F:** ok) yes.

F: Do you have any other idea?

P5: The other difference is that when we go to the clinic, we explain our problem and receive treatment (**F:** Hmm) while in clinical research, they investigate into the problem before they give you treatment - they investigate the problem and from the investigations they are able to find the best treatment for the disease.

F: Alright, any other views? Ladies, feel free to express yourselves! What is the difference between clinical research and the health care you access from the clinic every day? [No reply]

F: Please, express your views when we ask you a question because if you don't express them and keep quiet, we will spend a long time in here (**P6:** Laughs)

P7: We go to the clinic to receive treatment for ailments while in research we go to visit sick people in the village, those suffering from malaria or TB. After visiting them, we inform the doctors at the clinic about the people suffering. So this is different from the health care we get from the clinic everyday.

F: Ok, do have any other views? We are talking about the difference between clinical research and health care (**P5:** Yes) so, is there any other difference between the two?

P1: Yes, there is a difference between the two because when you are sick you rush to the clinic to get medical attention.

F: You have just talked about one side that when you are sick you rash to the clinic, what do you say about clinical research? [**P1:** Laughs]

P1: In clinical research, they advise us to go to the clinic when we are sick and to rush any seriously sick person to the hospital. I don't know if I am right.

F: We have already told you that there is neither a correct answer nor a wrong one. We are just interested in getting your views (**P6:** Agrees). So, do you have any other opinion on the

difference between clinical research and health care? [No reply] Don't you have any? [Silence]

P3: At the hospital we get treatment when we are sick while research can be conducted even if one is not sick (**F:** hmm) hmm.

F: Ok.

P4: The difference is that we get medical treatment when sick whereas in research you are given all sorts of assistance even if you are not sick

F: Hmm, those are their views, what about others?

P9: Health personnel most of the times help us in form of food while at the hospital we get assistance in form of medicine.

F: Hmm, other views? What do others say is there any difference between health research and health care?

F: All of us answered that there is a difference not so? (**All:** yes) so we would like you to explain the difference.

P2: The difference is that you go to the hospital when you are not feeling well while in research you can enroll even if you are ok, depending on the type of research whether they are trying to find out if you have certain diseases.

F: Ok, do you think that people who participate in clinical research understand the difference between the two?

P1: It is difficult to know because people think differently. However, I am sure that many people know that research is different from medical treatment.

P9: I also think that many people understand the difference because normally people are asked to participate in research whilst people go to the hospital to receive treatment on their own when they don't feel well.

F: Hmm, what do the rest of you say?

P7: Well, I agree with those who have said that many people understand the difference between clinical research and clinical care. In clinical research, people are always asked to give their permission before they participate and in most cases nurses are the ones who ask people to participate in research. If one does not want to participate he/she is free to refuse. Those who participate are the ones who are willing and give their permission.

F: Alright do you have other views?

ALL: Silence.

F: Ok, let's talk about the study you are participating in. What are the benefits for people who are participating in this study?

P2: One of the benefits is that we might be protected from being infected by the virus. The nurse told us that there is a possibility that one can be prevented from becoming infected.

F: Hmm, did the nurse say that the use of the gel protects you from HIV infection?

P5 + P3: No.

P3: The nurse said that the gel could prevent one from becoming infected after testing it first (**P5:** chips in and says; this is what they are trying to find out and it does not mean that the gels work)

F: Hmm, so what are the benefits to you in this study?

P10: One of the benefits is that whenever we are sick and come to the hospital, we will be treated faster than our friends – we were told that whenever we become sick we should always come to the clinic for treatment.

F: So, is that a benefit to you?

P10: Yes, because we are given this special treatment due to the fact that we are participating in this study.

F: Ok, now what are the disadvantages of taking part in this study?

P1: One disadvantage is that we take long when we come to the clinic for the study. Some of us come early in the morning and we go back home very late in the afternoon.

F: Hmm, is there another disadvantage of taking part in this study?

P8: Another disadvantage is that when one applies the gel on the vagina, it itches and it is discomforting to some people.

F: Ok, sometimes we hear that some people enroll in clinical research in order to get better medical treatment; is it true that people enroll in clinical research conducted at the hospital in order to access better medical treatment?

ALL: Yes.

P2: As we have already explained, people who participate in clinical research are given better treatment than other people. This is why people do not refuse to participate in research.

F: Do you know some people who refused to take part in this study?

P8: Yes some refused to take part because there were rumors that people who use the gels would become barren.

P4: A neighbor of mine discouraged me from participating but I told her that it is my right to participate or not.

F: Hmm, was your neighbor also approached to take part in the study?

P4: Yes, the sister (Nurse) asked her to participate but she refused because of the rumors people were circulating about the gels.

F: What rumors were they?

P4: The rumors that people who use the gels can not bear children and that one can become infected with the virus.

F: Do you mean that some people associated the gels with HIV transmission?

P5: Yes, there were rumors that people who used the gels would become HIV positive because the researchers had put the virus in the gels to see if people who used the gels would contract it (P2 chips in and says; but those were just false rumors!).

F: So, how did you dispel those rumors or what convinced you to come forward and participate in the study despite those rumors?

P5: We knew that those were just false rumors and the nurses who approached us explained to us that the rumors were not true. Moreover people who circulated those rumors had not listened to what the nurses said about the gels – they just fabricated those stories.

F: So, what exactly motivated you to participate in the study?

P6: I was asked by the nurse to take part in this study and since I have been participating in other studies conducted by the Johns Hopkins, I decided to take part in this study as well.
F: So, what was the main reason why you decided to participate in this particular study?

P6: I was just interested in taking part in this study.

F: Hmm, what about the rest of you – why did you decide to take part in this study?

P3: I wanted to know my status because we were told that they would test us for HIV.

F: Hmm, Madam over there, what do you say?

P7: Anyway, when we were asked to take part in the research, we were told that the researchers would provide us with treatment whenever we fell sick (**F:** Hmm).
They would also test us for HIV at each and every visit and prescribe drugs for the cure of any diseases one was suffering from. So, how could I refuse such a free service?

OTHERS: Laugh (in agreement).

F: **So, did you accept to participate in the study because they were providing free services?**

P7: **Yes.**

F: **Do you mean that you pay for the services rendered to you at the hospital?**

P1: **No, we don't pay for the services but sometimes we are told that there are no drugs at**

the hospital pharmacy and they ask us to buy drugs at private pharmacies which we can't

afford.

P8: **and sometimes they just give us the very same drugs like panadol… (Speaks faintly)**

F: **Can you raise up your voice please so that it may be recorded (points to recorder)?**

P8: **I said they give us panadol all the time** (F: **Hmm) [kids noise] so when we heard that**

they were providing drugs free of charge, we decided to join [P8: **continues speaking but**

cannot be heard because of kids' noise]

P10: In my case, I just wanted to know what was happening in the research since they were looking for people to participate in the research (**F:** Hmm). Yes.

F: Alright.

P3: They had actually explained to us what was to happen in the research before they asked us participate.

F: Ok, can you explain the arms in which people were assigned to in this study?

P1: During the consent process, we were told that we would randomly be assigned to four groups. In the groups, some would receive gels and others would receive nothing.

P7: We were also told that we would not know the arms to which we would be assigned. However, in my case I was in a group in which we received gels.

F: Hmm, do you the type of gel you received?

P7: No, I don't know the names of the gels. We just knew that some of us were given the gels.

F: Alright, how did they assign you to the different groups/arms?

P8: We don't know how we were assigned to the groups.

P3: We were given numbers and each one chose the gel which corresponded to her number.

F: Who generated the numbers? Where did they come from?

P5: I remember that the nurse explained that it was done by a computer.

F: Hmm, do you think the nurses explained clearly how you were assigned to the arms?

P10: Yes, they explained clearly. As my colleagues have stated, the nurses explained that it was the computer which assigned us to the different groups and that the nurses would not know to which group each one belonged. We understood that the nurses were not assigning us to the groups.

F: Hmm, what do others say?

P7: As she has said, it was very clear.

F: Ok, did each one of you expect to be in the group in which you are?

P7: No, nobody knew she would be in the group in which she is. It was just by chance as the nurse explained.
F: Hmm, what about you madam?

P2: It is true that nobody knew in advance that she would belong to a particular group. It was determined by the computer and nobody had the right to choose to which group she would belong.

F: So, how do you feel about being in your assigned group?

P6: In my case, I am happy that I am in this group. Of course, I know some people are not happy that they are in a group in which they are not receiving anything.

P4: There is nobody to blame about this – can you blame the computer for assigning you to your group? No, it was just by chance that we were assigned to these groups (**P8:** chips in and says; it is a pity that they arranged that some people should not receive gels when we were told that they are testing gels).

F: In your opinion, who decided that some people should receive gels and others should not receive gels?

P8: I think it was the researchers themselves because the computer could not make such a decision.

P4: A machine can not make a decision.

F: How are the things you receive in this study distributed to you?

P8: What type of things are you talking about? Are you talking about the gels or the soap and other materials?

F: I mean the gels.

P8: After getting the numbers we were given an envelop that corresponded to our number. Inside the envelop, we would find the gel and nurses would explain how to use the gels to each individual.

F: Did the doctors or the study staff know what the participants received?

P10: No, they didn't know.

P7: The study staff provided instructions but they didn't know what we were getting.

F: How did you know that they didn't know what you were getting?

P4: During the consent process, they stated that they would not know what each one would receive.

P8: But eventually, they would know those who were not receiving anything because they could complain that they were not receive anything.

F: Ok, what is a placebo? Let's hear from you first because you have not spoken for long.

P1: It's difficult to explain what it is.

F: No, it is not difficult – I want you to explain what you know about a placebo.

P1: It is a kind of medication which does not function like the actual medicine.

F: What do you mean by that?

P3: I think what she wants to say is that it is something which looks like the gel but it is not the actual that is being tested.

F: Is that what the nurse explained?

P3: Yes, the nurse explained that some people would receive a placebo, something which looks like the gel but it is not the actual gel and others would receive totally nothing.

F: So, do you know people who received the placebo gel?

P6: No, we wouldn't know but we could know those who didn't receive anything.

F: Why wouldn't you know those who received placebo gels?

P6: Because the placebo gels were like the other gels and we wouldn't differentiate the two.

F: Hmm, what do the rest of you say about placebo gels and those who received them?

P9: As she has explained, nobody knew that she was getting a placebo gel and none of us would know the people who were getting the placebo gels.

F: Alright, if at the end of the study they told you that you received placebo gels during the study, how would you feel?

P8: It would be ok because it was part of the arrangement of this study and we were all contributing to the success of the study.

P10: Aah it would be discouraging to some of us because we all felt we were receiving the actual gel.

F: And you madam, how would you feel?

P2: I would also feel bad because I thought the gel I was receiving was protecting me from HIV.

F: So, what would you do?

P2: I would just regret about it.

F: Ok, do you think it is possible for you to become infected with the virus whilst you are participating in the study?

P7: Yes, if one does not follow the instructions, she can easily become infected with the virus. What's important is to follow the counseling we receive from the nurses.

F: Hmm.

P5: Everybody is potentially a victim of the epidemic – but we need to take care of ourselves. However, the study itself would not expose us to the virus.

F: Hmm, how would you feel if you were told that you are HIV-positive?

P9: If it's me, I would accept it because nowadays having the virus does not mean the end of the day. There are many people around us who are living with HIV/AIDS and are living positively. After all, ARVs are available and are saving many lives.

F: Hmm, how would other people feel about it?

P3: If one becomes HIV positive because of her careless behaviour, then it is her own fault but if she becomes HIV infected because of using the gels, which I doubt, then it would be unfair – she would have to claim for compensation and ask the researchers to provide treatment for her.

F: How do you think the gels could cause one to become HIV positive?

ALL: Silence.

F: I mean if you say one becomes infected with the virus because of using the gels, how could this be possible?

P7: In my view, one can not become infected because of using the gels. If she becomes infected, it would be because of not following the instructions from the nurses or being careless about her life just like the other people who are getting infected with the virus.

F: So, were told that it was possible for one to become infected in the course of her participation in the study?

ALL: Yes (**P8:** If one did not follow the instructions we were given before took part in the study).

F: Hmm, do you have any other views on this issue?

ALL: Silence

F: Silence means you don't have any other views on this *(Kachetechete sausa nyama)*, not so?

ALL: Yes.

F: Ok, why do you think they are using a placebo in this study?

P9: The nurse said they wanted to compare the different groups at the end of the study.

F: So, why would they use a placebo if they wanted to compare the different groups?

ALL: Silence.

F: Didn't the nurse explain why some people were receiving placebo gels in this study?

P5: What she said was that the researchers wanted to find out if the gels were effective in preventing HIV transmission. In this case, with the use of the placebo gels, they would be able to know whether the gels were more effective than the placebo gels.

F: Hmm, is there anybody who would like to add on this?

P3: The fact is that the nurse did not explain clearly why some people were receiving placebo gels, am I not right? [Others say *eeh* to show agreement] .

F: Ok, why do you think the researchers decided to double blind the study?

P8: What do you mean by that?

F: I think you stated that both you and the study staff did not know what you were receiving, not so?

ALL: Yes.

F: Yes, so the term "double-blind" means both you the research participants and the researchers did not know what you were receiving.

P8: You are right but in this study the researchers knew what we were receiving.

F: Hmm did they know what each one of you was receiving?

P8: No, I mean that they knew that we were receiving two different types of gels plus a placebo gel and that others were getting nothing.

F: Yes, but they didn't know what each one of you was assigned to receive, not so?

ALL: Yes.

F: So, my question is why they choose "double-blind" in this study? Why they decide that both they and you should not know what you were receiving?

P9: They were afraid that if one knew that she was receiving a placebo gel, she would withdraw from the study.

F: So, how would that affect the researchers?

P9: They would not be able to recruit a good number of people because some would have dropped out.

F: Ok, is there any other reason why they chose "double-blind" in this study?

ALL: Silence.

F: Ok, so far, we have said that the researchers used placebo gels, they randomized you into different groups and that the study was double-blinded. Now do the terms, placebo, randomization and double-blind mean anything to you?

P4: Those words don't mean anything to us – perhaps they are significant to the researchers who chose them.

P5: Of course the nurse explained what they mean but it does not matter to us.

F: Did you consider the use of those terms before you decided to participate in the study?

P3 + P9: No we didn't.

P6: We were only worried with the placebo gels and those who didn't receive anything.

F: Finally, if you had power to change some things about the study, what would you have changed so that the objectives of study were very clear to the research participants?

10: I would not tell people that some will be receiving placebo gels or nothing for this would discourage some people and it would be as good as not taking part in the study.

F: Why would you not tell them about the placebo gels or that they would receive anything if this was the truth?

P10: It is not good to tell people because if one knows that she is not using the actual gel or that she is not receiving anything, next time, she will not be willing to participate in research.

F: Yah but I do think you would also complain if they lied to you and eventually you realized that some of you were receiving placebo gels or nothing.

P9: I think it is good to be told the truth. I appreciate that we were told the truth about our participation in this study.

F: What do you mean by the truth about your participation in the study?

P9: We were told the truth that there were no benefits in this study for our participation.

F: Once again, what would you have liked changed in the way information was given to you about the study?

P3: I would have loved it we knew what we were given whether we received PRO-Gel, Buffer-Gel or Placebo-Gel.

F: Don't you think that you would have changed your behavior if you knew what you were receiving?

P3: No, we wouldn't because we would have just known the truth about what we were getting.

F: Hmm, do you have anything else to add?

ALL: Silence.

F: Alright, we have talked about a lot of things in this discussion. I don't know if there is anybody who has a comment or a question about what we have discussed.

ALL: Silence.

F: Does this mean you don't have anything else to say or a question to ask?

ALL: Yes (meaning).

P8: I think we are all tired – we want to go.

F: Ok, if there are neither comments nor questions, then I would like to take this opportunity to thank you all for coming to participate in this discussion and for sharing your views with me. The ideas you have given will help us to achieve our goal. Thank you once again and I wish you all safe journeys back home.

ALL: Thank you very much.

END OF DISCUSSION

APPENDIX 26: LIST OF LOW SCORERS FROM BLANTYRE SITE (N=77)

	Participant Identifier	Total Score %	CATEGORY ON A TRIPPLE SCALE 1=0=49% 2=50-74% 3=75%+	CATEGORY ON A DUAL SCALE 1=0-74% 2=75%+
1.	058	50	2	1
2.	059	70	2	1
3.	061	73	2	1
4.	062	65	2	1
5.	063	58	2	1
6.	070	65	2	1
7.	073	60	2	1
8.	079	70	2	1
9.	083	70	2	1
10.	084	73	2	1
11.	085	68	2	1
12.	087	73	2	1
13.	088	63	2	1
14.	089	70	2	1
15.	093	65	2	1
16.	094	65	2	1
17.	096	68	2	1
18.	099	70	2	1
19.	100	65	2	1
20.	101	70	2	1
21.	102	65	2	1
22.	104	60	2	1
23.	105	60	2	1
24.	108	73	2	1
25.	112	58	2	1
26.	113	60	2	1
27.	115	68	2	1
28.	116	48	1	1
29.	120	55	2	1
30.	124	73	2	1
31.	125	68	2	1
32.	127	60	2	1
33.	131	70	2	1
34.	133	73	2	1
35.	134	55	2	1
36.	135	63	2	1
37.	136	68	2	1
38.	137	50	2	1
39.	139	58	2	1
40.	140	58	2	1
41.	141	60	2	1
42.	142	70	2	1
43.	143	60	2	1

44.	147	70	2	1
45.	150	58	2	1
46.	151	60	2	1
47.	153	68	2	1
48.	154	70	2	1
49.	155	40	1	1
50.	156	70	2	1
51.	157	58	2	1
52.	158	63	2	1
53.	161	70	2	1
54.	162	68	2	1
55.	163	53	2	1
56.	164	50	2	1
57.	167	70	2	1
58.	168	53	2	1
59.	169	68	2	1
60.	170	73	2	1
61.	171	68	2	1
62.	179	68	2	1
63.	181	73	2	1
64.	182	63	2	1
65.	183	70	2	1
66.	184	60	2	1
67.	187	73	2	1
68.	189	68	2	1
69.	191	60	2	1
70.	194	60	2	1
71.	196	68	2	1
72.	197	70	2	1
73.	198	40	1	1
74.	199	70	2	1
75.	200	68	2	1
76.	201	53	2	1
77.	202	50	2	1

Note: Participants with highlighted identifiers participated in the intervention phase of the study. Their residential address was still traceable at the time of the intervention and they were located by tracers and had ultimately availed themselves for the intervention.

APPENDIX 27: LIST OF LOW SCORERS FROM THE LILONGWE SITE
(N=47)

	Participant Identifier	Total Score %	CATEGORY ON A TRIPPLE SCALE 1=0=49% 2=50-74% 3=75%+	CATEGORY ON A DUAL SCALE 1=0-74% 2=75%+
1.	001	63	2	1
2.	002	60	2	1
3.	003	45	1	1
4.	004	70	2	1
5.	005	60	2	1
6.	006	53	2	1
7.	007	53	2	1
8.	008	65	2	1
9.	009	48	1	1
10.	010	53	2	1
11.	011	48	1	1
12.	012	53	2	1
13.	014	70	2	1
14.	015	53	1	1
15.	016	63	2	1
16.	018	60	2	1
17.	019	48	1	1
18.	020	70	2	1
19.	021	70	2	1
20.	022	60	2	1
21.	023	70	2	1
22.	024	63	2	1
23.	025	73	2	1
24.	026	58	2	1
25.	027	60	2	1
26.	028	65	2	1
27.	029	63	2	1
28.	031	63	2	1
29.	032	58	2	1
30.	033	60	2	1
31.	034	70	2	1
32.	035	60	2	1
33.	036	63	2	1
34.	038	63	2	1
35.	039	68	2	1
36.	040	65	2	1
37.	041	58	2	1
38.	042	70	2	1
39.	043	63	2	1
40.	044	68	2	1
41.	045	68	2	1
42.	046	58	2	1

43.	048	53	2	1
44.	050	68	2	1
45.	051	65	2	1
46.	052	65	2	1
47.	054	55	2	1