TITLE: A MODEL FOR OBTAINING PARENTAL INFORMED CONSENT FOR HIV CLINICAL TRIALS RESEARCH WITH PEDIATRIC PATIENTS

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ABSTRACT

All research involving human subjects should be conducted in accordance to the general ethical principles of autonomy or respect for persons, beneficence and justice. Competent adults can exercise their autonomy and can choose to take on risk for the sake of others, therefore are able to protect their own interests while in the pediatric research the 'best interests of the child' takes precedence over autonomy. In other words giving informed consent in the pediatric context, is not '*who decides'* but *'what is the best decision for the child'*. Due to lack of consensus gold standard to guide researchers and assess the quality of parental informed consent in Botswana, the practical and ethical challenges posed in obtaining parental informed consent for child enrolment in pediatric HIV clinical trials were examined. The study aimed to determine the readability of the consent forms used in pediatric HIV clinical trials; assess communication methods, practices and perceptions of the trial staff regarding the informed consent process; assess the extent to which parents recall and understand the information disclosed to them and their satisfaction with the informed consent process as well as to identify and describe the reasons for parental approval to child enrolment into HIV clinical trial studies. The study used a cross-sectional exploratory descriptive design and applied triangulation methods which included readability analysis of consent forms; in-depth interviews and two focus group discussions with trial staff who conduct the informed consent process as well as face-to-face semi-structured interviews conducted with 151 parents/guardians. Results showed that all the 10 consent forms analyzed for readability were found to be difficult to read as they were written for higher grade level than that of most participants. Majority of trial staff were females with relevant qualifications in various medical disciplines and multiple tasks. Majority of trial staff were of the opinion that possession of good background knowledge of participants' culture; research ethics regulations, clinical trials research, and pre-assessment of readability of consent forms were an asset to obtaining valid informed consent. Trial staff were of the opinion that the information disclosed to the parents was too much and complex for comprehension and valid decision making. The common method of disclosing information was found to be mainly the paternalistic type which does not promote autonomy of the parents. The parents who participated in this study were mostly females, with low education levels, social economic status and mainly from the rural areas. Bivariate analyses from the parents' results showed that the age, previous experience in research and relationship of parent to the child were significantly associated with the parents' ability to recall disclosed information. Motivation of

the parent to child enrolment was significantly associated with the numbers of clinic visits, previous experience in research, being a biological parent and being paid for participation in the study. Overall, findings seemed to suggest that the main motivation factor for child enrolment into HIV clinical trials by parents was the illness of the child and accessing health care for the child rather than altruism. This raises questions about the autonomy, voluntariness of the parents and the validity of the consent obtained. These findings were used to develop a model. The study demonstrated the need to develop a standard model consent form to guide research involving children, the importance of researchers having knowledge of participants' culture and the need for availability of context standard guidelines and laws to guide researchers conducting research involving children.

KEY WORDS

Autonomy; Comprehension; Decision-Making; Human Immunodeficiency Virus (HIV); Clinical Trial; Information Disclosure; Informed consent; Model; Parent; Parental Permission; Pediatric; Readability; Research Ethic; voluntariness; Vulnerable

DECLARATION

I, Mary Kasule declare that **"A MODEL FOR OBTAINING PARENTAL INFORMED CONSENT FOR HIV CLINICAL TRIALS RESEARCH WITH PEDIATRIC PATIENTS"** is my own work, that it has not been submitted for any degree or examination in any other university, and that all the sources I have used or quoted have been indicated and acknowledged by complete references.

Signature …… Date ……

Supervisor ……..

Signed …….. Date …….

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TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

ACHERE	Advisory Committee on Human Radiation Experiments
AIDS	Acquired Immuno-Deficiency Syndrome
ANOVA	Analysis of Variance
CFR	Code of Federal Regulations
CIOMS	Council for International Organization of Medical Science
CSO	Central Statistics Office
CT	Clinical Trial
FDA	Food and Drug Administration
FKGL	Flesch Kincaid Grade Level
FKRE	Flesch Kincaid Reading Ease
GCP	Good Clinical Practice
GDP	Gross Domestic Product
HIV	Human Immunodeficiency Virus
HRDC	Health Research and Development Committee
ICH	International Conference of Harmonization
ICH-GCP	International Conference of Harmonization-Good Clinical Practice
IRB	Institutional Review Board
MFDP	Ministry of Finance and Development Planning
OVC	Orphans and Vulnerable Children
P	Participant
R	Respondent
REC	Research Ethics Committee
SADC	Southern Africa Development Cooperation
SMOG	Simplified Measure of Gobbledygook
UNAIDS	United Nations Program on HIV/AIDS
UNICEF	United Nations Children's Fund
WHO	World Health Organization
WMA	World Medical Association

LIST OF ACRONYMS

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CHAPTER ONE

1.0 Introduction

All research involving human subjects should be conducted in accordance to the general ethical principles of autonomy or respect for persons, beneficence and justice (Faden and Beauchamp, 1986). Autonomy requires that those who are capable of deliberation about their personal choices should be treated with respect for their capacity for "self-determination" and those who are dependent or vulnerable should be afforded security against harm or abuse (Council for International Organization of Medical Science (CIOMS), 2000 p. 17).The most vital mechanism for ensuring autonomy is seeking informed consent when conducting research involving human subjects because it protects the individual's freedom of choice. The doctrine of informed consent is a product of the Declaration of Helsinki that was drafted by the World Medical Association in 1964 in an effort to ensure the protection of human research subjects. This process consists of four essential elements namely; full disclosure of information about the research, subject understanding of the information, voluntary consent and subject competence to consent (Faden and Beauchamp 1986; Levine 1986).

When children are involved in research especially non-therapeutic research that poses no prospects of direct benefit to them, issues of autonomy raise ethical and regulatory challenges because for practical and legal reasons, children are considered incapable of giving the necessary consent to expose themselves to research risks (CIOMS, 2002). This has raised debate regarding the legal and moral justification for involving children in research, as well as the requirement for extra protections and safeguards to be put in place to ensure protection through various research regulations (Weisstub, 1998). Safeguarding includes; protecting children from maltreatment, preventing impairment of a child's health or development and ensuring that children are growing up in circumstances consistent with the provision of safe and effective care (Furey, Kay, Barley *et al*., 2010). In addition, Beauchamp and Childress, (2008) argue that children must be afforded extra protection from unwarranted research risks, especially since they are a vulnerable population who lack adequate autonomy to understand and evaluate research risks for themselves. The safeguards and extra protection are obtained through seeking 'parental permission' or permission from legally authorized persons to enrol a child in research. Therefore 'permission' rather than 'consent' is used to more accurately

capture the ethical consideration involved in seeking parental approval before a child is enrolled in a clinical trial or any other type of research. Ross (2006) explains this as a legal and moral responsibility of the parent who raises the child and shoulders all social, emotional, moral and legal obligations. Parental permission also reflects respect for the parent's autonomy, authority and responsibility to determine the proper development and upbringing of the child. Furthermore, Weisstub (1998) explains that parental permission offers some external evaluation of the research's inherent risks, apart from that of the investigators and the ethics committees. Although the latter are better positioned to objectively evaluate the risks created, parents are arguably in a better position to evaluate the possible subjective risks (physical, psychological or otherwise) presented in relation to their child. Although 'permission' is a more accurate term for the parental decision-making role, common practice in the research environment is to refer to this process as 'consent'. For the sake of consistency with terminology, the researcher has continued to use the word 'consent' throughout this thesis. In addition, depending on the age, maturity and psychological development of the child, CIOMS (2002) guideline 14, recommends that as a means of respecting the developmental autonomy of the child and probably educating the child on the importance of moral consciousness, the 'assent' of the child is also required. This is to ensure understanding and positive agreement of the child to participate in the trial, to the extent that he/she is capable. This thesis however will not deal with assent because the topic requires a distinct line of investigation because different ethical challenges arise when competent children are involved in clinical trials.

Despite the legal and ethical restrictions on research involving children because of their vulnerability, clinical investigations involving children have been recently recognized as a scientific necessity to ensure the efficacy and safety of pediatric drugs, vaccines and diagnostics. Chan (2006, p.21) observed that lack of such investigations could result in a paucity of safety and effectiveness of data on children's drugs and biological products. This would ultimately result in therapies that were assumed in the absence of research to be safe and effective causing harm to children. Although the involvement of children in research is crucial, Weisstub (1998) cautions that this research must be scientifically necessary ethically sound, with an appropriate balance of risks and benefits, and parental permission must be sought. In response to these requirements, many domestic and international regulations have been developed to ensure protection of the rights and welfare of children. These requirements however make the application of the ethical principle of autonomy in pediatric research

different from that in the adult research context. Chappuy, Doz & Blance (2006 p.112) differentiate the two contexts as follows. Competent adults can exercise their autonomy and can choose to take on risk for the sake of others, therefore are able to protect their own interests while in the pediatric research context the 'best interests of the child' legal standard takes precedence over autonomy. In other words application of informed consent in the pediatric context, is not '*who decides'* but *'what is the best decision for the child'*.

Against this background, the current thesis examines the practices as well as practical and ethical challenges posed in obtaining parental informed consent for child enrolment in pediatric Human Immunodeficiency Virus (HIV) clinical trials conducted in Botswana. It focuses on the informed consent forms, the information disclosure process, parental comprehension of the information provided and the decision-making process, and voluntariness. The study also reviews the existing ethical theories of autonomy, models of informed consent, researcher-participant/patient interaction models and public health models so as to develop one that will guide the process of obtaining parental informed consent in Botswana.

1.1 Motivation

The researcher's interest in issues relating to consent came from working as the Botswana Research Ethics Committee (REC) administrator and as a member of the University of Botswana Institutional Review Board (IRB). The work partly involved reviewing consent forms written in English. These forms were overly long some ranging from 11-22 pages and used complex scientific language. These challenges are a major ethical issue especially for studies involving vulnerable groups such as children. A preliminary study conducted by the researcher (Kasule, 2009- unpublished: International Bioethics Training Practicum) to analyze the readability and understandability of consent forms used in clinical trials in Botswana showed that the consent forms were difficult to read and prepared at a level much higher than the recommended 6-8th grade according to United States standards . Although English is the Botswana official language, a large percentage of Batswana use the language mainly orally and may have difficulty understanding the information presented in a consent form written in English at a level of sophistication like a clinical trial consent form.

Due to the above concerns and the fact that currently there is no consensus gold standard used to guide researchers and assess the quality of parental informed consent in Botswana, this study used a holistic approach unlike many studies that have looked at improving particular steps of the informed consent process. This was done in three phases. The study initially analyzed the informed consent forms used by trial staff to conduct the informed consent process for ease of readability and understandability. The second phase involved identification of methods commonly used by trial staff to disclose information to the parents; how trial staff facilitate understanding, decision-making and promote voluntariness. The third phase involved an examination of parental perceptions about the informed consent process through assessing their awareness about the elements of the informed consent process disclosed, understanding of the elements, factors influencing their decision-making and voluntariness. I argue that both the trial staff and parents face challenges during the consent process and understanding how the two parties fulfil their obligation to reach a valid informed decision is important in improving parental informed process.

In this thesis the term 'parent' is used synonymously to refer to a biological parent, adoptive parent, or guardian as described in the International Conference of Harmonization (ICH) 11 (2000). Categorization of pediatric patient will also be based on the same document as shown below:

- Preterm new born infants
- Term new born infants (0 to 27 days)
- Infants and toddlers (28 days to 23 months)
- Children (2 to 11 years)
- Adolescents (12 to 16-18 years (dependent on region)

As mentioned earlier, among the above categories are competent children that participate in HIV clinical trials in Botswana. However this thesis will not deal with "assent" because the process of assent or decision making by children in the research setting is a separate process warranting ethical consideration. Therefore I have chosen to focus on parents as decision-makers.

1.2 Statement of the problem

1.2.1 Background to the Problem

The HIV pandemic has offered opportunities for the proliferation of pediatric HIV clinical trials in sub-Saharan countries including Botswana due to the worldwide need to discover new drugs and vaccines and develop new strategies for treatment and prevention. HIV has been a major public health problem for the past three decades and has gradually shifted from exclusively adult populations to include the paediatric populations as well (United Nations AIDS (UNAIDS) Agency, 2010). Worldwide, at the end of 2009, there were 2.5 million children living with HIV, 400 000 became newly infected and of the 1.8 million people who died of AIDS one in seven were children (UNAIDS, 2010). Botswana is one of the nine southern African countries that continue to bear the global burden of HIV and AIDS with an estimated 350 557 people living with HIV and of these 19125 are children aged 0-14 years (Botswana HIV/AIDS Impact Survey III, 2008). Despite increased availability of antiretroviral therapy in the developing world, children remain a neglected population because, as noted by Keeton (2007), the development of medicines for children lags years behind those of adults.

For the above reason, the World Health Organization (WHO, 2006) and other bodies such as the FDA (Food and Drug Administration, 2003) and the Clinical Trials Directive 2001/20/EC of the European Parliament and of the Council recommend and promote pediatric research into childhood diseases and other conditions that particularly affect children. The Clinical Trials Directive 2001/20/EC of the European Parliament and of the Council in particular recognise the need for investigation of medicinal products in the vulnerable population of children (i.e. minors in the meaning of the Clinical Trials Directive) and says in part:

> *"... There is a need for clinical trials involving children to improve the treatment available to them. Children represent a vulnerable population with developmental, physiological and psychological differences from adults, which make age and development-related research important for their benefit. Medicinal products, including vaccines, for children need to be tested scientifically before widespread use. This can only be achieved by ensuring that medicinal products which are likely to be of significant clinical value for children are fully studied. The clinical trials required for this purpose should be carried out under conditions affording the best possible protection for the subjects."* (p.34)

This urgency and importance of the goals of HIV preventive (in this case vaccine) and treatment, research can however overshadow the need to protect the well-being and human rights of vulnerable trial participants like children. Therefore the National Bioethics Advisory Commission (1998) stipulates that promoting and protecting the rights of trial participants is as important as advancing science because medical research is also about human development. Protecting trial participants rights may also help to promote good science and public confidence in the research and its findings.

One important mechanism that needs to be put in place when conducting research involving children is obtaining informed consent from their parents or guardians. This procedure represents the ethical position adopted towards volunteers in clinical trials as it gives meaning to the ethical principle of autonomy. The conceptual framework for the process of obtaining informed consent is focused around information sharing, understanding, voluntariness and competence. The World Medical Association Declaration of Helsinki (2004) states that in order for informed consent to occur potential participants must be informed about what the study entails, be able to distinguish between research and standard clinical treatments; understand the potential for medical or other benefits; and understand the potential for discomfort, toxicity or other risks that occur as a result of participation in research. Potential research participants must also be made aware of their rights to withdraw from participation any time. However, in the case of clinical trials involving non-consenting participants such as pediatric patients, the principle of informed consent may be compromised.

Article 2(j) of the Clinical Trials Directive (2001/20/EC, p.121) gives a comprehensive definition of the term informed consent, as well as the situations and process of obtaining it, as follows:

> "*A decision, which must be written, dated and signed, to take part in a clinical trial taken freely after being duly informed of its nature, significance, implications and risks. The decision must be made by any person capable of giving consent or, where the person is not capable of giving consent, by his or her legal representative; if the person concerned is unable to read, oral consent in the presence of at least one witness may be given in exceptional cases, as provided for in national legislation."(p. 37)*

This position is similar to that of the ICH/WHO Good Clinical Practice (2000). However, Ellis and Bochener (1999) cited in Delany (2005, p.4) observe that the process of obtaining informed consent is highly subjective and complex, as they note that:

> *"Informed consent is dependent as much on how we feel in conversation, our relationships with those giving information, how information is given, as with the substantive content of what we are actually told. Informed consent is volatile, emotional and processual. People make up their minds, change, hold on, become confused, disagree, rationalize, blame, accept responsibility, reinterpret, misinterpret, and do cost-benefit analyses and then act on what their emotions instruct them to do instead, or do not act, and simply do not know what to do".(p. 4)*

This observation indicates that giving valid consent involves intellectual competence, moral and emotional maturity, as well as cognitive capacity which enables individuals to have autonomy and rights. Since children do not have these attributes due to their developmental limitations, their participation in clinical research as consenting individuals would be considered unethical (Fombad, 2005). Therefore they depend on their parents' judgment and beliefs regarding issues of consenting to research (Lederer & Grodin, 1994).

Although a large body of bioethics literature on obtaining informed consent from adult participants in clinical research has been reported (Sugarman, McCrory, Powell, and Krasney, 1999), only a few studies have been reported on obtaining parental consent for child participation in clinical research (Rothman &Rothman, 2005). This is despite the fact that the use of children in human experiments dates back to the 1700s when clinicians used children with measles, pertussis, syphilis, gonorrhoea and other infectious diseases for human experiments (Katz, 1972). It was not until the 1900s that public controversy over such research practices led to the establishment of committees that issued recommendations and legislative proposals for ethical research conduct (Vollmann and Winau, 1996). Even after all these proposals, protections for child participants were still lacking. For example, even the Nuremberg Code (1949) and the Universal Declaration of Human Rights (1948) which was later adopted in 1966 as the International Covenant on Civil and Political Rights that were designed to protect the integrity of research subjects did not specifically target child participants in clinical research. Similarly, the initial World Medical Association of the Declaration (WMA) of Helsinki (1964) did not provide for research involving children, however its revisions dedicated a section 'Guidance Note 1' to research involving children

and set the conditions under which such research should be conducted and consented as well as confidentiality issues.

During the 1960s, criticism of unethical practices in research involving children gained new attention as a result of an article by Henry Beecher (1996) in which mentally retarded institutionalized children were deliberately fed extracts of fecal solutions from hepatitis infected patients and later injected with a more purified form of hepatitis. Faden and Beauchamp (1986), report that one of the main ethical concerns with this study was the inadequacy of the process for securing parental consent. Although this study contributed to public health, it also raised debate over the drive for tighter regulation on children participation in clinical research. Even then, there are still reports of unethical research involving children being conducted. For example, the 1996 Trovan clinical trial (Abdullah v. Pfizer, 2003) conducted by Pfizer during an epidemic of meningococcal meningitis in Nigeria where researchers were alleged not to have obtained informed consent from the parents/guardians of children that were recruited in this study. Such incidents call for improved regulatory frameworks. Currently several international and national organizations have issued ethical guidance on clinical trials with specific provision on participation of children (CIOMS, 1993 and revised in 2002; the International Council on Harmonization (ICH) Guidelines for Good Clinical Practice (2000).

Controversy still rages within pediatric research over ethical rules and regulations that guide research involving children. Some researchers (Punch, 1998; Swain, 1998; Small, 2001; Goodwin, 2003) have argued that the ethical rules and regulations of the informed consent process do not necessarily translate well to pediatric research; partly because the ethical dilemmas that arise in pediatric research are context-specific. Other researchers (Homan & Bulmer, 1982; Punch, 1998) argue that adhering to specific ethical rules in relation to research can affect the very issue that is being studied, such that it becomes impossible to conduct research involving children. Given that over 50% of medicines used in children are not licensed for use either for the disease states or for the age group (Tan, Cranswick, Rayner, and Chapman, 2003). This particular argument is plausible in pediatric research. Another challenge to obtaining parental informed consent is the commitment to uphold the child's rights (Alderson, 2004; Homan & Bulmer, 1982). Within pediatric research for instance it is doubtful if consent is indeed a process of sharing information that facilitates the individual's right to self-determination as Tait, Voepel-Lewis and Gauger (2011) claim. Yet, despite its

good intentions, the process of obtaining informed consent is rarely examined. As such, there are only limited studies with respect to parental consent practices within pediatric research and only a few of them deal with the broad aspects of the process (Pace et al., 2005; Eder 2007; Marshall 2006; Rajaraman, Jesuraj and Geiter, 2011). These few studies of obtaining parental consent for pediatric research suggest inadequacies in competence, information, understanding, or voluntariness for valid consent to occur.

1.2.2. Formulation of the problem

This study followed an inter-disciplinary approach in that it applies related concepts from other disciplines of public health, science, socio-sciences, health sciences and research ethics to examine the process of obtaining parental informed consent in Botswana. These approaches allowed assessing the readability and comprehension of the text of consent forms used by trial staff to conduct the consent process; the trial staffs' perspectives of the informed consent process; parents' perspectives on information disclosure and comprehension and voluntariness in decision making.

The background to parental informed consent described above demonstrates the nature of challenges that can be encountered in obtaining valid parental informed consent. Currently there is a paucity of literature in Botswana about the adequacy of obtaining parental informed consent and the factors that influence parents' decision making. Studies conducted thus far have mainly concentrated on adult informed consent (Shaibu, 2007; 2006). Drawing from my experiences as a reviewer of the informed consent forms submitted for approval to the Research Ethics Committee, the overly lengthy consent forms contribute to readability difficulties, voluminous and complex information that inhibits comprehension leading to invalid decisions and consent. Furthermore, the high HIV prevalence rates of 17.6% in the general population (NACA, 2008), and the government commitment to combating HIV/AIDS and other opportunistic infections have led to an increase in volume and complexity of children HIV clinical trials being conducted in Botswana. However, the country ethics review capacity and regulatory oversight lags behind these developments.

Secondly, the challenge facing pediatric research in Botswana is that most of the researchers who conduct pediatric HIV clinical trials are from outside Botswana. This is bound to raise

challenges of comprehension due to language and cultural differences. It must also be noted that most of the clinical trials conducted in Botswana are multisite studies where the consent forms are developed by institutions outside Botswana. This is likely to raise problems of lack of sensitivity on the part of the researchers to the values and culture of Botswana and failure to contextualize the information provided to participants. Furthermore, differences in socio-economic status, authority/power, and health care systems between the trial staff and parents may also have an influence on the voluntariness with which decisions are made by the parents. Low levels of literacy (Maruatona & Cervero, 2004), and high rates of income inequalities may also contribute to the challenges posed to obtaining valid parental informed consent (Joint United Nations Programme on HIV/AIDS, 2004). Additionally, it is doubtful that parents with chronically sick children asked to enrol their children in clinical trials would be expected to decline such participation.

Thirdly, at the moment Botswana lacks an established research ethics regulatory framework governing the conduct of pediatric research in terms of research guidelines, standard operating procedures and a legislation Act. Only a draft of the Botswana Clinical Trials Guidelines (v. 2008) is available. However the document does not comprehensively cover issues of child participation in research. Also available is a consent form guide document (Botswana Ministry of Health, Research Unit 2005), which caters for all types of research and has no special provision for child participants. This means that, there is no standardized way for researchers to prepare consent forms for child participation in clinical trials. As noted earlier, Botswana has signed and ratified to the United Nations Convention for Children's Rights that compel countries to respect and protect children's rights, but these have not been translated into policies regarding participation of children in research (Fombad, 2005). Additionally the laws, policies and practices guiding children's health rights regarding HIV treatment and care reveal inconsistencies and anomalies requiring harmonization (Kuwabara, 2008).

The fourth concern is the lack of a clear legislation regarding age of consent to participation in research or dealing with the capacity of children to make medical decisions. Currently the age of consent in Botswana is 21 years (section 49 of the Interpretation Act, 1984)applies for consent to participation in research but the Roman-Dutch law principles dealing with children's legal capacity to perform legal acts also applies (Fombad, 2005). This situation raises ethical challenges considering that children 14 years and above have the capacity to

make choices. The definition of a child also varies according to different settings. For example according to Botswana Children's Act (1981), Chapter 28:04, Part 1, Preliminary (ss-1-2), a "child" is defined as any person under the age of 14 years. Under this Act, children under the age of 14 years require a fully informed consent of the parent to whom most of the information is commonly discussed with. In the context of pediatric research, the above laws create an ethical dilemma for the trial staff in enrolling children in clinical trials, as it is not clear at which age limit parental consent is required for child participation in research. In addition, parents that are under 21 cannot consent for their children's participation in research regardless of their capacity and competence to do so. Such parents are denied the opportunity of their children to benefit from research participation where the research has prospects of benefit. Furthermore, considering the burden of nursing a chronically ill child, poverty, cultural and literacy levels might influence decision making of parents to child enrolment into research.

The other complexity about seeking parental informed consent revolves around the conflict between Botswana culture and the international instruments like the Convention on the Rights of the Child (United Nations General Assembly, 1989) and the African Charter on the Rights and Welfare of the Child (1990) which Botswana has ratified to, but have not been fully incorporated into law. These two instruments emphasize that "the best interest of the child must be the primary consideration and children are rights holders". However, Botswana culture as cited in Fombad (2005) like many other African cultures, believes that adults know what is best for the children and they are in a position to articulate the view of the children. Therefore the fact that parents might be torn between the requirements of the laws and their culture might affect the validity of the consent given.

In conclusion, the challenges recounted above imply that obtaining valid parental informed consent in Botswana is problematic and a model would go a long way in alleviating the problem.

1.3 Rationale

There is a paucity of literature in Botswana about the adequacy of the parental consenting process and the factors that influence decision-making limit a deeper understanding of the process which would help facilitate designing a parental consent model that can guide the

process in Botswana. The ethical conduct of research requires a comprehensive ethical and regulatory oversight framework, which currently is inadequate or non-existent in Botswana. It is also worth noting that most of the clinical trials conducted in Botswana are multisite studies, institutions outside Botswana develop the consent documents and most of the mainly investigators who conduct the clinical trials are from outside of Botswana. This is likely to raise a problem of lack of sensitivity of the investigators to the values and culture of the Botswana communities and fails to contextualize some of the information provided to participants. Currently no studies documenting the challenges of obtaining informed consent for child participation in HIV clinical research have been documented in Botswana although such studies are very important in ensuring that children's rights and welfare as well as those of the parents or guardians who enrol their children in clinical trials are protected. The specific objectives of the study are presented in the following section.

1.3.1 Aim of the study

The general aim of this thesis was to conduct a situational analysis of the current practices of obtaining parental consent for pediatric HIV clinical trials conducted in Botswana in order to evaluate the quality of the process and use the findings to develop a conceptual model that can be used as a framework to guide the parental consent process.

1.3.2 Objectives of the study

The study set out to:

- To determine the readability and comprehension of the consent forms used to obtain consent from parents who enrol their children in HIV clinical trials in Botswana.
- To identify the communication methods, practices and perceptions of the trial staff regarding informed consent information disclosure.
- To assess the extent to which parents are able to recall and understand the information disclosed to them and their satisfaction with the informed consent process
- To identify and describe the reasons for parental approval to child enrolment into trial studies.
- To develop a model to enhance and strengthen the process of informed consent for child participation in HIV clinical trials relevant to Botswana.

1.3.3 Research questions

It is evident from the above discussion that obtaining parental informed consent for child participants in HIV clinical trials poses challenges. The research aimed to examine the above mentioned challenges by answering the following research questions:

- How readable and understandable are the consent forms used to obtain parental informed consent?
- How effective are the trial staff–parent communication methods and practices from the trial staff and parents perspective?
- To what extent do parents recall and understand the information provided during the communication processes?
- What are the parental perceptions of, and levels of satisfaction with, the informed consent process?
- What motivates parents to enrol their children in HIV clinical trials?
- To what extent is the parental decision to enrol their children in HIV clinical trials voluntary?
- How can the process of informed consent for child participation in HIV clinical trials conducted in Botswana be enhanced?

1.4 Research framework

This thesis followed a cross-sectional exploratory design (Creswell, 2003) to conduct a holistic analysis of the current practices of obtaining parental consent for pediatric HIV clinical trials conducted in Botswana. Mixed methods both qualitative and quantitative were followed, based on the data collected from consent forms readability analysis, in-depth interview transcripts, focus group transcripts and face-to-face parent interviews using completed semi-structured questionnaires respectively.

1.4.1 Assumptions

The following assumptions guided this study:

- That the language used in the consent form is complex and difficult for parents to read and understand so as to make an informed decision which is in the best interest of the child.

- That differences between the researcher and parent due to socioeconomic diversities make it difficult for researchers to obtain adequate parental informed consent
- That parental understanding of the difference between clinical practice and research is doubtful.
- That a parental decision to enrol children in HIV clinical trials is not voluntary.
- That social coercion and monetary inducement due to high levels of poverty, language difficulties, and lack of true understanding of the entire study purposes influence parents to enrol their children in HIV clinical trials
- That the counselling process prior to and during the HIV clinical trials is not done in a friendly and enabling environment, therefore not effective for obtaining valid parental informed consent
- That parental informed consent is based on Western standards and models

1.5 Methodology

The thesis utilized a cross-sectional exploratory descriptive design and applied mixed quantitative and qualitative methods for data collection and analysis. Further, the thesis drew from the consequentialist and non-consequentialist theories of informed consent, and the significant models that guide autonomous decision-making and researcher/patient-participant interaction.

This thesis was conducted in two phases. Phase One involved a situational analysis of the current parental consenting process to generate concepts that were used for model development. The Creswell (2003) dominant-less-dominant model that uses a single dominant paradigm with an alternative less dominant component drawn from different

paradigms was adopted. The qualitative component, which used a purposively selected smaller sample of trial staff and consent forms, formed the less-dominant component. Qualitative data collection techniques involved the use of in-depth interviews with 11 trial staff and two focus group discussions with a total of 18 trial staff who conduct the consent process. Data collection and analysis for the qualitative component of the thesis were conducted simultaneously in order to generate data for concept formation and development. The dominant component was the quantitative survey involving a larger sample of parents. Face-to-face interviews with from 151 parents were conducted using a semi-structured questionnaire. Descriptive methods were used in reporting the quantitative data. Chi-Square-tests and ANOVA were determined. Furthermore, linear regressions assessed the relationship between demographic factors, levels of understanding.

1.6 Operational terms

1.6.1 Readability

In this thesis, the term 'readability' is used to refer to the reading ease and the grade level an individual should have obtained to be able to understand the text easily on first reading of the consent form that was used to recruit parents who enrol their children in HIV clinical trials. This understanding id borrowed from Johnson, (1998).

1.6.2 Informed consent

In this thesis, the term 'informed consent' is used to refer to the process by which a parent voluntarily confirms his or her willingness to child enrolment in the HIV clinical trial, after having been informed of all relevant aspects of the trial.

1.6.3 Clinical trials

In this thesis the term 'Clinical trials' refers to clinical trials conducted to test drug safety and efficacy in children.

1.6.4 Autonomy/Respect for persons

In this thesis these two terms are used interchangeably to refer to the parent's self-determination and freedom to decision-making regarding child enrolment in HIV clinical trials.

1.6.5 Model

In this thesis the term 'model' refers to 'a diagram' of proposed relationships among a set of concepts, factors, or variables about a particular hypothesis, question, context, problem or topics'. This is in line with Earp & Ennett (1991, pg 163) definition.

1.6.6 Child

In this thesis 'child' refers to anyone under the age of 21 years as stipulated by the Botswana Laws' Matrimonial Causes Act (1973)

1.6.7 Parent

In this thesis, the term 'parent' refers to any legal caregiver of the child. This may include the biological parent(s), grandparent(s), and/or any other member of the extended family, or institutions such as orphanages.

1.6.8 Trial staff

Using insights from the ICH (2000) guidelines, this thesis uses the term 'trial staff' to refer to the investigator, or the person designated by the investigator to inform the parent of all the pertinent aspects of the clinical trial. This includes people who research institutions may designate as research nurse, study nurse, study coordinator, or recruiter.

1.6.9 Pediatric population

For the purposes of this thesis, 'pediatric populations' will include newborns (birth to 1 month of age); infants (1month to 2 years of age); children (2 to 12 years of age) and

adolescents (12 to 21 years of age) as sourced at: http://www.fda.gov / (US Department of Health and Human Services, Food and Drug Administration)

1.7 Organization of the thesis

The thesis comprises of five chapters as follows:
Chapter one presents the introduction, background to the problem, statement of the problem, the theoretical framework, and the rationale of the study. It also states the aims, objectives, assumptions, and the research questions. Chapter Two presents the literature reviewed. Chapter Three presents the methodology. The chapter covers the research design, sampling techniques, description of the sample, and data collection and analysis. Chapter Four presents the findings and discussion. Chapter Five deals with the conclusions and Chapter Six presents the model.

1.8 Conclusion

This chapter provided a broad account of informed consent in the research context and its regulatory framework. The chapter also described the motivation of the study, and discussed informed consent in the context of public health and individual bioethics. The chapter also discussed the conceptualization of the study and showed how the topic was refined by literature. The chapter also outlined the research framework, and the overall design.

The next chapter examines the literature that guided this thesis.

CHAPTER TWO

LITERATURE REVIEW

2.0. Introduction

This chapter reviews the literature on informed consent for pediatric research starting with examining the relationship between public health ethics, individual ethics and pediatric research. It also explores literature on the assessment of readability and comprehension of the consent forms; the perceptions and challenges regarding information disclosure; parental understanding of the information disclosed; decision-making process and voluntariness to child enrolment into pediatric HIV clinical trials. A review of the ethical theories, models of informed consent and models of physician-parent interaction aimed at improving parental informed consent process is also conducted.

2.1 Public health ethics and pediatric research

HIV clinical trials can be regarded both as public health and individual interventions. This means investigators have to apply both public health ethics and individual-based bioethics in decision making about involving children in research. Public health ethics is population-based, as a specialty area distinct from bioethics with an individual-based focus. According to the Institute of Medicine (IOM, 1998), public health is the societal approach to protecting and promoting health rather than individual oriented actions to achieve this goal. Research like HIV clinical trials combines both public health ethics and bioethics because it ensures minimization of threats of disease in the community as well as among individuals. Winslow's (1920, p.148) cited in Noland, Troxler and Torrens Salami (2004, p. 24), classical definition of 'public health' is instructive in HIV pediatric research. He defined public health as:

> *"the science and the art of **preventing disease, prolonging life,** and **promoting physical health and efficiency** through organized community efforts for the sanitation of the environment, **the control of community infections,** the education of the individual in principles of personal hygiene, and the organization of medical and nursing service for **early diagnosis and treatment of disease**" [boldface own emphasis] (Noland, Troxler and Torrens Salami (2004), p. 24)*

Acknowledging that Winslow was certainly not thinking about pediatric HIV clinical trials in the 1920's, today these clinical trials are an essential part of public health interventions aimed at preventing this disease, prolonging life, promoting physical health, including early diagnosis and treatment of the disease. In this regard both public health ethics and bioethics respect and value individual dignity and worth as stated in the United Nations' 1948 Universal Declaration of Human Rights. However the relationship between public health ethics and research especially with vulnerable populations like children is a complex one. While individual research ethics refers to the moral deliberation, choice and accountability on the part of the individual throughout the research process (Edwards & Mauthner, 2002, p. 14), from a public health research ethics perspective, a wide range of ethical issues arise due the tension between societal rights versus individual liberties regarding autonomy. In this case, the question that arises is, "What is the right thing to do?" in making decisions that will affect both the public's and the individual's health.

There is currently a growing interest and recognition of the difference between public health ethics and bioethics regarding participants' right to voluntary and informed consent. Since individual ethics and public health ethics differ in terms of who is protected; the individual versus the community, Lappe (1986) noted that individual rights could be compromised for the sake of community interests. So there is need for a balance such that benefit outweighs the risk and the absolute level of infringement on individual rights is minimized. Involving children in HIV clinical trials might create such tension; extra safeguards must be put in place to protect their safety and wellbeing taking into account the model of 'best interests of the child' as stipulated by the Belmont Report (1978).

Regarding the justification and explaining the dilemmas that surround the decisions by investigators to involve children in research, several ethical theories have been suggested. For example Deyhle, Hess, & Lecompte (1992), cited in Miles &Huberman (1994, p 289) suggested two key ethical theories. The first one is the Mills' teleological or consequentialist theory which judges actions according to primary ends or their specific consequences, benefits and costs for various audiences. The second one is Kant's (1993, p.70) deontological or non-consequentialist theory based on duties and rights and respects individuals as ends in themselves. Kant's categorical and practical rules raise questions like: (a) would I like this action to be applied to everyone including me? (b) will I treat every person I encounter as an end and not as a means to something I want? Furthermore, several models of informed

consent linked to the above theories have been proposed to describe the doctor-patient relationship in sharing of information and facilitating understanding about the disease and treatment that can be applicable to the research setting. For example, the 'Event Model' (Wear, 1998); the 'Transparency Standard Model' (Brody, 1987); the 'Shared Decision Making Model' (Charles, 1998); the 'Process Model' (Lidz, Appelbaum & Meisel, 1988); and the 'Conversational Model' (Katz,) described in detail in section 2.4.1 below. The next section looks at the legal requirements for obtaining parental consent.

2.2 History of research involving children and existing regulations

Scientific experimentation with human subjects has historically been tainted with scandals of abuse which are only being investigated in the 21st century, the latest being the Obama Presidential Commission for the Study of Bioethical Issues (2011). Some of the worst abuses and exploitation of children who participated in medical experiments without the knowledge or consent of their caretakers have been documented and are reported (Advisory Committee on Human Radiation Experiments (ACHERE), 1995), cited in Vollman & Winau, (1996). This kind of research reflects a gruesome history of studies involving children and would be categorized as 'greater than minimal risk' with no prospects of direct benefit to the individual except to future populations (International Conference on Harmonization (ICH)-Good Clinical Practice (GCP) guidelines 2000). Most of these experiments either resulted in death, severe birth deformities or disabilities like brain damage. Ultimately, since 1945 many codes and regulations have been put in place to ensure adequate protection of child subjects, particularly in developing countries that often do not have adequate regulatory institutions or standards governing clinical research.

Table 2.1 History of unethical research involving children

1896	Dr. Arthur Wentworth performs spinal taps on 29 children at Children's Hospital in Boston to determine if procedure is harmful.
1931	75 children die in Lubeck, Germany from pediatrician's experiment with tuberculosis vaccine.
1946-1974	The Atomic Energy Commission authorized experiments in which mentally retarded children were fed radioactive oatmeal without the consent of their parents or being informed that their children were subjects of an experiment, and without any expectation of a positive benefit.
1949-1953	Atomic Energy Commission studies of mentally disabled school children fed radioactive isotopes at Fernald and Wrentham schools
1953	New born Daniel Burton rendered blind at Brooklyn Doctor's Hospital during study on RLF and the use of oxygen
1958-1960	Injection of hepatitis into mentally disabled children at Willowbrook School on Staten Island in an attempt to find vaccine.
1962	Thalidomide withdrawn from the market after thousands of birth deformities blamed in part on misleading results of animal studies.
1990	More than 1500 six-month old black and Hispanic babies in Los Angeles are given an "experimental" measles vaccine that had never been licensed for use in the United States. The Center for Disease Control later admits that parents were never informed that the vaccine being injected to their children was experimental.
1996	About 200 children in Nigeria treated with an experimental drug Trovan were negatively affected; 11 died and many others were left severely disabled with blindness, deafness, brain damage, and paralysis.
1998	-Three children die at St. Jude Children's Hospital in Memphis during participation in clinical trial for acute lymphoblastic leukemia. -One year-old Gage Stevens dies at Children's Hospital in Pittsburgh during participation in Propulsid clinical trial for infant acid reflux. -18-year-old Jesse Gelsinger dies after being injected with 37 trillion particles of adenovirus in gene therapy experiment at University of Pennsylvania. His death triggers a still on-going re-evaluation of the conflicts of interest plaguing human subject research.
2001	Biotech company in Pennsylvania asks the FDA for permission to conduct placebo trials on infants in Latin America born with serious lung disease though such tests would be illegal in U.S.
2004	The state Health Department launched a probe into potentially dangerous drug research conducted on HIV-infected infants and children at a Manhattan foster-care agency.

Source: Vollman & Winau (1996).

Examples of codes and regulations include; the Declaration of Helsinki (1964); World Health Organization (WHO) guidelines for Good Clinical Practice (1995); the 2002 CIOMS); the ICH-GCP guidelines (1996); U.S. Department of Health and Human Services, Common Rule, Code of Federal Regulations Title 45 CFR 46, Subpart D, 1979).

The Common Rule is also applicable to research conducted in

Botswana as stated in section 101. All these guidelines emphasize the necessity of parental permission; children giving assent where appropriate after assessment of their capacity and maturity and advocating for extra protections to be put in place whenever children are involved as subjects in research.

More recent regulations include the Joint United Nations Program on HIV/AIDS (2000), and the UNAIDS Guidance Document on Ethical Considerations in HIV Preventive Vaccine Research (available at: http://data.unaids.org/publications) accessed on 20 September, 2012) offer guidance for HIV studies involving children. The documents have specific guidance that identify children as a vulnerable population and support the ethical principle of autonomy in research. For purposes of this thesis, the specific relevant guidelines are cited in full below:

- *Guidance Point 7: vulnerable populations where relevant the research protocol should describe the social contexts of a proposed research population that create conditions for possible exploitation or increased vulnerability among potential research participants, as well as the steps that will be taken to overcome these and protect the dignity, safety and welfare of the participants. This point applies to children as they are categorized as a vulnerable population (p. 22)*

- *Guidance Point 12: independent and informed consent based on complete, accurate, appropriately conveyed and understood information should be obtained from each individual while being screened for eligibility for participation in an HIV preventive vaccine trial, and before s/he is actually enrolled in the trial (p.32.*

- *Guidance Point 13: special measures should be taken to protect persons who are, or may be, limited in their ability to provide informed consent (p. 36).*

- *Guidance Point 15: a plan for monitoring the initial and continued adequacy of the informed consent process and risk-reduction interventions should be agreed upon before the trial commences (p.39).*

- *Guidance Point 18: children should be included in the clinical trials to verify safety, immunogenicity, and efficacy from their standpoint as future recipients of HIV preventive vaccine (p.46).*

Despite all the above safeguards, evidence from recent abuses like the 1996 Trovan clinical trial mentioned in Chapter One shows that ethical and practical challenges still arise whenever children are involved in clinical trials or research in general. Therefore, substantive and procedural protections must be put in place before children are enrolled in clinical trials, in order to uphold the ethical principle of autonomy.

2.3 Informed Consent in Clinical trials involving children

The need for studies involving children despite the vulnerability of these subjects was defended in chapter one. I examine herein detail the justification and further clarify the basis of parental informed consent. Sugarman et al. (1999) explained that informed consent is based on the ethical principle of autonomy and the core requirements for obtaining valid informed consent include; possession of decision-making capacity (competency to participate in the informed consent process); the individual must be fully and accurately informed; and the consent must be given voluntarily. As mentioned earlier, children do not have these competences so their consent to research is provided by the parent or legal guardian as a safeguard and protection from research risks (Kopelman and Murphy, 2004).

Several foundational ethical theories of autonomy that guide the informed consent process mentioned earlier are discussed in detail below. The first one is the Kant's *deontological or non-consequentialist theory* of autonomy was developed by Kant (1993, p. 52). This theory places value on the intentions of the individual rather than the outcomes (consequences) of any action. The theory also focuses on rules, obligations and duties of the individual, and acting from duty is viewed as ethical (Waller, 2005). One of the key criticisms of applying a strictly deontological approach to healthcare is that it can lead to conflicts of interest between equally entitled individuals. For example the non-consequentialist theory would regard seeking parental informed consent as a rule, duty or obligation irrespective of the overall expected consequences of doing so. For example, a researcher conducting HIV pediatric clinical trial that exposes children to risks and has no direct benefit to the child would be a contradicting his/her obligation and the duty of non-maleficence. Furthermore, evidence of non-consequentialist views in public health is exhibited in legislations such as Public Health Acts that regulate individuals that can endanger public health and safety. For example regulations like no smoking in public places contradict the individual respect for person and

goes against individual liberties. Kopelman (2005) noted that although the mission of public health is to achieve the greatest health benefit for the greatest number of people, individual rights need to be protected and exposure to undue risk must be avoided. Therefore individuals and institutions that are involved in the conducting of HIV clinical trials have an obligation to ensure that child participants' rights are protected and their wellbeing is safeguarded and one way of doing this is through seeking parental consent.

The second ethical theory of autonomy known as the Mills (cited in Delany, 2005) teleological or consequentialist theory of autonomy holds the view that the correct moral response is related to the outcome, or consequence, of the act therefore contradicting the non-consequentialist theory. Its central aim is the premise of 'maximizing the greatest good for the greatest number'. The 'good' referred to can be expressed in a variety of ways and may refer to values or 'utility' such as happiness, being pain-free or symptom-free or any other life enhancing outcome. As an ethical theory, consequentialism is attractive as there is always an outcome and the correct moral response is the one that will produce the greatest good for the greatest number. However, it does have limitations as it can endorse acts that could be contrary to the rights of individuals even if the end result is one which would improve care for many others. For example in this thesis, the theory would imply that, if a few children were enrolled in an HIV clinical trial testing a new drug regardless of their parents' consent and the children are exposed to some risk, this would be acceptable as long as the general pediatric population benefits from the outcome. According to Mill's consequentialist theory, the end justifies the means. Therefore the decision with the best overall expected consequences or which benefits the majority is the one we ought to take. The theory therefore upholds the public health model in its prioritizing the population over the individual. By inference Alderson (2004) observes that public health professionals would be in support of this theory since they are said to act for the "common good" (Weed & McKeown, 1998). Beauchamp and Childress (1994) however argued that from a population point of view, this might imply that any given intervention must result in more good than harm; and that the public health model assumes that the appropriate mode of evaluating options is balancing risks and benefits. This is because the mission of public health is to achieve the greatest health benefit for the greatest number of people. If we oversimplify the public health approach which is interested in securing the greatest benefits for the most people, consequentialism appears to permit, or even require that the most fundamental interests of individuals be sacrificed in order to produce the best overall outcome. It could also mean that

the origin of good or pleasure is irrelevant as long as the outcome benefits most people. However it is important to note that most public health interventions are intended to benefit the entire population without knowingly harming individuals or groups (Public Health Encyclopedia :http://www.endnotes.com/public-health-encyclopedia). Thus when researchers involve children as participants in clinical trials, their belief is that since all children will benefit when an effective intervention is discovered it is right to put a few children at risk for the benefit of many. This contradicts the non-consequentialists who believe that this should not be done at the expense of sacrificing the children's fundamental rights or interests to produce the best overall outcome. Therefore justification of informed consent according to the consequentialist theory would raise dilemmas for both the researcher and parent, as it would contradict the ethical principle of autonomy of the participants' right to self-determination.

2.3.1 The consent form

An important element of informed consent is full information disclosure and according to CIOMS (2002), this information needs to be documented and communicated in a language understood by the potential participant. However data from studies on informed consent readability shows that consent forms and consent information templates are usually written at about the 11th grade level or higher than the recommended 6th - 8th grade. This therefore defeats the achievement of the goal of comprehension (Briguglio, Cardella, Fox, Hopper, TenHave, 1995; Johnson, 1998; Friedman and Hoffman-Goetz, 2006; Knapp, Raynor, Silcock, Parkinson, 2009; Kithinji and Kass, 2010). Equal interest has been shown in determining the nature and adequacy of various consent procedures in research and clinical contexts (Sugarman, McCrovy, and Hubal, 1999; Flory and Emanuel, 2004; Ryan, Prictor, McLaughlin and Hill, 2008). For example, research has focused on the value to the consent process of various educational approaches and materials (brochures, videotapes, and information sheets) and has found that the use of such materials enhances comprehension (Cooley, Moriarty, Berger, Selm-Orr, Coyle and Short, 1995; Doak, Doak, Doak and Root, 1996; Fureman, Meyers, McLella, Metzger and Woody, 1997; Agre, Stieglitz and Milstein, 2006). Some authors however argue that in clinical research, both patients and providers place little weight on the value of informed consent (Lidz, Meisel, Osterweis, Holden, Marx and Munetz, 1983). Sugarman, Popkin, Fortney and Rivera (2001) recommended that informed consent should never be focused merely on the written form, which constitutes only

a fragment of the process, but should be considered as a document and a record that shows that ethically relevant information has been discussed and understood to lead to a valid and voluntary decision. More importantly, informed consent should be considered as an evolving process as opposed to a statistic one-time event.

Some studies have exposed the misunderstanding that the informed consent process was synonymous to the consent form; and that the consent form is either seen by consenters as a legal document or as a contract that is signed once information has been exchanged.Getz and Borfitz (2002) highlight the need to distinguish the informed consent process from the consent form and for investigators to take an active role in ensuring that consent is voluntary and informed. For example, the authors noted that one out of seven adult participants reported that they did not even read the consent form before giving their consent. Additionally, as noted by Federman, Hanna and Rodrigues (2002), sometimes it is sponsors and research institutional risk managers who deliberately fail to treat the informed consent process as an on-going, interactive dialogue between research staff and research participants. It is important that the process involves the disclosure and exchange of relevant information, discussion of that information, and assessment of the individual's understanding of the discussion throughout the duration of the study.

With child participants, one of the major ethical challenges of conducting research is the complexity of the informed consent process because proxy consent has to be obtained from a consenting parent or guardian (Federman, Hanna and Rodrigues, 2002). Certain perspectives from developing countries on this complexity have attributed it to the fact that the international ethical codes and regulations governing the informed consent process are based on western legal perspectives that have to be interpreted in accordance with local laws and procedures applicable in the host countries (Bwakure-Dangarembizi, Musesengwa, Mhute and Vhembo, 2012). Some authors have observed that although there is a large body of literature describing issues that govern practices related to informed consent and the insufficiency of obtaining competent adult informed consent (Benatar, 2000; Molyneux, Wassenaar, Peshu & Marsh, 2005).; Geissler and Pool, 2005), there is a paucity of literature regarding informed consent in studies involving children (Pace, Talisuna, Wendler, Maiso, Wabwire-Mangen, Bakyaita, Okiria, Garrett-Mayer, Emanuel, and Grady, 2005). Another observation by Erb and Sugarman (2000) is that the consent process has been investigated as

a fragmented process, unit by unit and not in its entirety. This thesis will attempt to attend to these gaps.

2.3.2 The Legal and ethical challenges of conducting pediatric trials

The legal definition of a child is one the challenges in obtaining parental consent in different settings. Therefore the next task in the review of literature was to ascertain the definition of a child in Botswana. Botswana law is not very clear about the legal definition of a child because various Acts and statutes define a child differently. For instance, according to the legislation of Botswana, the Botswana Children's Act (1981) a child is any person under the age fourteen; the Botswana Adoption Act (Chapter 28-01, 1952), defines a child as someone below the age of nineteen; the Botswana Matrimonial Causes Act (1973) defines a child as someone below the age of twenty one; the Botswana Affiliation of Proceedings Act (1999) defines a child as someone below the age of sixteen; while the Botswana Laws Interpretation Act 20 (1984) makes the age of majority 21 years. In reality however, children in Botswana, younger than 21 as the law of majority puts it have children as elsewhere and some have had to take on responsibility of their siblings due to the loss of their parents to AIDS. In this case such children would be considered mature minors who can give parental consent (Maundeni, 2005).There is no evidence in the literature reviewed on Botswana's specifying the legal age of consent to participate in research. It is therefore safe to regard the age of majority which is 21 years as legal age to participation in research. Therefore in Botswana children under the age of 21 need parental permission and/or assent where appropriate to participate in research although some have the competence and capacity to consent.

It is also important to understand the legal ethical definition of a parent in the Botswana text because a parent is the decision maker in the informed consent process. We scanned the literature to establish who is regarded as a parent in the Botswana context so as to know who qualifies to give parental informed consent. For this purpose, the review included a brief examination of authoritative writings on the matter by Fombad (2005) and revealed a complicated understanding of 'parent'. According to this author, Botswana has a dual legal system combining Roman Dutch Law and Customary Law and therefore, children guardianship rights depend on the law applied. Previously under Customary Law, women in Botswana had no rights regarding child custody, but since the abolition of the Marital Power of 2005 which regarded women as minors, both partners are now accorded equal power in a

family even though this has to be in a marriage registered under community of property. Therefore for married women, their guardianship rights to children depend on the legal system under which she was married. A woman married under the Customary Law or with the stipulation of community of property is viewed as a legal minor and requires her husband's consent in making decisions about the child. Secondly, under Customary Law unmarried fathers do not automatically have parental responsibility for their children but the same law treats men as the head of the family and they have guardianship rights over women and children. Under the same law, the child's maternal grandfather has the duty of supporting his unmarried daughter's child. In the opinion of Ditswanelo (1997) this situation reflects the view that a woman remains her father's "property" until marriage, at which time she becomes her husband's property. Although under Roman Dutch law, women have legal custody over their children (Cailleba and Kumar, 2010), under Customary Law, unmarried women fall under the guardianship of their fathers and if such women have children, the responsible parent who can give parental consent would be this grandfather. Consequently, in Botswana being a biological parent does not accord that individual legal representation of the child because in many cases the legal representative of a child could be the grandparents or other members of the immediate or extended family.

Other twists to the understanding of 'parent' are incidences of children being their own caretakers themselves. Such incidences are very common in Botswana as evidenced from the number of orphans which escalated drastically due to the high prevalence of HIV (Government of Botswana, 2008). In other cases children were placed under the custody of relatives (Maundeni, 2009). By 2007, Botswana had an estimated 137,805 orphans and vulnerable children (OVC), representing 17.2% of the number of children below the age of 18 years (Government of Botswana, 2008). Over 68% of such orphans are taken in by female-headed households, 34% live with grandparents, and 11% are cared for by other relatives (UNICEF, 2005). Despite these legal categories, in this thesis the term "parent" will refer to any legal caregiver of the child. We note that in view of the many factors influencing parental decision making discussed above, these differences in understanding of 'parent' have a bearing on the validity of the consent granted. In view of the above discussions it seems culture and the law can have a bearing on the process of obtaining parental informed consent in the Botswana context. Therefore the next section examines how these two attributes are linked to parental informed consent.

2.3.3 Botswana Culture and the law

Alderson (2004) makes the claim that it is well established in law that parents make decisions regarding child's rearing including decisions related to the child's welfare and health care. If we accept this claim, then the parents or legal guardians have the responsibility to consent to the children's medical research. However, in many communities, culture rather than the law carries greater force. For example, in Botswana, cultural practices regarding gender can affect obtaining valid informed consent since women are generally regarded as legal minors dependent on men (Brown, 1983). Unfortunately, women in Botswana are mainly the caregivers for the sick, the elderly and those orphaned (Maundeni, 2009). Furthermore, although Botswana has child-specific legislation, namely the Botswana Children's Act (1981), Chapter 28:04, Part 1, Preliminary (ss-1-2), and the Act mainly deals with children in need of care and juvenile offenders and at the core of the Act is the 'Best Interest of the Child' principle. This principle requires that when dealing with children all parties concerned should be guided by what is in the best interest of the child. However, in pediatric research the protection of the subject becomes particularly critical because the parent who is a third party is making the decision about participation and this decision is supposed to be in the subject's best interest. Sometimes the decision might be for the parent's personal interest instead of the best interest of the child.

Another safeguard for children's rights is the United Nations' Universal Declaration of Human Rights. Article 1(http://www.un.org/events/humanrights/) of this declaration states that: "We are all born free and equal in dignity and rights. Therefore when children are involved in clinical trials or research in general assent must be obtained regardless of the anticipated benefits from the research in order to protect the dignity, privacy and confidentiality of child participants. However as mentioned in Chapter One this study focuses only on parental consent.

Regarding autonomy and the age of consent, we reviewed literature concerning the age at which children become competent to make decisions by themselves. Traditionally in law, competence has always been regarded as a function of age but the ages at which children can do certain things have been defined by the country's relevant laws, a notion which is being increasingly questioned in relation to matters concerning health care (De Lourdes, Larcher, and Kurz, 2003). According to Alderson (2004) younger children may be able to consent to

research only if they have enough maturity and ability to understand the benefits and risks of what is being proposed and its alternatives. This has introduced the concept of 'mature minor' or 'emancipated minors' to refer to groups of children whose age ranges from 14-18 years being regarded as mature enough to give their own consent without the permission of the parent, particularly, where it is assumed that the decision is beneficial for the adolescent and he/she does not want the parents to be involved. Unfortunately many developing countries including Botswana have no laws defining the age at which a child can consent to research.

2.3.4 Pediatric clinical trials

A clinical trial is defined as a study in which participants are assigned to receive one or more interventions (or no intervention) so that researchers can evaluate the effects of the interventions on biomedical or health-related outcomes (National Institute of Health (NIH) at: http://www.clinicalTrials.gov). The interventions are determined by the study protocol and participants may receive diagnostic, therapeutic, or other types of interventions. In order to protect the best interest of children that are enrolled in HIV clinical trials, child specific-guidelines have been laid down in many international research regulations. For example the conduct of clinical trials is mainly guided by the ICH-GCP guidelines (2000); specifically section 2.6.3 which stipulates the requirements of involving children in clinical trials.

DeMets, Friedman and Furberg (2010), categorize clinical trials as Phases I - IV according to sample size as explained below:

Phase I clinical trials test a new biomedical intervention in a small group of human subjects (20-80 subjects) for the first time to evaluate safety (dosage and side effects).

Phase II studies the biomedical or behavioral intervention in a larger group (hundreds) to determine the efficacy and to further evaluate its safety.

Phase III studies investigate the efficacy of biomedical or behavioral intervention in large groups of human subjects (several hundred to several thousands) by comparing the intervention to other standard or experimental interventions as

well as to monitor adverse effects, and to collect information that will allow the intervention to be used safely.

Phase IV studies are conducted after the intervention has been marketed. These studies are designed to monitor effectiveness of the approved intervention in the general population and to collect information about any adverse effects with wide spread use.

Research ethics requires that such clinical trials be conducted in accordance with the three basic ethical principles of biomedical research in humans, namely: autonomy, beneficence and justice. The next section discusses the research governance framework.

2.3.5 Research regulatory Frameworks in the wake of HIV/AIDS

The HIV/AIDS epidemic in Botswana led to an escalation of scientific and medical research on HIV/AIDS including pediatric HIV research in the past two decades. Unfortunately, like in many developing countries, the provision of a regulatory framework to guide the process has not kept pace with this increase (Pace, Talisuna, Wendler, Maiso, Wabwire-Mangen, Bakyaita, Okiria, Garrett-Mayer, Emanuel, and Grady, 2005). Although the Botswana Legislation Public Health Act [Chapter 63:01 (e)] (1971) mandates the Ministry of Health to promote, regulate, and carry out research in connection with prevention and treatment of human diseases and to prepare and publish reports and statistics or other information relative to public health and HIV clinical trials, this Act does not provide for guidelines and regulations for ethical conduct of this research.

Effective regulatory frameworks are critical for the conducting of clinical trials involving human subjects given that clinical trials have the potential to invade the right to personal autonomy and personal dignity of participants and also carry risks. Unfortunately the regulatory framework for the conduct of clinical trials in Botswana is very basic at the moment. Reference to clinical trials is only found in Part IV, Regulation 18 (1-20) of the Botswana Drugs and Related Substance Act of 1992. Clinical trials are also conducted in accordance with Botswana Ministry of Health, Health Research Clinical Trials Guidelines (2008) that guides the National Research Ethics Committee on how to review and approve research proposals and the Botswana Ministry of Health Guide-Consent Form (2005) used as

a template to guide researchers conducting both research involving adults and children. Regarding the involvement of children in research Section 3.4.6 of the Botswana Clinical Trials guidelines (2008) states that:

> *"When children are involved in research, the regulations require that the assent of the child and the consent of the parent(s) must be sought. Given that children have not reached their full intellectual and emotional capacities and are legally unable to give valid consent, involving children in research requires the permission of their parents or legally authorized representatives. The Health Research and Development Committee (HRDC) will determine whether the permission of both parents is necessary, and the conditions under which one parent may be considered "not reasonably available".* (Page 26)

However, in the literature reviewed, there is no evidence of explicit national guidelines for research involving children. Additionally, Botswana does not have national guidelines specific for HIV clinical trials research however international guidelines are adapted to Botswana. Unfortunately, as noted earlier, the adapted international guidelines are based on western laws that need to be contextualized to the local setting. It is however important to note that although Botswana recognizes the rights of the child and has ratified to two important international conventions dealing with the rights of the child namely, the United Nations Convention on the Rights of the Child (CRC), (1989) and the African Charter on the Rights and Welfare of the Child (1990), these have not been translated into law and policy (Fombad, 2005). These conventions are very important as far as the children's rights especially in the context of HIV/AIDS testing and treatment are concerned regarding children's rights to informed consent. Most important are Article 3 of the CRC and Article 4 of African Charter which emphasize that the short and long term best interests of the child must be the primary consideration in all decisions and actions that may affect the present and future of the children. Zuch, Mason-Jones, Mathews and Henly (2012) report that South Africa is one of the few countries in Africa that has a legislation protecting children participating in health-related research under the law through the South African National Health Act, No 61, (2004) implemented on March 1, 2012. The law mandates active consent from a parent or legal guardian for all research conducted with research participants under the age of 18 years. Such legal acknowledgment of parental authority and responsibility is also needed in Botswana. Considering all what has been so far discussed about the requirements and informed consent and the inadequacies in the process, the next section discusses the factors that affect parental informed consent

2.4 Factors affecting Parental informed consent

Parental informed consent unlike adult informed consent is unique because it focuses more on parental decision making and the assumption that parents know their children intimately and care deeply for their welfare. Some consensus has emerged on the basic ethical requirements for pediatric clinical trials. First and foremost, Guideline 9 of CIOMS states that children must be protected from unnecessary research risks, especially since they are considered a vulnerable population who lack adequate capacity to understand and evaluate research risks for themselves before participation in research (CIOMS, 2002). At this point, it is important to differentiate between the term competence and capacity when it comes to parental informed consent. Beauchamp and Childress (2001), describe the term competence as a legal term which assumes adults to be competent and able to make decisions for themselves unless proven otherwise. Thus, the law considers children as incompetent and dependent regardless of their maturity until the legal age of majority. Capacity on the other hand is described as the ability of an individual to make decisions if he/she can understand the problem, risks and benefits of alternatives and can express a choice (Kipnis and Gerhard, 1995). Therefore the term capacity could be a more useful description to describe an individual's ability to make decisions about participation in research, because although parents may be legally competent, they may possess inadequate decisional capacity to give informed consent on behalf of the child especially when burdened with a child suffering from a chronic disease like HIV. This is likely to destabilize the parent's emotional stability and rendering the parent vulnerable. This situation could be considered as a limitation in applying informed consent directly in pediatrics. However, courts recognize the parent's rights to make decisions (proxy consent) for minor children based on parental autonomy since all responsibility of for the child's care lies with them (Cooper and Koch, 1996).

Despite the legal rights, parents who make decisions on behalf of the child must be committed to the child's interests, must have adequate knowledge and information, emotional stability and ability to make reasoned or rational judgments (Childress, 1997). Therefore different approaches like 'best *interest of the child'* and '*rational-parent standard'* are applied as the theoretical basis for parental decision making. The best interest of child standard weighs quality of life considerations, whereby the parent has to take into account the potential benefits of the intervention and the real and potential burdens of the treatment or research as judged by a reasonable person (Beauchamp and Childress, 1994). The rational-

parent standard requires the parent to demonstrate ability to prioritize options for the child using the parent's own coherent and consistent value system (Cooper and Koch, 1996). Therefore trial staff need to take into account these standards in determining and facilitating valid parental informed consent.

As mentioned in Chapter One section 1.0, when parents agree to child enrolment they are not giving informed consent but informed 'permission" (Zawistowski, 2003 p.408).The requirements for parental permission serve as an ethical obligation for trial staff to respect and protect vulnerable individuals (Faden and Beauchamp, 1986). This makes informed consent to have a limited application in pediatrics but rather parental permission applies. Parental permission ensures that the rights and welfare of children that participate in clinical trial research are protected and confirms that parents have control over their children's decisions and that the decisions are consistent with their values, interests and preferences (Fombad, 2005). Ross (2006 p.200) provides three additional attributes that qualify the parents to be the best representatives of the child regarding granting informed consent namely; (i) parental decision promotes children's best interests (ii) parents have the right to raise their children according to their own standards and values without state intervention, and (iii) they have the capacity to do a risk/benefit analysis before consenting to their child's enrolment into research studies. However, other than the law, competency and decisional capacity of the parent, there are a number of other factors that range from personal to social-environmental that can cause barriers in voluntary decision-making. For example, although literature shows that parental decision–making is likely to be based on the parent's cognitive and emotional reaction to the information provided (Faden and Beauchamp, 1986), some empirical studies have shown that often personal and cultural values play a major role in decision-making (Frimpong & Monash, 2007; Marshall, 2006; Shaibu, 2007) provided evidence of family and community participation in decision making in many developing countries. Other specific factors identified in the literature (Kyriaki, Panagiotou, Katsaragakis, Tsilika & Parpa, 2009 p.49) that may influence decision making include:

- parents' stress due the illness of the child
- trust of physician's assessment rather than parents own assessment of risks and benefits
- prospects of payments or reimbursements for participation

- access to improved medical care
- practical advantages like transport, a meal, or a chance to visit urban areas

This review also came across several recently published studies that shed light on why parents accept or decline to enrol their children in medical research and how they understand and balance risks against potential benefits (Tait, Voepel-Lewis, Malviya, 2003a; Greenley, Drotar, Zyzanski and Kodish; 2006; Tait, Voepel-Lewis, Malviya, 2003b; Rothmier, Lasley and Shapiro, 2003; & Hulst, Peters, van den Bos, 2005). These studies found that many parents had inadequate understanding of the information presented to them during the informed consent process. The studies also showed that factors like age, higher education level, lower anxiety, greater perceived clarity of information, greater degree of listening to the explanation of the research, greater degree of reading the consent document and perceptions of the study's importance, risks and benefits were significantly associated with greater parental understanding. Another example from a children's leukemia clinical trial showed that, approximately half of the parents failed to understand random assignment at the time of enrolment and even six months later (Greenley, Drotar, Zyzanski and Kodish, 2006). However, factors in the same study factors like being a member of a majority ethnic group, higher socioeconomic status, presence of a nurse during the informed consent, parental reading of the consent document and physician discussion of specific components of the randomized controlled trial were associated with better understanding.

A study that compared parents who consented to their child's research participation and those who declined, showed that the parents who exhibited less uncertainty in their decision making, were more trusting of the medical system and believed that the environment in which the consent was sought was less pressured (Tait et al, 2003b). Rothmier, Lasley and Shapiro (2003) found that although many parents exhibit altruistic motives such as a desire to contribute to medical knowledge, the most compelling motive for parents accepting to enrol their children is learning more about their child's illness, as well as access to care. While Hulst, Peters and van den Bos (2005) found payment for participation not to play a significant role in parental decisions, obtaining free medications gained importance as the socioeconomic status declined; and that although the severity of the child's illness did not decrease the probability of obtaining parental permission, parents who perceived that the research would be burdensome to the child were significantly less likely to consent.

Additionally, Lindegger and Richter (2000) cite social desirability as another factor that that can affect parental consent. The author explains social desirability as the tendency of volunteers to behave in what they deem socially acceptable in order to win a favour or avoid displeasure of the researcher as particularly prevalent in situations where differences in power and status exist between the consenter and parent particularly in poor resourced settings. Meisel and Roth (1983) caution that assessments of understanding test short-term memory other than tests of understanding rendering their findings unreliable. Nevertheless, the Declaration of Helsinki (1964) dictates that volunteers must have the freedom to make a decision about participation without any form of coercion as a fulfillment of the ethical principle of autonomy. On the basis of the many factors identified above, obtaining valid informed consent has been conceptualized by Lindegger and Richter (2000) as a framework of four overlapping core elements namely; information disclosure, understanding, social desirability, and freedom from coercion.

In conclusion, the big challenge for trial staff to try and minimize these negative influences during the informed consent process. This thesis will examine the factors that affect obtaining parental informed consent for HIV pediatric studies conducted in Botswana and use the findings to develop a model that can enhance the process that suits this context. The next section examines literature on the nature of each of the steps of this process.

2.5 Information disclosure process

As indicated in the previous section, obtaining valid informed consent has been conceptualized by Lindegger and Richter (2000) as a framework of four overlapping core elements namely; information disclosure, understanding, social desirability, and freedom from coercion. The first step in the informed consent process is the provision of full and transparent information. According to the Nuffield Council on Bioethics (1995), this information protects research subjects from acts of deception, manipulation, deliberate misdescription of what is proposed, lack of disclosure of material facts, or conflicts of interest. Gaps in how information is communicated to potential have been identified. For instance, in a multi-center study by Williams and Zwitter (1994, p. 905) that asked research investigators about information they had disclosed to potential participants, 58% indicated having disclosed full information, 42% only gave information on the proposed treatment,

while 12% had not informed patients about the trial prior to randomization and 38% did not tell the patients about randomization while 5% did not seek consent at all. In the same study, however at least more than 90% of the investigators had provided the participant with a copy of the consent form, an opportunity to read before coming for the next visit and information about risks. However less than 56% of the investigators had emphasized randomization and only 8.5 % had made a formal assessment of understanding. This shows that some key information may not be communicated at all.

In response to this gap, three standards of disclosure were developed as a guide to ethical communication of information (Beauchamp and Childress, 1994, p. 148). Although these standards were developed for treatment purposes, they could also apply to HIV clinical trials settings which combine treatment and research. These standards include: (i) the professional practice standard, (ii) the reasonable person standard and (iii) the subjective standard. The professional practice standard is determined by the medical community and it emphasizes the patient's best medical interest. This standard is frequently criticized because it assumes that the physician is capable of determining what is in the patient's best interest implying paternalism. The reasonable person standard supposes a "hypothetical reasonable person" (Beauchamp & Childress, 1994, p.148) and takes into consideration the patient's need for information, rather than the physician's opinion of the patient's needs. This shows respect for the patient's autonomy and his/her right to self-determination which is central to obtaining valid informed consent. The difficulty with this standard is that it is difficult to determine what a reasonable person is. According to Beauchamp and Childress (1994), the most preferred standard of information disclosure is the subjective standard. This standard emphasizes that for the principle of autonomy to be maximized, the level of disclosure of relevant information should be tailored to the person's individual needs. In addition, Argard (2005, p.634) acknowledges the difficulty associated with setting strict standards for information adequacy across different clinical and research contexts and recommends that the subjective standard procedure could be the best since it acknowledges that the information provided should be tailored to match the specific information needs of the potential participants taking into account their culture, values, beliefs and health status. However, Pedroni and Pimple (2001 at: http//www.poynter.indiana.edu) added that, in practice, the best way to facilitate informed consent may be to design consent forms and other informational materials to satisfy a reasonable person standard, supplemented by conversations intended to elicit and answer any questions that are not otherwise addressed.

Therefore, information should be presented at a level that the person understands, based on their intellectual ability, and taking into consideration cultural differences, functional limitations and language barriers.

Certain basic elements have to be disclosed in order to fulfil the requirement of full information disclosure. For purposes of this thesis, these elements are summarized in Table 2.2 and will be used to assess recall of information and comprehension in Chapter Three.

Table 2.2: Basic elements of informed consent

	Basic elements of informed consent
1	A statement that the study involves research; an explanation of the purposes of the research and the expected duration of the subject's participation; a description of the procedures to be followed; and the identification of any procedures which are experimental
2	A statement that taking part is voluntary; refusal to take part will involve no penalty or loss of benefits to which the subject is otherwise entitled; and the subject may stop taking part at any time without penalty, or loss of benefits to which the subject is otherwise entitled
3	A description of any reasonably foreseeable risks or discomforts to the subject from the study procedures - these may be potential physical, psychological, legal or social risks
4	A description of any benefits to the subject or to others which may reasonably be expected from the research
5	A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject
6	A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained
7	For research involving more than minimal risk, an explanation as to whether any compensation is available for injury and an explanation as to whether medical treatments are available if injury occurs, and if so, what they consist of, or where further information may be obtained
8	An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, whom to contact in the event of a research-related injury to the subject, and a 24 hour phone number for the PI.

Source: ICH-Harmonized Tripartite Guideline (Guideline for Good Clinical Practice E6 (R1, 1996)

As shown in table 7.2, consent forms carry large amounts of information in order to fulfil the legal and ethical requirements. However the quality and quantity of information to be disclosed depends on the objective of the investigator or person designated by the investigator to fully inform the subject of all relevant information, for the subject to reflectively select what s/he wants and for the investigator to execute what has been selected (ICH-GCP 2002, section 4.8.5). Some international regulations have added more to the basic elements. For example, CIOMS (2008), guideline 19 requires more details namely, the alternative procedures or treatments available; what responsibility, if any, lies with the

investigator to provide medical service to the subject; and provision of free treatment for injuries related to research. Studies that have analyzed inclusion of these elements found that majority of forms include all the elements and participants were aware of these elements. For instance, a study by Silverman (2001) that analyzed 267 Phase I clinical trials consent forms showed that 99% of the participants knew that the trial was research, 92 % knew that the purpose was safety testing, 99% knew that they had a right to withdraw, 67% knew death as a risk and 84% knew that there were unknown risks while only 5% knew cure as a possible benefit.

Federman, Hanna and Rodrigues (2002) however caution that the idea of the process of informed consent as a provision for sharing information and educating the research participant has fallen prey to the idea of being a document to be signed by the participant, constructed by the research sponsor or site to comply with the regulations. The same authors further elaborate that, in clinical research, these documents typically include lengthy descriptions of diagnoses, prognoses, treatment alternatives, risks and benefits of the alternative treatments, the risk of no treatment, the right to refuse, the commitment to provide care even in the face of refusal, and the injury compensation policy of the sponsoring institution. These details seem to indicate that the purpose of the document is to be compliant with regulations while the spirit of the document is clearly the articulation of every possible danger so that any subsequent participant complaint can be countered with the argument that the participant had been informed and had accepted this risk. Therefore research investigators have to be cautious and sensitive to these intentions by those who prepare the consent forms.

Regarding the critical issue of language, CIOMS (2002) and the National Consensus Conference (1997, p: 32) recommend that information provided to a participant about the study be provided in a language he/she can understand, at their level of comprehension and be allowed time to ask questions, obtain answers and to reflect and give due consideration to their decision. Although this information is normally given in a written document, in the case of illiterate participants or those who speak a language with no written form, it is given verbally. Often consent forms are translated from one language to one that a participant is comfortable with. An analysis of the comprehension of a survey translated into 11 languages (Yuling and Landreth, 2009) concluded that translations must reflect the cultural values and social practices of the research setting. For example, issues like the general linguistic rules governing the use of the language for information exchange, the language-specific rules, such as the sentence structure or discourse structure of a language that may be different from the

language originally used to prepare the document e.g. English language. This can result in different presentation of information in a target language and the cultural norms of doing certain things in a given culture, such as appropriate level of politeness in expressing a message. If cultural norms and social values are not observed there is a danger that the information conveyed to participants may be incomplete or misunderstood.

The nature of the process of obtaining valid informed consent has been considered as both a legal and ethical obligation to distinguish, the legal indemnity stems from the understanding between the researchers and volunteer (Richter and Lindegger, 2002, p.317). That is why Faden and Beauchamp (2003) refer to the ethical approach as signifying the autonomous authorization based on understanding and absence of control by others, and the legal approach as the social rules of consent based on legal authorization as determined by the rules. These two obligations lead to different decisions and guidelines when it comes to information disclosure. Faden and Beauchamp (cited in Richter and Lindegger, 2000 p.315) observed that commonly, it is primarily the legal approach that receives focus in practice with emphasis on the documentation of itemized checklists of what is included in informed consent. However, Meisel and Kuczewski (1996, p.2523) noted that regarding the quality and quantity of information to be disclosed to a volunteer, the legal approach would be concerned with liability necessitating all the information to be disclosed. The ethical approach however, would be concerned with the moral facilitation leading to shared decision-making but this approach can be undermined by excessive information. Marshall (2004) doubts whether providing consent forms that contain all the defined key elements necessarily offers the would-be participants the opportunity to be fully informed and able to make autonomous decisions. Consent information is usually represented in a written document; the next section examines the qualities of this document that facilitate decision making and valid consent.

2.5.1 Readability and comprehension of the consent form

When parents are presented with the option of enrolling their children in HIV clinical trial, they have to undergo a consenting process for the investigators to obtain their valid informed consent. In most cases the informed consent information is presented in a written document called an informed consent form which the parents must read or it must be read to them to understand the information provided and make an informed decision. Ability to read and understand a text requires a combination of literacy skills and a certain level of formal

education and the importance of literacy and education as part of the social and economic determinants of health is well documented (WHO: http://www.who.int /topics/social_determinants/). The Ad Hoc Committee on Health Literacy, 1999, (cited in Kickbusch, 2001, p.293) stresses that education influences an individual's ability to navigate the health care system, to interpret health information and to communicate effectively with physicians and other professionals. However it also notes that most health professional are not aware of their patient's low literacy levels or that most patients are embarrassed to indicate to them that they have not understood. There is need to assess individual literacy competence in order to judge levels of comprehension of information provided.

Literacy levels are related to public health outcomes and literacy is context and content specific. Therefore in the health context we talk of health literacy. A distinction needs to be made between general literacy and health literacy. Health literacy has been defined differently defined by many authors but they all capture the issues of the context in which the health literacy demands are made and the skills that people bring to that situation. For example, Ratzan& Parker (2000) cited in Nielsen-Bohlman, Panzer and Kinding (2004 p.32) define health literacy as " the degree to which individuals have the capacity to obtain, process and understand basic health information and services needed to make appropriate health decisions". Nielsen-Bohlman, Panzer and Kinding (2004 p.37) associate this process to a collection of skills namely; an individual's ability to read, write and understand written language that is familiar. The same author also associates it to back ground knowledge of print literacy; reading or text literacy, related to characteristics of the text being read, such as complexity and format and functional literacy as well as the use of literacy in order to perform a particular task. Therefore, Rudd (2003) cited in Nielsen-Bohlman, Panzer and Kinding (2004 p.32) argues that health literacy is a shared function of the individual's education system, culture, societal factors and the health system.

Various methods are used to assess readability and comprehension of informed consent forms. The readability of consent forms can be determined using a wide range of readability formulas. These are formulas commonly used to predict the ability of a reader to read and comprehend a written text. The formulas can only be used on text written in English.

The scores generated from these formulas are an indication of how difficult or easy it is for a reader to read and understand a text and the number of years of education that a person needs

to be able to understand the text on the first reading. In general, readability is determined by analysing word and sentence length in the text. Online computer software programs like the online utility :http://www.online-utility.org/english/ that use a combination of formulas namely; the Flesch-Kincaid Reading Ease (FKRE) and Flesch-Kincaid Grade Level (FKGL), Gunning-Fog index, the Simplified Measure of Gobbledygook (SMOG) and Fog formulas exist for the purpose. Johnson (2004) noted that the formulas work mainly by measuring the number of words in a sentence and the number of letters or syllables per word as well as the semantic factor (the difficulty of the words) and the syntactic factor (the difficulty of the sentence). The Flesch Kincaid Reading Ease Scores range from 0-100, the higher the score the easier it is to read the text. Generally, scores below 30 are very difficult to read and can only be read by individuals that have graduate education. Scores above 90 are very easy to read and can be read by individuals with a fifth grade education. Texts written for the public are recommended to be at 6th -8th grade reading level (Johnson, 1998). However the message behind all these formulas is that if you use shorter average sentence lengths and fewer big-lettered words, you can increase the readability level, the speed and ease of reading.

Regarding the use of the above methods, Chall (1995) however cautioned that, although these methods are easy to use and have the ability to broadly predict text difficulty, they cannot be regarded as a precise final measure. Thus factors beyond those measured by formulas need to be considered. Bruce, Rubin and Starr (1981) argue that readability factors mainly deal with sentence length and word difficulty, but miss out on discourse cohesion, number of inferences required, number of items to remember, complexity of ideas, rhetorical structure, dialect, and background knowledge required. The same authors also note that because formulas are measurements based on a text isolated from the context of its use, they cannot reflect reader-specific factors such as motivation, interest, values and purpose.

The recommended reading age of consent form is 6-8th grade based on the American reading age system (Johnson, 1998). For subjects in Botswana these recommended levels may not apply because of differences in education systems and language. Furthermore, although the adult literacy level in Botswana is currently at 83% , it means that about 17% of the adult population performs below basic reading level and do not have the proficiency necessary to perform more than basic literacy activities (Maruatona, Cervero and Ronald, 2004). The

question therefore for Botswana would be; how can evidence derived from American based formulas be relevant to respondents in Botswana settings with different linguistic, educational, literacy, cultural and social practices? In the absence of appropriate readability assessment tools, the readability formulas provide an estimation of the challenges for readers in Botswana and an indication of the levels of difficulties in understandability of informed consent information.

The result of manipulating consent forms to meet regulatory requirements is increased length, complexity, linguistic sophistication, and generally daunting nature of such documents. Consequently, consent forms are not conducive to increasing understanding, but rather serve to overwhelm participants. Hochhauser (2004) identified certain factors to consider when a reader reads a text, and one of these is the difficulty of assembling words into meaningful sentences. So another area of concern we found in the literature is the readability and comprehension of the consent form. When the information about the study is disclosed using a written informed consent document, the readability and comprehension of the text is very critical for conveying study information to enable a potential participant to arrive at a decision concerning their willingness to participate in it. Readability refers to the ease with which a written text can be read and understood. Johnson (2004) uses it to refer to all the factors that affect success in textual reading and understanding including the interest level and motivation of the reader, the legibility of the print, and the complexity of words and sentences in relation to the reading ability of the reader. The same author also noted that the determination of readability addresses the problem of matching individual reading levels to the difficulty of the text. Ideally, the goal is to develop consent forms that are both short and written in simple and comprehensible language so that they facilitate a greater level of understanding and enable potential subjects to make truly informed decisions about research study participation.

The South African Department of Health (2006) observed that consent forms often present highly complex information that must be understood by patients. The complexity of these forms is a major barrier to comprehension for many research volunteers especially those with low literacy skills. Some of the barriers to comprehension identified include the form's excessive length, lack of adequate time to read the form, high reading levels, and poor format and layout of the form; barriers which Hochhauser (2004) rightly says increase risks to both

the researcher and participants, lead to therapeutic misconceptions, poor enrolment and failure to follow up.

2.5.2 Researcher/participant communication models

Physician -participant interactions have been studied and patterns of behavior have been theorized in the form of models mostly in clinical settings but only a few studies have looked at the process in research settings. For example, Kodish, Michelle, Robert, et al. (2004) observed that physician-patient interactions in clinical trial settings differ from the researcher-participant ones in that in the former there is a greater need to discuss with patients their potential concerns, examine their feelings and expectations from the treatment plan. This is because the objective of the physician-patient interaction is for the physician to provide the patient with all relevant information, for the patient to reflectively select the medical interventions he or she wants and for the physician to execute the selected interventions and provide explanations and feedback to enable informed decision-making (Brown, Weston and Stewart (1989).

A great deal of variance in physician-patient communication styles mainly in clinical settings has been observed (Korsch, Freemon, and Negrete (1971) and this can compromise the success of the communication process. The basic principle that governs informed consent is autonomy or respect for persons which have become symbols of integrity (Beauchamp and Childress, 2001). Several models of informed consent linked to ethical theories have been proposed and are used to explain how the informed consent process is integrated into the ethical principle of autonomy and how they are applicable to autonomous decision making in the informed consent practice (Delany, 2005). These models namely, the 'Event Model' (Wear, 1998), the 'Transparency Standard Model' (Brody, 1989), and the 'Shared Decision Making Model' (Charles, 1997), have been observed not to promote autonomy as they are essentially prescriptive, describing what the physician should say in communication encounters and dictate the elements to be complied with. On the other hand, two other models of informed consent process namely; the 'Process Model' (Lidz, Appelbaum & Meisel, 1988); and the 'Conversation Model' (Katz, 2000); cited in Delany (2005, p.73-84) were found applicable to autonomous decision-making because they promote thinking and

reflection on the value and meaning of autonomy. A brief overview of the Process Model and Conversational model is given below.

(i) The Process Model

Developed by Lidz, Appelbaum & Meisel (1988), this model this model sets out three requisites for successful decision-making namely; the recognition and delineation of roles; acknowledgement of the differences in values and beliefs about health and illness; and clarification of the relative values and expectations held by those involved in the informed consent process about illness, treatment or research. Thus this model recognizes the patient's/participant's expert knowledge of the history and context of their problem and regards them as part of the treatment or research team. The model also promotes mutual sharing of information, calls for respect for autonomy and time to reflect on proposed options, risks, and benefits during the informed consent process.

(ii) The Conversation Model of Interaction

Developed by Katz (2000), this model marks a shift from the traditional paternalistic prescriptive models. It involves active reflection on the values, motivations, expectations and interests that may influence implementation of the informed consent process (Delany, 2005). This thesis will adapt this model because of its capacity for recognizing that 'meaningful clinical conversation rests in a particular understanding and assumption of patient/participant autonomy and right to self-determination.

As a guide to describing patient-doctor relationship in communicating information, four models were developed by Emanuel and Emanuel (1992). Although the models do not specifically refer to the principle of autonomy and are mostly applied in treatment settings, they reflect the necessary communication methods and the need for upholding autonomy in the doctor-patient relationship so are applicable to clinical research settings like HIV clinical trials. These models include the 'Paternalistic model', the 'Informative model', the 'Interpretive model' and the 'Deliberative model' used to explain the assumptions made by physicians or researchers during the interaction process of obtaining informed. The models are summarized in Table 2.2 below and a brief overview of each model is given.

The section below gives a brief interpretation of the assumptions of each of the above models.

(iii) The paternalistic model

As shown in Table 2.2, this model is seen as the traditional one-way practice which assumes that the physician and patient share common values and the physician acts in the best interest of the patient to restore the patient's health or alleviate pain using selected information that will encourage the patient to consent to the intervention. This would be considered paternalist but it depends on the characteristic of the patient. For example, patient preference of the physician style, some patients may prefer an informative physician while others may prefer not to know. Emanuel and Emanuel (1992, p. 222) also suggested that age, gender, socio-economic status, education and type of diagnosis may affect the extent to which patients play an active role in information disclosure interaction process.

(iv) The informative model

Table 2.2 shows that this model assumes that participants know their own values and preferences and the physician just provides the means (information) for the patient to exercise control and make an informed decision. This model treats the patient as a consumer, thereby allowing them choice, therefore it could be said to facilitate autonomous decision making.

(v) The interpretive model

This model as shown in Table 2.2 assumes that participants may have conflicting or not fully formed values that may require clarification. The physician in this case acts as an advisor or a counselor to provide both factual information and help to interpret relevant patient values.

Table 2.3: The four models for guiding physician-patient communication

	Models			
	Informative	**Interpretive**	**Deliberative**	**Paternalistic**
Patient Values	Defined, fixed and known to the patient	Conflicting or not fully formed values that may require clarification.	Open to development and revision through moral discussion	Objectives shared by the physician and patient
Physician Obligation	Providing factual information and implementing patient's selected intervention	Elucidating and interpreting relevant patient values as well as informing the patient and implementing the patient's selected intervention	Articulating and persuading the patient of the most admirable values as informing the patient and implementing the patient's selected intervention	Promoting the patient's well-being independent of the patient's preferences
Conception of patient's autonomy	Choice of control over medical care	Self-understanding relevant to medical care	Moral self-development relevant to medical care	Conforming to objective values
Conception of patient's roles	Competent technical expert	Counsellor or advisor	Friend or teacher	Guardian

Source: Emanuel & Emanuel (1992, p.222)

(i) The deliberative model

In this model physicians play the role of participant's teacher or friend and provide factual information and the values underlying the choices with the assumption that participant's values are open to development. This means the physician helps the participant to determine and choose the best health related values that can be realized. In this case the participant's autonomy will comprise of moral self-development and determination in decision–making which are relevant components of autonomy. This thesis will draw from each of these models in the development of the model for obtaining parental informed consent.

The next section reviews literature on the understanding or comprehension of the information disclosed.

2.5 Comprehension of information

Literature on adult individual's understanding of and decisions about their own participation in research is considerably more extensive than the corresponding literature on parents making decisions about their child's participation in research. The reasoning that the decisions that adults make on their own behalf are generally relevant to the understanding of the information provided. However, many studies (Ruccione, Kramer, Moore and Perin, 1991; Levi, Marsick, Drotar and Kodish, 2000) have reported that parents may have anxieties associated with making decisions on behalf of their child, especially one's sick child and that this may put particular stress on an adult's comprehension, reasoning, and decision-making capacities.

Most research evaluating people's understanding of the difference between research and usual clinical care has involved adults consenting to research participation in their own right. It generally indicates that avoiding or overcoming the therapeutic misconception can be a formidable challenge. As Appelbaum, Roth, Lidz, Benson and Winsdale (1987) observed, subjects have the ability of maintaining their therapeutic misconceptions, while they gave the appearance of having a good general understanding of the study. Other studies also suggest that research participants may have difficulty understanding the purpose of research (Daugherty, Ratain, Grochowski, Stocking, Kodish, Mick and Siegler, 1995). A review of 61 studies about attitudes toward clinical trials by Edwards, Lilford and Hewison (1998) found that people mentioned self-interest more often than altruism as the reason for participating in trials. Often, however, the specific questions and methods were not fully described to provide a clear picture of the results. These authors also cite three studies from the 1990s that reported a near majority or majority of physicians believed that research participants did not understand the information given them or did not realize that they were participating in research.

Furthermore, other studies have suggested that research participants frequently have expectations of benefit (Daugherty et al., 1995, Schutta and Burnett, 2000). Likewise, although participants may understand and approve the knowledge-generating purpose of research in general, participants may view their own participation primarily in terms of benefit to themselves (Cassileth, Lusk, Miller and Hurwitz, 1982; Bevan, Chee, McGhee and

McInnes, 1993; Aby, Pheley and Steinberg, 1996; Hutchison, 1998). An interview survey conducted by the Advisory Committee on Human Radiation Experiments (ACHRE, 1995) on a fairly large sample of more than 1800 patients at 19 health care institutions reported a number of interesting findings about people's understanding of research participation. A third of those surveyed believed that patients who participated in medical research usually or always benefited medically compared with those who did not. About two-thirds of the patients who had participated in research indicated that they had done so to obtain better treatment; a similar percentage reported that being in research gave them hope. The researchers, however, reported that patients who had been in diagnostic, epidemiologic, or survey research were more likely to differentiate between research and treatment than those who had participated in studies testing a potentially therapeutic intervention.

Other reports have shown that some patients consider research participation may not necessarily result in improvement in their condition from the intervention being tested, but they may expect to receive better diagnostic evaluation, closer medical monitoring and follow-up, and more information about their condition (Mattson, Curb, and McArdle 1985; ACHRE, 1995; Yoder, O'Rourke, Etnyre, Spears and Brown, 1997; Madsen, Holm, Davidsen, and Riis, 2000). For example, for Danish patients in a trial of interventions for inflammatory bowel disease, an important reason for participating in the research was "the expectation of being 'a special patient' during the trial" (Madsen et al., 2000, p. 463).

According to Meisel and Roth (1983), the following factors have been observed as determinants of participants' ability to comprehend information:

- Lack of provision of psychological information required to make informed decisions such as recognition of personal value systems that allow potential participants to evaluate information.
- Separation of patients' understanding and judgment (objective) of facts from their attitudes or feelings (subjective) about those facts.
- Failure to assess comprehension of implications as well as facts.
- Impact of emotional factors on participants' ability to evaluate information (anxiety arising from excess information or apprehension of risk).
- Giving matters related to legal liability priority and not what the participant would like to know or what they consider would be helpful to have been told.

Therefore in addition to factors that influence readability, personal factors like values, emotional factors, attitudes and feelings should also be considered when seeking informed consent as they may influence comprehension.

Beauchamp and Childress (2001) suggested that information given to participants requires a level of adequate comprehension and appreciation for meaningful deliberation about a decision. The authors refer to this as substantial understanding which means that autonomous decisions must reflect what one intends to do; which is only possible if the individual adequately comprehends the relevant information. Marshall (2006) provided evidence from empirical studies on informed consent which suggest that even when provided with information about the nature of research, participants systematically misinterpret the risk/benefit ratio of participating in research because they fail to understand the underlying scientific methodology. In such cases, what the participants actually authorize differs substantially from what they intend to authorize, and thus informed consent is frustrated. For example, Pace et al. (2005) found that although most respondents in comprehension of consent to a randomized trial among HIV positive individuals in Thailand said they were well informed, only one third correctly reported that half of the participants would receive the experimental therapy. Such misunderstandings may arise from use of complex epidemiological terms like randomized assignment, placebo control groups, double blinded procedures and fixed treatment protocols. The case of parental comprehension may also affected by the anxiety and fear created by the illness of the child and need to access health services for the child (Ross, 2006). As observed in this section autonomous decision-making can only result from adequate comprehension of information disclosed. The next section examines the decision-making component of informed consent.

2.6 Decision-making

Decisional capacity is critical in decision-making to participation in research. Decisional capacity refers to an individual's psychological abilities to form rational decisions (Raphael, 2007). Appelbaum and Grisso (1988) identified four elements related to decisional capacity first described by namely; the ability to communicate a choice, the ability to understand the relevant information, the ability to appreciate a situation and its consequences and the ability to reason rationally. Arnold and Feldman (1986 p. 340) noted that an individual's choice is

influenced not only by the perceptions of his/her goals but the anxiety and confusion experienced while making the decision. In research an individual capable of informed choice should demonstrate the ability to understand the nature of research participation, appreciate the consequences of such participation, exhibit the ability to deliberate on alternatives, including the ability not to participate in research and evidence ability to make a reasoned choice (Appelbaum and Grisso, 1998). As mentioned earlier, children have no legal authority to make decisions, therefore surrogate decisions are made on their behalf by the parents. Cooper and Koch, (1996) cited in Zawistowski, (2003 p.408), suggested that the *rational-parent standard* approach is the best approach to apply for surrogate decision making in case of younger children who lack the capacity to demonstrate intelligence. This standard requires the surrogate to demonstrate the ability to prioritize options for the child using the parent's own coherent and consistent value system.

All international guidelines recognize the principle of "respect for persons" and emphasize the importance of freedom of choice and personal decision-making. However, according to Arnold & Feldman (1986), the major concern about decision-making is that rational decision-making is of the assumption that all decision-makers have mental capacities for analysis and evaluation to do so. However, the same author observed that persons giving consent must have reasonably stable preferences, goals, and values with which they genuinely identify, suggesting that a certain level of maturity is necessary. Additionally, decision-making further requires that prospective subjects are able to assess the possible consequences of participation or non-participation with respect to their individual interests, and must be able to come to a reliable decision as a result of these deliberations.

Despite having the requisite skills, women and children may not be able to exercise their decision-making capacity because of the environments and cultures that significantly limit opportunities for individual choice. Marshall (2004) observed that historically, beliefs and values about autonomy and personal decisional capacity are grounded within social and cultural patterns of the community obligations and family ties. As noted by Molyneux et. al. (2005), in the western culture decision making is individual while in non-western settings decision-making involves family and sometimes the community; and Ajayi (1980) observed that in certain regions of the world, respect for family and community elders strongly influences a community's receptivity to participation in medical research. A survey of 540 investigators from developing countries found that 66% of the investigators thought that the

informed consent process focused too much on the individual rather than community or family in research with adults, while 19% sought consent from another family member other than the participant especially where verbal consent was sought (Kass & Hyder, 2001). A study by Loue, Okello & Kawuma (1996), reported that in Uganda the civil law recognizes an 18-year old male living with his parents as having a right to make his own decisions but according to customary law he has to obtain consent from his father prior to entering into obligation or contracts whereas most Ugandan women seek the consent of their husbands before making any decision regarding their participation into research.

CIOMS (2002) states that only the informed consent of the woman herself is required for her participation and that in no case should the permission of a spouse or partner replace the requirement of individual informed consent. If women wish to consult with their husbands or partners or seek voluntarily to obtain their permission before deciding to enrol in research, that is not only ethically permissible but in some contexts highly desirable. A strict requirement of authorization of spouse or partner however violates the substantiate principle of respect for persons. However in most developing countries setting, this is not the case, although there are exceptions that would include approaching a woman's husband or partner /father before speaking with her directly (Macklin, 2004).

2.7 Voluntariness and consent authorization

In order for individuals to exercise their autonomy they must have the capacity to make free choices without coercion or undue influence (Schiffman and Kanuk, 1997) which reflects voluntariness. However, voluntariness is a difficult concept to operationalize because although legally children have rights, they cannot express their developing autonomy because they lack the legal rights, intellectual and emotional maturity, therefore parents or guardians consent on their behalf (Karim, Karim, Coovadia, & Susser, 1998; Beauchamp & Childress, 2001). In Botswana like in many developing countries, the health care of children is mostly a woman's responsibility. However, decision-making by women may be compromised by gender bias and power issues (Wassenaar, Bardorf & Richter, 2005). For example, Marshall (2004) found that nearly one-third of more than 400 participants married women interviewed in Nigeria to participate in the hypertension and breast cancer study needed permission from their spouses. Pace, et.al. (2005) also noted that voluntariness can be compromised by the

stress caused by the nature of illness of the child as well as other socio-economic factors and these may erode decision making capacity.

Some studies have considered refusal to participate, feeling of pressure to join a study and freedom to withdraw as indicators of voluntariness. For example Gross (2002) reported that in a cardiac intervention study only 7% of the potential participants refused to participate Pace et al. (2005) reported that 58% of the parents in malaria treatment study done in Uganda felt pressured to join because of their children's illness while only 48% of Bangladesh pregnant women involved in an iron supplement trial knew they could quit the study anytime. Issues of information disclosure, understanding and voluntariness among parents who enrol their children in HIV pediatric studies have not been critically analyzed in Botswana. Therefore the thesis aims to assess the current situation and develop a conceptual model for obtaining parental informed consent for HIV clinical trials involving pediatric populations.

2.8 Conclusion

This chapter discussed literature under the elements of informed consent, the need to involve children in clinical research, regulatory challenges of research involving children and parental consent and the key steps of the informed consent. The literature highlighted the ethical and practical challenges encountered in conducting research involving children focusing on parental informed consent. Further, it emerged that parental informed consent in research involving is critical but there is a paucity of literature on parental informed consent in sub-Saharan Africa including Botswana. Literature also showed that the process of informed consent is inadequately implemented and consent forms are becoming longer and more complex for ease of readability and comprehension by potential participants. Furthermore potential participants' understanding is variable and lacking especially in certain aspects of clinical trials like randomization and freedom to quit a study. Therefore more research is required to embrace these issues in order to enhance the understanding of the informed consent process as well as improve the process and voluntary decision making in a variety of settings. The next chapter describes the procedures that were followed to collect and analyse data for this thesis.

CHAPTER THREE

METHODOLOGY

3.0. Introduction

This chapter reports on the methodology used in this thesis. The chapter begins by giving a brief overview of the research methodology, and provides a brief explanation of the research design and its appropriateness in addressing the research questions. Finally, it describes the tools and instruments used for data collection, data collection procedures, and analysis, as well as the ways in which ethical issues material to the study were addressed.

3.1 Research Design

This thesis followed a cross-sectional exploratory design (Creswell, 2003) to conduct a holistic analysis of the current practices of obtaining parental consent for pediatric HIV clinical trials conducted in Botswana. A mixed methods approach using both qualitative and quantitative techniques was followed, including a readability assessment, in-depth interviews, focus groups and face-to-face semi-structured interviews. According to Wiersma (1995), qualitative research investigates the complex phenomena experienced by participants by examining people's words and actions in descriptive ways thereby allowing the researcher to operate in a natural setting. This paradigm was relevant to this study since it was examining the informed consent process as used in the context of a clinical trials research environment. As noted in chapter one, the general aim of this study was to conduct a situational analysis of the current practices of obtaining parental consent for pediatric HIV clinical trials conducted in Botswana in order to use the findings to develop a conceptual model that can be used as a framework to guide future parental consent processes. On the other hand the quantitative method was used as a triangulation technique to strengthen the findings obtained from the qualitative data by cross-checking information collected from the parents.

3.2. Study Setting

3.2.1. The country

Botswana is a landlocked semi-arid country situated in Southern Africa. It is bordered by South Africa, Namibia, and Zimbabwe. According to Botswana Central Statistics Office (CSO), Botswana has an estimated population of 1.8 million (CSO, 2009a) which is sparsely distributed in a land of about 582 000 km2. This terrain makes distribution of services quite a challenge. About 34% of the population is less than 15 years old. Most of this population is concentrated in the south eastern part of the country where the soil conditions are more favorable to arable production and, in Gaborone, the capital city, employment opportunities are more prevalent. It is estimated that more than 40% of the population lives in rural areas (CSO, 2009b). Although most biomedical research institutions are located in urban areas, many of those seeking medical care for their children come from rural areas.

Botswana is a middle-income country whose economy has been rated as one of the strongest in Africa as well as in the Southern Africa Development Corporation (SADC) region. The Ministry of Finance and Development Planning (MFDP), 2011 reported a Gross Domestic Product (GDP) average growth of 8% and this economic growth is mainly been attributed to the mining sector, in particular the diamond industry, which accounts for 80% of export revenue (MFDP, 2006b). Revenue from exports together with returns from various types of taxes (e.g. non-mineral income tax, and export duties), non-tax items (e.g. mineral royalties and dividends, fees, charges and sundry) and grants constitute government general revenue and is used to fund all government activities. .

Despite the above successes, poverty and unemployment are still some of the major challenges facing the country. Unemployment rate is estimated at 31.6% (CSO, 2009b). High rates of income inequalities have led to an estimated percentage of 21% of the population living below the national poverty line (CSO, 2011).The Botswana 2009/2010 Core Welfare Indicators Survey (BCWIS) showed that persistent poverty is more prevalent in rural areas and among female-headed households especially among the youth and lowly-skilled people (UNICEF, 2011). Therefore the above situation might have a bearing on obtaining valid informed consent from study participants in Botswana like has been suggested elsewhere. For

example, Marshall, (2006) cited literacy levels, language and poverty as some of the factors that influence obtaining valid consent.

The 2003 Sentinel Survey showed that in 2001 Botswana life expectancy at birth had dropped from 66 years in 1966 to 56 years in 2001 (Republic of Botswana/ United Nations, 2004). The Second National Literacy Survey 2003 reported a lower literacy rate among males (47%) than among females (53%). An estimated 70 per cent of the population is ethno-linguistically homogenous and speaks Setswana which is the national language, although English is considered as the official language. The other 30 per cent of the population speaks about 28 other languages (Maruatona & Cervero, 2004).

3.3. Study sites

Institutions that conduct pediatric HIV clinical trials in Botswana were used for this study.

3.4. Study population

This study utilized two populations: (i) trial staff directly involved in consent processes for pediatric HIV clinical trials and (ii) parents who had previously provided consent for their children's inclusion in a clinical trial. With permission from the research institutions, a total of 29 research staff participated in the qualitative portion of the study: 11 in in-depth interviews and 18 in two focus groups discussions. The quantitative component of this study comprised a sample of 151 parents of children 0-20 years of age whose children had been enrolled in HIV clinical trials at the selected sites.

3.5 Measures and instruments

A summary of variables and instruments that were used to measure the independent variables is shown in Table 3.1. The study used a triangulation method to allow for a holistic examination of the informed consent process. The triangulation of data enabled comparing of data from different sources. In addition to the instruments used to examine the informed consent process, information gathered from the focus groups were used to support and clarify other findings and were not the source of measurable data itself. Using illustrative examples

from the focus groups helped to confirm and give an in-depth understanding of the methods and practices used in obtaining parental informed consent process at the selected sites.

Table 3.1: Variables measured and instruments used

Variables		Instruments
Dependent variable	Readability of consent form	Readability Calculator
Independent Variables: Consent form Readability	Total Number of pages	Readability Calculator/formulas http://www.online-utility.org/english/
	Total number of words	
	Average number of sentences	
	Average number of syllables per word	
	Average number of words per sentence	
	Reading Ease	
	Reading Grade level	
Independent variables: Trial staff	Demographic characteristics	Consenter In-depth interview & Focus Group Guide
	Perceptions of parent	
	Involvement in consent form drafting	
	Information disclosure methods and practices	
	Facilitation and assessment of understanding	
	Facilitation of shared decision making	
Independent variables : Parent	Demographic characteristics of the parent and child	Face-to Face interview
	Information disclosed	
	Parents' perceptions about information disclosed	
	Manner in which information was provided	
	Information provided	
	Importance of information provided	
	Level of understanding	
	Voluntariness: Choose not to participate, feel pressure to join and knowing that one can refuse or withdraw	

3.6. Sampling Techniques and Sample size

3.6.1 Consent forms

The purpose of analyzing the consent forms using readability formulas was to assess text readability. A nonprobability purposeful sampling technique was used to select 10 pediatric biomedical research consent forms used in HIV clinical trial studies. These studies were categorized as of greater than minimal risk as they were mainly Phase I, II and III trials (Food

and Drug Administration (FDA) 21CFR 50.51, 2001) and eligible for children 0-18 years. These forms had also been approved by the national ethics committee, were registered at the clinical trials registry at http://www.clinicaltrials.gov/ and had been used to seek consent from parents/guardians during the pediatric clinical trials between 2008 -2010. For anonymity the 10 consent forms were coded as CT1 to CT10.

3.6.2 Trial Staff

Two samples were used to collect qualitative data from trial staff securing permission from parents to enrol their children in HIV clinical trials at the four selected sites. The sample was obtained using a non-probability purposive sample technique. Ten (10) of the eleven (11) trial staff who participated in the in-depth interviews were Batswana nationals and one was non-Motswana. For anonymity purposes the country of origin of this participant is withheld. The two focus group discussions were composed of only Batswana trial staff. The inclusion criteria was as follows: Direct involvement in the consenting of parents/guardians, a minimum qualification of a diploma in any medical/Health science field or social-behavioral field, at least a minimum of 1 year working experience in a research environment involving children as research subjects.

A non-probability purposive sampling technique was appropriate to select the consenters because only a few pediatric HIV clinical trials are conducted in Botswana and the country has a few research institutions that conduct pediatric research. The method also helped in the development of explanations from the emerging data during the data analysis process since the qualitative approach was guided by the 'grounded theory'. It was necessary to keep selecting new samples in order to build interpretive theories from emerging data to elaborate on developed theories. The sample of consenters was determined by the data that was being generated. According to Strauss & Corbin, (1998), it is impossible to know how many participants to involve in a qualitative study. A total of eleven (n=11) trial staff participated in the in-depth interviews and a total of eighteen (18) trial staff participated in the two focus groups discussions. The focus group discussion at site A comprised of 8 participants while the one at site B comprised of 10 participants. Only individuals who worked as HIV clinical trial staff and were involved in the seeking of parental informed consent were for recruitment of children in HIV clinical trials were selected.

3.6.3 Parents

Data collected from the parents constituted the quantitative component of the study as described in section 3.1. A random sampling technique was used to draw from a sampling frame of parents who had previously agreed to the enrolment of their children in HIV clinical trials. This technique was adopted because very little is known about the population regarding the practices and quality of parental informed consent process in Botswana; this allowed each parent/guardian to stand an equal chance of being selected and generate generalizable results. The sample size for the quantitative component of the study was calculated as shown below. The parent sample size was calculated according to proportions. Since no such surveys had ever been conducted before in Botswana, a 50% proportion was used in calculating the parent/guardian sample size using the formula below. The sample size was determined using Cochran's sample size calculation formula for categorical data to enable detection of difference at α=.05 and margin of error =.06 (Bartlett, Kotrlik & Higgins, 2001, Israel, 1992)

Sample size calculation

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

$$n = Z^*Z\,[P\,(1-p)\,(D^*D)]$$

P= True proportion of factor in the population, or the expected frequency value

D= Maximum difference between the sample mean and population mean or expected frequency Value minus (-) Worst acceptable value

Z= Area under normal curve correspondence to the desired confidence level.

Assumptions

The sample to be taken must be a simple random or otherwise a representative sample.

Values necessary for calculating the sample size:

The total estimated population of parents that had agreed to enrolment of their children in HIV clinical trials was = 600

An expected frequency (P) of good scores of 50% is recommended for dichotomous variables as it results in maximization of variance and produces maximum sample size (Bartlett, Kortik & Higgins, 2001).

In order to calculate "n", a confidence interval of 6 percent, worst acceptable frequency of 56 percent or 44 percent and confidence level of 95 percent were used.

Value for Z at 95 percent confidence level = 1.960

Calculation for 'n'

P= Expected frequency values = 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= Z*Z [P (1-P) (D*D)]

n= 1.960*1.960[0.50(1-0.5) (0.06*0.60)

n= 1.960*1.960[0.50(1-0.50) (0.0036)

n= 1.960*1.960[.25/0.0036]

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 (600x 0.05= 30), 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 600 participants as follows:

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

S= 267/ [1+ (266.78/600)

S=267/ [1+.444]

S= 267/1.444

S= 184

Out of the calculated sample size of 184 parents, only 151 parents agreed to participate in the study.

3.7 Procedures for data collection

3.7.1. Readability assessment

The readability of the consent forms was qualitatively assessed by means of the Flesch–Kincaid Reading Ease and Flesch–Kincaid Grade Level, using a computer Readability Calculator: http://www.online-utility.org/english/.The software generates scores of the reading ease of the text and the grade level needed in order to be able to understand the text easily on the first reading. Ten (10) copies of coded consent forms CT1 to CT 10 written in English that underwent ethics review and used at least at one of the study sites between the years 2008-2010 were scanned as a Text and Image file then saved as Rich Text File. Each consent form was cleaned for scanning errors and copied separately from the word document and pasted unto the 'Reading Calculator' software space provided. The software automatically generated the readability scores. The variables included total number of pages and words, average number of sentences, syllables per word, and words per sentence, and Flesch Kincaid Reading Ease and Grade level which were used as predictors to calculate the descriptive statistics.

A limitation with using this method of evaluating readability in this study is that all readability calculators are designed to predict an approximate representation of the US grade levels needed to comprehend text written in English which might not be applicable for the Botswana setting. Secondly, readability tests alone may not be the only evaluator of the suitability of text, which is another limitation. Other factors may need to be considered such as the size of type and length of line, sentence structure, the number of words per page, the use of color, the use of diagrams, the page layout, and the use of space between paragraphs (Johnson, 2004). Some words used in the research context do not exist in Setswana or have different meanings.

3.7. 2 Collection of data from trial staff

Qualitative data was collected from trial staff at the selected sites using in-depth interviews and focus group discussions. Informed consent was sought from each of the potential participants and those who agreed to participate signed a consent document (Appendix1). In-depth interviews were conducted by a trained research assistant in English to elicit

information regarding trial staff demographic characteristics; parents' age, education, social economic status, previous research experience and importance of knowledge of culture of parents; information disclosure, parental understanding of clinical trial and decision making. The instrument used for the in-depth interview guide (Appendix 2) contained mostly open-ended questions which allowed participants to freely express their opinions. Interviews were held in each participant's office. Every effort was made to maintain anonymity, privacy and confidentiality during the in-depth interviews. Therefore when reporting the results, trial staff who participated in the in-depth interviews were referred to as *'respondents'*. On average each interview lasted between 45 minutes to an hour. Since all the trial staff work in close proximity to each other and interviews were conducted on different days, there was a moderate risk of bias given that participants would have had the opportunity to discuss interview questions with others who had not yet been interviewed. To the extent that this occurred, it is unlikely that it would have resulted in inaccurate information.

Two focus group discussions were held with a total sample of 18 trial staff using a focus group guide as an instrument (Appendix 3). The focus group discussion at site A comprised of 8 participants while the one at site B comprised of 10 participants. The two groups were small enough (8-10 people), homogeneous regarding demographics, academic qualification (all had attained tertiary education), and all of them worked for research institutions that conduct HIV clinical trials as trial staff involved in conducting the consent process. The homogenisity helped to avoid inhibition of group interaction, assisted in in exploring the topic in greater depth unlike when if the groups were heterogeneous and helped to eliminate idiosyncratic individual characteristics from data. The groups also provided information that met the specific set objectives.

The focus group guide instrument consisted of open-ended questions which created a more interactive environment in which more in-depth discussions about the informed consent process were encouraged. Focus groups were audiotaped and notes and observations were recorded by the facilitators. For anonymity purposes, the trial staff who participated in the focus group discussions were referred to *as 'participants'*. Individual informed consent (Appendix 4) and group informed consent (Appendix 5) were sought from all participants. The focus group guide comprised of open-ended questions that were grouped into five main categories that elicited information on the perceptions of the trial staff about characteristics of parents who agree to child enrolment into HIV clinical trials (age, education, social

economic status, previous research experience and perceived importance of participant's familiarity with cultural background of parents on the consenting process); the drafting of the consent form document; information disclosure, parental understanding of clinical trial and decision making. According to Babbie & Moutom (2005), focus group discussions tend to allow a space in which people create meaning among themselves other than individually.

A trained professional facilitator with bioethics and epidemiology training as well as experience in these fields, and unknown to the participants facilitated the focus group discussions with an observer taking notes. The discussions were audio-taped. The two focus groups were facilitated by the same facilitators and the two groups were coded as A and B for anonymity to ensure confidentiality. Invitations were sent out to participants at all the selected sites. The two focus group discussions took place in separate locations on separate days. Discussions were held in English because all participants were fluent in English. Focus group A comprised of 8 trial staff who were given codes P 1 to P8used to address the trial staff during the discussions and transcribing. However, for reporting the results the trial staff were referred to as participants. Discussions for group A were held in a research setting located in a rural area where the participants worked. Focus group B comprised of 10 participants who worked at urban sites. The participants were given codes P1 to P 10 and these codes were only used to address the participants during the sessions and for transcription purposes but were not used in the write up of the results and discussion for confidentiality purposes. Each session lasted on average one to one and half hours. The discussions started off with introductions, getting to know about the background of the participants, followed by discussions on the documentation of the consent form, information disclosure, parental recall of information disclosed, motivation and voluntariness to participate, and ended with a wrap up in which the participants were thanked and promised to be given feedback about the findings. The wrap up also gave the participants an opportunity to ask questions and give further input. Soon after each session the facilitators verified whether the tape recorders had worked by listening to the recordings, they also noted any major observations made about the discussions.

3.7.3 Data collection from the parents

Quantitative data was collected by two trained research assistants using a slightly modified semi-structured questionnaire instrument adopted from Pace et al., (2005). The research assistants read out the questions to the parents and filled in the responses from the parents. Of the 184 participants included in the sample, 25 did not respond and questionnaires from 8 participants were not included in the analysis because they contained too many missing cases. Before the parents were interviewed, consent was sought from each of them by the research assistant reading out the consent form to them and explaining what the study was about either in English (Appendix 6) or in Setswana (Appendix 7). The questions from the semi-structured questionnaire were read to the parents/guardians who had agreed to participate in the study and had previously agreed to child enrolment in a pediatric HIV clinical trial in a language that they preferred, using either the English semi-structured questionnaire (Appendix 8) or the Setswana semi-structured questionnaire (Appendix 9) by the research assistants. This was in order to enhance understanding and accommodate low literacy levels and overcome possible parental inabilities in read and write. In addition the research assistant wrote down any observations and notes. Every parent participated once irrespective of the number of children she had on the study or number of times he/she visits the site clinic. Each session lasted 30-45 minutes. Participants signed or put a thumb print on the consent form to acknowledge agreement to participation in the study.

3.8. Procedure for Data Analysis

3.8.1 Analysis of Readability Assessment

A sample of 10 pediatric biomedical research consent forms was included in the analysis. The number of pages and words, average number sentences, syllables per word and words per sentence as well as Flesch-Kincaid Reading Ease and Grade Level Scores generated by the Readability Calculator were copied from the computer generated data into Excel sheets. Readability statistics were then calculated including the mean, standard deviation and range. The Flesch-Kincaid Reading Ease and Grade Level Scores were mapped against the corresponding readability levels based on the value scale as shown in Table 1. It is generally understood that texts written for the public should be at 6^{th}-8^{th} grade level (Johnson, 1998). Descriptive statistics were calculated in SPSS and the indicators were compared to the

readability scores using the t-test in SPSS to determine the relationship between the indicator variables was also calculated.

Table 3.2: Interpretation of Flesch Reading Ease score to Readability level

KFRE Score	Reading Ease	Number of years of formal education
0–29	Very difficult	College Graduate
30–49	Difficult	13th -16th grade
50–59	Fairly difficult	10th -11th grade
60–69	Standard	8th-9th grade
70–79	Fairly easy	7th grade
80–89	Easy	6th grade
90–100	Very easy	5th grade

Source: Flesch (1948) and Dubay (2004).

3.8.2 Analysis of qualitative data

Audio-taped data collected from the in-depth interviews and focus group discussions (appendix 13 and 14) were transcribed. The data were analyzed simultaneously as it was being collected. According to Seidel (1998), qualitative data analysis involves noticing interesting things from the data, collecting them and thinking about them. Audio-taped data from twelve (11) separate in-depth interviews and two focus group discussions were transcribed verbatim to generate a record of what each respondent had said. The transcripts were read over and over thoroughly before further analysis to observe trends.

Open coding was done from each of the in-depth interview transcripts using different colour highlighters to generate coding units of analysis or concepts commonly referred to as categories and sub categories. Miles and Huberman (1994, p.56) described coding units as "tags or labels" for assigning units of meaning to the descriptive or inferential information compiled during a study. The categories identified were typed, printed cut out and pasted on smaller cards. These coding units included words, phrases, sentences and or entire paragraphs about, demographic data, observations made during the sessions, and opinions about certain

topics like the consent form, information disclosure, parental understanding and voluntariness. According to Charmaz (1983:112), codes serve to summarize, synthesize, and sort the many observations made of the data, so it is a fundamental means of developing the analysis. Researchers use codes to pull together and categorize a series of otherwise discrete events, statements, and observations which they identify in the data.

Axial coding was performed from the many coding units or concepts earlier to regroup or disintegrate the data by selecting key codes and concepts of interest in order to generate a central scheme. This was done through concept formation and development. Concept formation involved comparison of categories and subcategories generated from open coding to explore differences and similarities across events or occurrences within the data collected. Through this process further codes that emerged were observed and collected. The new concepts formed were further explored in greater depth and incorporated into 'core variable' or main theme which according to (Hutchinson, 1993:193). During this process any codes that were overlapping or irrelevant were discarded. Records had to be read over and over again to generate patterns and the data sequence that could generate concepts of comprehensible patterns. A summary of the process is shown in figure 3.2 below. The transcripts from the focus group discussions were not coded as they were only used to provide examples that supported the readability results, in-depth interview results and parent interviews.

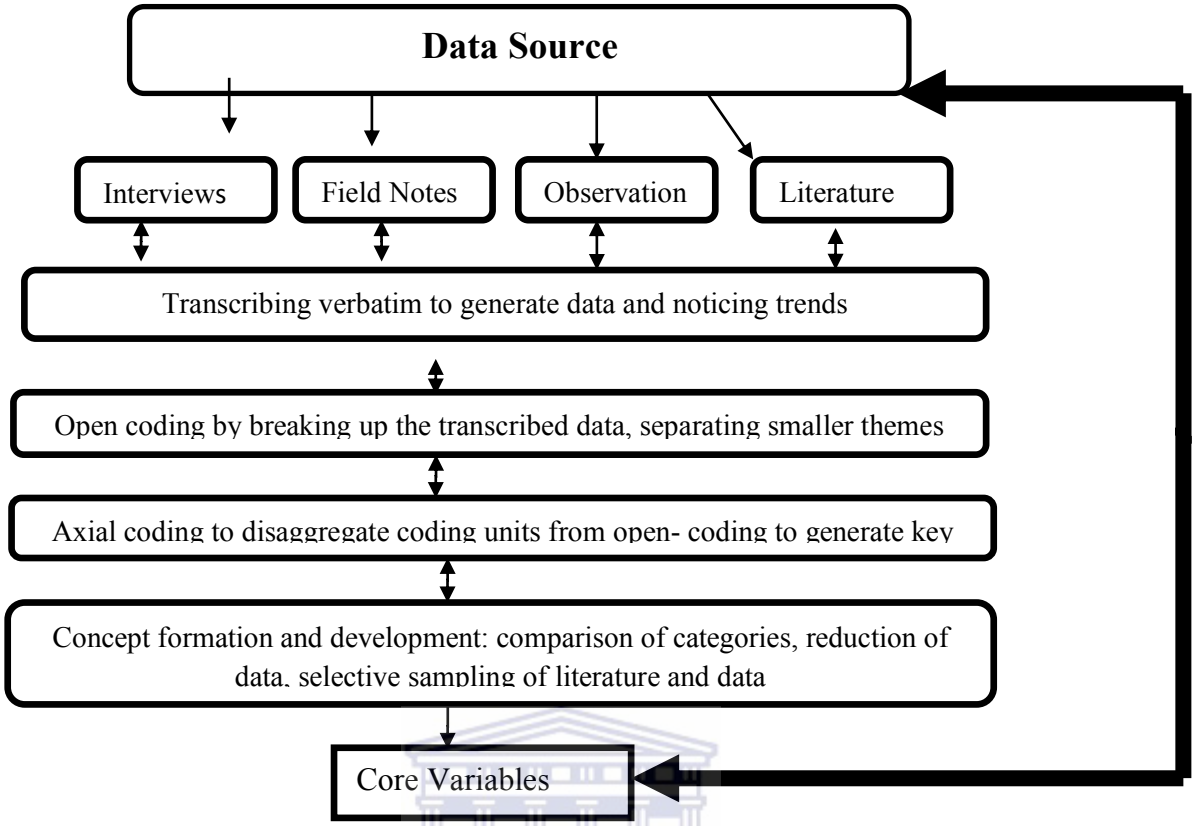

Figure 3.1: Showing connections among data generation, treatment and analysis.

3.8.3 Qualitative data notions of objectivity

- **Trustworthiness**

Trustworthiness is an approach used to clarify the notion of objectivity as it is manifested in qualitative research (Babbie and Mouton, 2005). Trustworthiness of this study was enhanced by ensuring that data collection occurs until saturation occurs. The triangulation methods used in this study ensured that information is collected about the different variables from different viewpoints because different questions were asked, from different sources using different methods. The data was also collected using different materials e.g. audio tapes, observation notes and memos. Consultation with my supervisors and colleagues with experience in the field of bioethics but outside the context of this study was done to review perceptions, insights and analyses. A thorough data check was done to correct for obvious errors.

- **Credibility, dependability and confirmabilty**

Guba and Lincoln, (1984) state that in qualitative research, there can be no credibility without dependability. Credibility refers to the notion of compatibility between the constructed realities that exist in the minds of the respondents and those that are attributed to them (Babbie and Mouton, 2005). Dependability refers to the fact that an inquiry must provide results that if it were to be repeated with the same or similar respondents in the same context, the findings would be the same (Babbie and Mouton, 2005). In order to ensure that the results of this study were credible, the researcher ensured that data was collected both from parents and trial staff until saturation was reached through prolonged engagement. Triangulation methods were also used to enhance validity by combining document analysis, in-depth interviews, focus groups, and observations whose results were compared and contrasted in order to reach as rich a picture of the situation as possible and to increase credibility. Referential adequacy was also ensured by the use of different methods to document findings e.g. audio taping and note making from observations were used. Peer debriefing was also conducted through constantly consulting with experienced scholars in the field of bioethics. These included my former lecturers and colleagues from the international Bioethics course as well as my two supervisors. Credibility was also ensured though continuously double checking the sources of my data and the interpretations that were being generated from data. This allowed correction of errors and assessing the overall adequacy of the data. The researcher attempted to ensure dependability through the use of what Babbie and Mouton, (2005) refers to as inquiry audit. This was achieved through the use of triangulation methods and critically examining the data gathered against the results, interpretations and recommendations to ensure that they are supported by the data gathered. The same technique also ensured confirmability. Confirmability refers to the degree to which the findings are the product of focus of the inquiry and not the biases of the researcher (Babbie and Mouton, 2005).

- **Transferability**

Transferability is the extent to which the findings can be applied in other contexts or with other respondents (Babbie and Morton, 2005). The researcher cannot claim that the qualitative knowledge gained from this study can be will have relevance in another context or could be generalized. Therefore in order to try and ensure transferability, the researcher used

the purposive sampling technique in order to maximize the range of specific information that could be obtained from key informants.

3.8.4 Quantitative data analysis

Descriptive statistics were run for the quantitative data in this thesis. Questions from the 151 parents/guardian interviews were analyzed using SPSS software 16.0. The data were cleaned and analysis was done. Frequencies and distributions were created for all dependent variables. For categorical variables, calculations were made and proportions were compared in each category via Chi-Square $\chi 2$ tests where the observed values were large or Fischer's exact test where the observed values were small. The dependent variables were aggregated outcome measures from the demographic data, information disclosure, understanding/ and perceived voluntariness gathered from the parent semi-structured questionnaire.

The analysis from both the quantitative and qualitative approaches were then interpreted and compared. The mixed methods allowed for confirmation, cross-validation, or corroboration of findings within a single study, and were meant to offset the weaknesses inherent with the use of one method by using strengths from each method.

For validation purposes, instruments used were pre-tested. The researcher's in-depth interview instrument and the parent/guardian semi-structured interview instruments were pre-tested on a few trial staff and parents respectively in order to identify any difficulty with the methods or instruments and to investigate the accuracy and appropriateness of the instruments to be used.

3.9. Quantitative data notions of objectivity

- **Validity and Reliability**

Validity refers to the extent to which an empirical measure adequately reflects the real meaning of the concept under consideration (Babbie and Mouton, 2005). To ensure validity the researcher used a slightly modified semi-structured questionnaire instrument adopted from Pace et al., (2005). The tool was peer-reviewed and pre-tested before being

administered for this study. Babbie and Mouton (2005) refers to the term reliability as a way of ensuring that someone else using the same method in the same circumstances should be able to obtain the same findings i.e. the findings are repeatable . This was achieved by the use of a slightly modified questionnaire that had been previously used in a similar study (Pace et al., 2005). An attempt to avoid threat to validity and reliability was made through the use of an exploratory design since the researcher had limited knowledge about the topic. In addition, use of an already established tool during data collection also helped in avoiding threats to validity and reliability.

3.10 Ethical Considerations

- Permission to review and approve this study was sought from the Health Research and Development Committee which serves as the national research ethics committee of the Botswana Ministry of Health (Appendix 11) and the ethics committee at the University of Western Cape. Permission was also sought from the institutions where data were collected.
- The three (3) research assistants and the two (2) focus group discussions facilitors had Good Clinical Practice (GCP) training.
- Participation was voluntary and informed consent was sought from each parent either in English (Appendix 7) or Setswana (Appendix 8) and each trial staff during the in-depth interviews (Appendix 1) and individual and group consent was sought from each trial staff who participated in the focus group discussion (Appendix 4 and 5 respectively) after full disclosure of information about the study.
- The research was conducted in accordance with the three basic ethical principles, of Respect for persons, Beneficence and Justice.
- Access to the data was restricted only to the research team using a password and backups in different locations will be created to minimize data loss.
- Interviews with trial staff were conducted in private offices and the parent/guardian semi-structured interview guides for the parents were translated into the local language (Setswana). The research assistants were fluent in both Setswana and English.
- Personal identity of the trial staff and parents were kept anonymous. Codes were used in identifying the questionnaires used and addressing the participants during all trial

staff and parent interviews and focus group discussions. Data collected was be entered in a computer and secured using a password.

3.12 Conclusion

This chapter elucidated on the methodology that was followed in this thesis, including the research design, sampling techniques, data collection and analysis methods. The research design was described and reasons for its choice outline. The purposive and random sampling techniques used to select the samples were also described and reasons for their suitability mentioned. Details of the tools used namely; the in-depth interview guide, focus group guide and semi-structured questionnaire were also described in the data collection section (section 3.6). The qualitative and quantitative data analysis methods and their relevance to the study were also described. The study validity, reliably and trustworthiness as well as the ethical considerations put in place to protect the research participants and study sites were also explained. The findings from this study are described in chapter four and five.

CHAPTER FOUR

RESULTS FROM CONSENT FORM READABILITY ANALYSES, TRIAL STAFF IN-DEPTH INTERVIEWS AND FOCUS GROUP DISCUSSIONS

4.0 Introduction

The study investigated the parental informed consent process for pediatric HIV clinical trials with a purpose to develop a model that can guide future consenting processes. This chapter presents results from informed consent form readability analyses, trial staff in-depth interviews and focus group discussions. Results are presented according to the five thematic areas of the informed consent process namely; communication, comprehension, motivation, decision making and voluntariness. The presentation however begins with a summary of the quantitative descriptive data on the informed consent forms that were analyzed (Table 4.1) and the demographic information of the trial staff (Table 4.2) so as to provide background information about the population.

4.1 Summary of the quantitative descriptive data

A summary of quantitative data collected from the ten (10) consent form analyzed and the demographic characteristics of the trial staff is shown in Tables 4.1 and Table 4.2 respectively.

Table 4.1: Summary of the Descriptive statistics of the consent form readability (n=10)

Variable	*Descriptive Statistics*			
	Min	*Max*	*Mean*	*SD*
No of pages	*7*	*21*	*12.7*	*5.293*
No. of words/form	*3224*	*8297*	*5003*	*1714.919*
Avg. No of sentences/form	*162*	*382*	*254*	*0.377*
Avg. No. of Syllables/word	*1.59*	*1.66*	*1.59*	*0.337*
Avg. No. of words/sentence	*16.45*	*24.96*	*21.88*	*2.5729*
FKRE	*41.92*	*57.05*	*50.29*	*4.9253*
FKGL	*9.35*	*13.61*	*11.50*	*1.259*

Overall out of the ten (10) consent forms analyzed the length of the consent forms ranged from 7-21 pages with a mean length of 13 pages. The mean KFRE of 50.9 shows that the reading ease of the consent forms was lower than the standard of 60-69. This shows the text was fairly difficult to read. The mean FKGL of 11.50 also shows that the consent forms were written for higher grade level participants than the recommended 6-8th grade level.

Table 4.2 above shows a summary of the demographic characteristics of the trial staff who participated in the in-depth interviews. The demographic characteristics helped in identifying the information relevant to the process of communicating clinical trial information and facilitated in identification of the adequacy (or otherwise) of the professional qualifications of the trial staff. The mean age of those involved in the in-depth interviews was 40 years. Eight participants were female. The education levels of the trial staff ranged from bachelor's degrees, diplomas and certificates. A number of them had postgraduate qualifications. All the trial staff reported having completed training in Good Clinical Practice (GCP) and the training was done every two years or in some cases each time they started a new study. Some trial staff had more than one type of training in human subjects protection offered either done online or thorough seminars or workshops. All trial staff had some form of pediatric training and experience.

Table 4.2 Summary of the descriptive statistics of trial staff demographic data (n=11)

Variable	*Frequency*
Gender	*8*
Female	
Male	*3*
Age	
30-40	*7*
40-50	*4*
Education Level	
Diploma	*6*
Degree	*4*
Certificate	*1*
****Occupation***	
Research Nurse	*4*
Study Coordinator	*5*
Social Worker	*1*
Medical Doctor	*1*
****Training in bioethics***	
Good Clinical Practice (GCP)	*11*
GCP and CITI	*1*
GCP and workshops	*4*
GCP& Human subjects protection (HSP)	*1*
****Pediatrics***	
Basic training	*9*
Specialization in pediatrics	*1*
Experience in Pediatrics	*5*
Neither training nor experience	*1*

CITI=Collaborative Institutional Training initiative, GCP=Good Clinical Practice training, HSP=Human Subjects Protection
Some respondents had more than one qualification in bioethics and pediatrics
** Trial Staff had more than one of the listed variables therefore the total is more than eleven (11)*

4.2 Communication

Communication process is a very vital first step in the informed consent process where potential participants are provided with full and transparent information to protect them from acts of deception, manipulation, deliberate misdescription of what is proposed, lack of disclosure of material facts, or conflicts of interest as well protection of their rights and welfare. The process also ensures the researcher that the legal and indemnity requirement are

met. During this step, it is important that potential participants also understand the implications of participating in research. Findings on trial staff perceptions about the communication process of the informed consent process are reported under the subsections below starting with results from the readability of the consent forms used to seek consent from parents for child enrollment into pediatric HIV clinical trials.

4.2.1 Readability of informed consent forms

It is on the basis of how readable and comprehensible informed consent forms are that potential study participants are empowered to make an informed voluntary shared decision. The study analyzed the readability of ten (10) informed consent forms. Table 4.3 shows that overall, most (n=7) of the consent forms were longer than 12 pages, the longest being 21 pages implying that they would require a lot time to read and understand. More importantly, the KFRE and FKGL which were used to determine the reading ease and grade level respectively revealed a mean FKRE score of 50.29 ± 4.920 indicating that the forms were difficult to read while the mean FKGL of 11.50, $p<0.001$) indicated that the forms were written at a grade level far higher than the average grade level of the parents who were asked to read them. The FKRE and FKGL scores are however based on the English metrics and so, for second language readers in Botswana, the scores show that the difficulty is far too high.

Table 4.3: Readability scores for the consent forms (*n*=10)

			Readability scores				
Clinical Trial (n=10	*No. of* Pages	*No. of words*	*Avg. No. of Sentences*	*Avg No. Syllables/ word*	*Avg. No. of words /sentence*	*FKRE*	*FKGL*
1	*7*	*3594.0*	*162.0*	*1.6*	*22.2*	*46.0*	*12.35*
2	*20*	*8297.0*	*382.0*	*1.59*	*21.72*	*49.89*	*11.69*
3	*11*	*4001.0*	*188.0*	*1.59*	*21.28*	*50.88*	*11.45*
4	*7*	*3224.0*	*196.0*	*1.59*	*16.45*	*55.92*	*9.55*
5	*7*	*3358.0*	*194.0*	*1.56*	*17.31*	*57.05*	*9.6*
6	*12*	*4663.0*	*205.0*	*1.66*	*21.77*	*44.69*	*12.43*
7	*12*	*4805.0*	*206.0*	*1.54*	*23.33*	*53.05*	*11.66*
8	*21*	*5790.0*	*232.0*	*1.65*	*24.96*	*41.92*	*13.61*
9	*12*	*4958.0*	*241.0*	*1.56*	*20.57*	*53.85*	*10.86*
10	*18*	*7449.0*	*334.0*	*1.59*	*22.3*	*49.73*	*11.86*
Mean	***12.7***	***5013.90***	***234.0***	***1.593***	***21.18***	***50.29***	***11.50***
SD	***5.293***	***1714.919***	***69.862***	***0.377***	***2.5729***	***4.9253***	***1.249***

FKRE= Flesch-Kincaid Reading Ease, FKGL= Flesch-Kincaid Grade Level

A correlation coefficient of r =.995 was found which indicated a strong linear relationship between the reading ease and length of sentences (mean =12.7), average number of words per sentence (mean =21.2) and average number of syllables per word (mean=1.59). The coefficient of determination (r^2) was also high at 99.1%. The overall ANOVA test was significant at $p < 0.001$ and (F=84.006) indicating that the length of sentences, average number of words per sentence and average number of syllables per word had a significant effect on the reading ease of the selected consent forms.

Results from analysis of the different sub-sections of selected elements that appeared in all the 10 consent forms (Table 4.4) showed that the mean KFRE score was 47.8, much lower that the recommended 60 and the KFGL was 11.5 higher than the recommended 6-8th grade.

Table 4.4: Mean scores of FKRE and FKGL of sub-parts of selected key elements of the consent forms (n=10)

Subsection	***Mean KFRE***	***Mean KFGL***
Participant rights	*62.5*	*8.3*
Statement of research	*58.0*	*9.4*
Study procedures	*55.0*	*11.1*
Risks	*50.6*	*11.4*
Benefits	*48.4*	*12.4*
Compensation for injuries as a result of participation in the study	*45.6*	*11.1*
Purpose of study	*44.6*	*12.5*
Payment for participation	*43.4*	*12.4*
Confidentiality	*39.2*	*13.1*
Cost of participation to parent	*31.5*	*13.9*
Mean Scores	***47.8***	***11.5***

4.3 Findings from In-depth interviews and focus group discussions

This section reports the findings from trial staffs' background knowledge about clinical trials, their perceptions about parent demographic characteristics and how these influence the informed consent process are reported. The section also reports about the perceptions of trial staff regarding their interaction with the parents during the information disclosure process; parents' comprehension of information disclosed to them; what motivates parents to enroll their children into HIV clinical trials and their voluntariness to participation in the trial studies. Throughout this chapter, for anonymity, privacy and confidentiality purposes the

eleven (11) trial staff who participated in the in-depth interviews will be referred to as *respondent(s)* while the 18 trial staff who participated in the focus group discussions will be referred to as *participant(s)*.

4.3.1Trial staff background knowledge about clinical trials

Trial staff are expected to have some basic knowledge about clinical trials especially the phases and risk categories in order to be able to conduct a risk benefit analysis to assist the potential participants make an informed choice. At the cost of yielding important benefits, pediatric HIV clinical trials carry significant risks that may arise from the investigational drugs being tested and/or those of social nature like confidentiality and stigmatization. Therefore, during the in-depth interviews, for the clinical trial they had conducted parental consent process for, respondents were asked to briefly explain its Phase and give examples of its risk categories. The immediate response to this question by most respondents was silence and facial expressions of doubt. However majority of respondents reported that they had conducted consent process mainly for Phase II and III clinical trials but indicated that they carried minimal risk as these two answers below show:
For example, answers like the ones below were given:

> "*A bit of risk because we do not know the side effects"*
> *"Low risk because we draw blood, so we prick them but I have not seen any danger"*

The same question about the phases of clinical trials their and risk categories were asked during both focus group discussions and there was silence in both groups, and whispers of not wanting to commit to answering the question which indicated doubt until one respondent asked the facilitator "*How do you categorize your phases?"* Another participant requested for further explanation on the criteria used to determine study *'risk categories'*. In one of the focus groups, participants were adamant that the clinical trials they had conducted the consent process for were all minimal risk given that some of the drugs used were already registered in Botswana with known side effects, or simply involved standard procedures like blood draws. It is clear that trial staff need further education on the issue of risk categories.

To assess the parents' potential to fully benefit from information communicated, the study examines at length how trial staff perceived the parents who enrol their children in the trials.

4.3.2 Perceptions of the trial staff about the characteristics of parents

Since communication involves a receiver, the study sought to establish how the trial staff viewed the recipients of the consenting information, the parents. During the in-depth interviews respondents were asked to comment on the age of parents who agreed to child enrolment into the HIV clinical trials, their education levels, social economic status, and previous research experiences. All respondents reported that the age of consent according to Botswana law is 21 years of age. Therefore only parents that were 21 years of age and above could enrol their children. Any parent below that age needed to be accompanied by someone 21 years old or above. One respondent elaborated as follows during the in-depth interviews*:*

> *"We enrol only children whose parents are 21 years and above because of the Botswana laws' limitation of the age of consent being 21. Those parents that [are] less than 21 have to be represented by their parents or grandparents. Sometimes even those above 21 bring an elder because they are the caregivers. This is very important because they take care of the children in the absence of the biological parents".*

Regarding parent's education level, respondents stated that majority of parents had low levels of education. For instance one respondent commented that:

> *"Majority of parents I see have primary education or junior school, only a few have secondary education and very few reached tertiary level".*

Two other respondents linked low education to the fact that parents reside in the rural areas while one of the respondents expressed a preference for parents with low education and said*:*

> *"I prefer those without much education because those with some education think they know and they give a lot of trouble with adherence".*

However, the general opinion was that the parents have very low education because, according to one, *"those with high education rarely come to our clinics because they can afford to go to private doctors".* More perceptions on the parents' education emerged from the focus group discussions. Several participants commented that the parents they interacted with had low health literacy although this was not elaborated and some even accused parents with high education of not interested in research. Because the point of recruitment was the public health facilities, parents from the middle and high social class cannot be reached because these social classes attend private clinics as one clearly put it:

"Only low to middle income class parents came to the research centres, those from high income class do not come because of stigma".

A participant from one of the focus groups said; *"we go to places where there is high burden of disease where recruitment will be quicker".*

Most focus group participants also perceived the parents as submissive as one respondent from one of the focus groups elaborated:

"*It is very interesting when you talk about levels of education…you find that majority of these people with low social economic status are submissive to the health personnel. The other reason might be that they do not know their rights, they believe that as a patient you have to listen so cannot say no to enrolment of a child".*

Regarding the socioeconomic status of the parents, all the respondents in the in-depth interviews and participants in the focus group discussions reported that majority of the parents came from a low socioeconomic class.

The study also sought to find out from trial staff if parents' previous experience in research affected the informed consent process in any way. During the in-depth interviews most of the respondents agreed that parents that had enrolled a child in research previously easily agreed to child subsequent enrolment and one respondent pointed out specifically that this could be attributed to the problem of possible lack of understanding of the difference between research and treatment (therapeutic misconception) among some parents as expressed below:

"Umm…… not a lot of parents have previous experience in research but I have realized that when I started to be involved in research in 2001 very few parents participated in research but by 2008 a lot of parents knew about research and the research centers. Some even decided to have more babies saying that the research centre will help them [with treatment]*."*

Another respondent observed that parents who had previously enrolled their children in HIV clinical trials showed enthusiasm:

"You find that most of our participants whenever a study they had enrolled their child in closes, most of them will come forward and ask if there are any other studies they can enrol their child in."

To assess whether the culture of a parent had an influence on the outcome of the informed consent process, respondents in the in-depth interviews were asked to comment on the importance of familiarity with parents' culture, values and beliefs before the start of the study. As expected, responses were unanimous that trial staff familiarity with parents' culture, especially language, values and social norms was very important and played a major role in the success or failure of the consenting process. During the in-depth interview the phrase *"very important"* was frequently heard. The five responses sampled below provide the many angles the issue of familiarity with culture can be understood:

> *"Culture promotes understanding of the parent's behavior and reactions, for example those parents who say must go back home and consult, and it is usually an indirect way of refusal".*
>
> *"I think you cannot take out the culture issue because before even any recruitment can start, we have to go through the Chief (Kgosi) of the village and the parents also can ask the trial staff whether they got permission from the chief! I also have experiences where parents admit that their babies are taking traditional medicines. I respect their culture so cannot stop them but advise. The issue of consultation with elders or spouses is also a problem because many parents cannot enrol their children before getting permission from the elders or the spouse. The child belongs to the family and the community because they are all caretakers".*
>
> *"Culture is very important* [passionately emphasized], *especially knowing the local language because it can determine the success of the consent processes. This knowledge helps to get all the details and understand the client".*
>
> *"Very important because HIV issues are delicate some language used can be offensive or taboo to the participant, some participants may even refuse to enrol their children if not culturally respected".*
>
> *"Batswana culture is diverse with different values and norms among people of the north and south, different languages also have a major impact, the way you talk with someone with respect also differs even how you ask how the patient is feeling so respect for persons is expressed differently".*

As these responses show, familiarity with culture involves several understandings: of etiquette in terms of a polite refusal; of protocol in terms of recognizing the Chief first and foremost; of taboos regarding HIV; and of the local language and its dialects and/or varieties. Participants in one of the focus group discussions had a lengthy discussion about the culture issue and yet more understandings of culture emerged:

"I think it is very important because what they believe in or their cultural background would in a very big way influence the decision that they make. For example if you are asking a mother to formula feed, you want to find out the cultural challenges she will face at home and in the society. When you understand that, then both of you are able to know how to work your way around it unlike when you do don't know. The mother will breast feed at home and formula feed only when she comes to the clinic".

"The parents feel involved and respected".

"It helps to understand how many people have an influence on the decision the parent makes. You might be talking directly to the baby's mother but her decision might be influenced by the grandmother. It also helps retention of participants in the study and the participants to give information to other people that are involved in the care of the child".

To summarize, the trial staff perceptions of the parents were examined from a variety of angles. Thus far, the study has identified factors that might affect the consenting process, namely, (i) that the legal age of consent disadvantages some parents (ii) that trial staff awareness of phases and risk categories is lacking (iii) that a rural location, poverty, parents' low education levels, and the inability to distinguish between research and treatment make parents vulnerable to consenting without fully understanding the process involved (iv) that familiarity of trial staff with the parents' culture is beneficial.

The next section will focus on the information disclosure process.

4.3.3 Information disclosure process

Iinformation disclosure was investigated from the point of view of the trial staff because they are the ones who perform this responsibility. The first step in information disclosure is drafting the informed consent document. Therefore, trial staff were asked about their involvement in the drafting process and their responses are presented.

During the in-depth interviews, most respondents reported non-involvement in the drafting of the consent forms except as translators but there was also some indication of unclear involvement in statements such as *"we use the format and contextualize it to the*

Botswana setting" and *"at times if consulted we could change some of the things!"* What came out clearly however, was that consent forms are developed by the researcher who was variously referred to by the respondents as *"the sponsor"*; *"the research team"*; *"the study coordinator and the doctors involved in the study"; or "the institution"*. One of the respondents summarized the process by saying:

> *"the last time I heard about the preparation of the consent document some of the coordinators --- they were translating. To tell the truth they are the ones who prepare the form. Then we have a site meeting where the head nurse and doctors give an input".*

Attention was drawn to the length of the consent forms and trial staff were asked for their comment. In one of the focus group discussions, one of participant remarked:

> *"it's like a book, so we have to read everywhere so the participant can understand to make a decision. Sometimes it can take more than one hour because they ask questions!"*

This was echoed by one participant who added that:

> *"the forms can be more than 20 pages long. But you will find that sometimes most of the pages are about the intervention which at the end of the day you can extract from* [that] *and put it aside and wait for the participant to consent then you can tell them about it. The translated version can go up to 25 pages".*

However, one of the respondents in the in-depth interviews did not see length as a disadvantage because, according to her:

> *"nurses are able to summarize the information from lengthy forms to about 6 pages, a page sometimes. Although they are long nurses with experience know how to pick the most important issues*"

Participants in one of the focus group discussions had mixed opinions regarding the excessive length of the consent form as captured by one of the participants saying:

> *"we are not saying we are happy but what we are saying is that if there could be a strategy that ensures that all the information is included without making it that lengthy".*

This dilemma was elaborated clearly during the in-depth interview as follows where one respondent said:

> *"In my opinion, I think the pages are ok although the package looks bulky. But if someone is at home with all the time to read they can understand. The form is well detailed unlike when you summarize. When you are the one doing the consenting you would understand but*

the potential participant who takes the form home to read would not understand. So may be encouraging the potential participants to read a few pages at a go until they understand would help. I think it is important that they get all the information".

Another respondent concluded the debate on the excessive length of the consent form by resignedly admitting that *"It's long and that is a problem, but it is worth it".*

And finally, a word to the form's readability from one participant in one of the focus group discussions:

"When designing a consent form you need to think of the bigger picture. For example who is going to read it? So if all the information is available in a short form it is ok. I have attended a workshop where we were asked; how long should a consent form be? We never reached a conclusion! Take into consideration all reader's needs".

And a wish to the future generation of researchers by one of the participants in the same group:

"I hope we can find the best way and I am hoping the PhD student will come back and tell us the best way. Because even if it is long, it is how you administer it that matters! Establish what the potential participant needs to know and start with that and take your time!"

The challenge therefore is how to involve the trial staff in the drafting process given their clear understanding that the consent form document is too long.

The information disclosure process was investigated further to identify the effectiveness of the procedures followed. The study sought to identify the communication practices followed and perceptions of the effectiveness of the procedures used for recruiting potential participants, the language used, initial source of information about the study, the quantity and complexity of information disclosed, elements of the informed consent document, and methods used to communicate information.

The most common method reported was the use of recruiters and advertisements in the form of posters and flyers posted at the clinics or other public places. Self-referrals, referrals from public clinics/hospitals, and the use of the investigator's health facility (clinic/hospital) to approach individuals already in their database were also reported. One respondent during the in-depth interview was able to provide a concise summary of the recruitment process:

> *"We hardly use the radio, but we use mainly posters put at the clinics. We also use the patient meetings, wards, antenatal clinics especially in the rural areas. A few patients come as self-referrals from private clinics. We identify a population that is need of ARVs (vulnerable) like the last study we did, we focused on ARV clinics so we were going there in advance to pick clients to talk to them in person or by phone, then we do home visits. Some of those who come to the clinic we get their contacts and some of them are in our database".*

Three (3) other respondents echoed similar recruitment procedures. For example one respondent said that: *"Our recruiters [they] go to the government clinics every morning and they talk to our patients".*

From the discussions it became clear that the primary language of communication was Setswana except in the case of one who reported using English only and mainly provided information to parents by reading the consent form to them. Two other respondents however indicated that they offer parents a choice to communicate either in Setswana or English: *"I talk to the parents in Setswana but some prefer English*, [chuckles] *most educated Batswana prefer to use English."* Another respondent noted the challenge of information complexity saying *"The information provided is complex but we try as much as possible to simplify. It seems Setswana has a way round many English words"*.

A participant from one of the focus group discussions complained about the consent form being translated only in Setswana while there are many other languages spoken by potential participants and argued that this problem needed to be addressed as it compromised parental understanding. Given the sensitivity with which language issues are debated in Botswana (Moeng, 2013), this speaker, quickly dropped the topic saying dismissively, *"use the day-to-day language*, *although I do not know how it will be considered by the national ethics committee, whether they will see it as ethical"*. Another participant captured the challenge of disclosing complex scientific information in a local language and the likelihood of misinformation in the following words:

> *"We do not have some of the words in Setswana, but as long as I tell them what I understand and break down the technical language".*

Majority (6) of the respondents complained during the in-depth interviews that the information given to parents was too much; two respondents rated the quantity as average;

and three said it was enough for the parents to make a decision. However, one respondent observed that having to listen to someone reading to you a lengthy text placed high demands on the parents' listening capability saying:

> *"too much? Yah, you can say they have too much information. When you think someone is here and you are reading a 20 page document, you can't really expect her to understand it all, it's too much information"*

In her own angry utterance below, one participant in one of the focus group discussions dramatized the meaninglessness of too much information and how this leads to confusing parents when she says with a shake of the head:

> *"Um.....to me, sometimes it feels like it's too much and sometimes I feel like we are just confusing her. We are telling the mother, that time when you came for registration, the baby is going to be tested.....then we start telling them…"*

Perhaps due to the respondents' GCP training, there was the reluctant acceptance that the information was *"too much, but necessary and part of the ethical principles"* and that it was *"enough for a person to make a decision"*.

One participant in one of the focus group discussions expressed doubt whether all of the information disclosed was useful to the parents and said:

> *"For a long consent form, about half of it is about drugs, so I concentrate on the section where the participant has been given a drug. Most of them cannot memorize the drug names"*.

As a way to minimize the confusion created by too much information, one respondent suggested making the consenting session as interactive as possible saying "*It's ok because after explaining you allow time to ask question"*.

During the in-depth interviews, respondents were asked the following questions relating to the complexity of the information provided with particular reference to the technical language used:

1. Considering the complexity of the technical language used in the consent form, what standard of disclosure do you use to disclose information to the parents?
2. How do you rate the complexity of the information you provide to the parents?

In response to the first question, the phrase *"all the information"* was heard from seven respondents during the in-depth interviews. In response to the second question, the phrase

"too complex" was echoed nine times implying that the problem of technical language is a real challenge and according to one of the respondents, *"Scientific terms can be very complex and are a challenge to explain".* There was no clear agreement on the accuracy of the translations from English to Setswana, with one respondent admitting that *"sometimes we lose the meaning of certain words when we explain in Setswana"*. Another stated that *"It depends on the study but most studies I have worked on have been very complex, but the translation covers how you can explain".* The issue of complexity of information was also discussed at length during one of the focus group discussions. In an effort to simplify the complex technical terms, one participant said:

> *"we do appreciate that Setswana has the written and spoken type, but we say some English words in Setswana way of translation, local language specialist need to be involved in the translation since the Setswana language has different dialects."*

The linguistic challenge was acknowledge by all the participants as real. It left many of them doubting whether so much technical and complex information was beneficial to the consenting process of a desperate and vulnerable parent.

During the in-depth interviews each respondent was asked to comment about the specific elements in the consent form they found most difficult to explain. Results showed that majority found explaining technical terms like 'randomization' and 'placebo' difficult and for as indicated by one of the respondents: "*It is difficult to bring out the meaning in Setswana",* while another respondent said:

> *"I describe it* [randomization] *as the distribution, but even myself I do not know. I would not say it has no effect because somewhere patients switch their medication to get to know which one works".*

'Risks' and 'study procedures' were elements of informed consent process that were specifically mentioned by several (5) respondents as difficult to explain. The demand to explain procedures clearly according to one of the respondents is *"because that is where most parents base their decision".* Another respondent said, but without explaining how, that she uses analogies for the difficult terms that do not exist in Setswana and added that *"It is difficult to explain, but I have long experience so am able to address most of the issues".* Very few respondents reported that they were comfortable communicating all the consenting elements with one of them outlining how she handles the task thus:

"I do not find any section difficult because I follow the form as it is, may be when it comes to difficult medical terms, I say them the simple way for example 'gastroenteritis' I would say diarrhea".

Another respondent added that:

"*It's not that easy because sometimes you end up using other words. Fortunately some of the parents can read English, so after that we give them the English version to read at home".*

Respondents were quite outspoken during the in-depth interviews about the issue of communication as the following comments indicate:

"To me communicating is not a problem. But many people feel Setswana is difficult to read. There are some other words that are difficult to understand. So to me it's important to master Setswana".

"I communicate to the parents verbally by reading to them in Setswana but the English consent form can be given to them to read during the session".

"*If the study is too long, I tell them by verbally reading but with time am able to give a summary, stop if a client has a question. Most clients are able to read so I encourage them to take the form home and read".*

"You try to explain everything but to a level of the patient's understanding in order to understand each other. These days people are knowledgeable and some have previous experience in research so this helps". [Chuckles]... *We tell them everything in case something goes wrong, we do not leave out any information".*

In the next section the study focuses on what respondents thought about levels of understanding.

4.4 Comprehension of information

Another theme that was analyzed was the perceptions of trial staff on the levels of understanding of the information disclosed to the parent. The next section presents the results from the trial staff's in-depth interviews and focus group discussions.

4.4.1. Trial staff perceptions about parental understanding of information disclosed

As part of assessing parents understanding of the information disclosed, trial staff were asked about their perceptions of parents' initial reaction to enrolling their child into an experimental study. They were also asked if parents understood the difference between research and treatment. To assess parental understanding the trial staff were also asked if parents asked any questions during the consenting process, what methods they used to test levels of understanding, and what they thought was a favorable duration for the consenting process.

Responses given during the in-depth interviews about their perceptions regarding parents' initial reaction to experimentation on their children were mixed. Some of the respondents described most parents as being *'anxious'*, while others said parents were expressionless but appeared frightened. One respondent described the parents as being *"more anxious than when they came"* and *"hopeful"*. Another respondent described the parents as *"mostly initially anxious"* especially for those whose children have never been tested for HIV by saying that *"I think some of them think there is something seriously wrong with the child"*. A few respondents said the parents looked *'ok'*, without elaborating. However, other observations were also made. For example, one respondent observed that *"Some parents are shy because the culture makes it difficult for them to express themselves"*.

Another respondent reported that:

> *"Some parents are happy because of the care they get at the research center. For example no long ques, more privacy and more time with the doctors and nurses. Even after the study closes they do not want to be transferred back to the public facilities".*

One respondent observed that parents from rural areas were eagerly keen on clinical trials and said thoughtfully,

> *"Um… one thing that I have noticed is that those from the rural areas when they hear about a study which is about to start, it is like when should I bring my child'?... it is not a struggle because they also believe in being tested. Also due to shortage of staff at the public clinics, the parents prefer coming to the research centres".*

During the in-depth interviews, the distinction between research and treatment was vaguely made by most trial staff; explanations given were shallow and it seemed as if the trial staff themselves were not really sure whether parental understanding of the difference occurs or

they just did not want to commit themselves. One respondent sounded almost unconcerned saying *"Some do* [understand the difference] *as they have participated in other studies",* while another said "We *try to explain"*. This was echoed by yet another *"Not really but we try until we feel they have understood"*. That trial staff are committed to proper conduct of the consenting process came from this response:

> "*Most of them say am happy because my child will be treated but we continue to explain the difference. We keep reminding them from the beginning that this is research"*.

Only one of the trial staff confidently said *"yes parents understand the difference between research and treatment"* but did not elaborate. From the focus group discussions, came this detailed explanation that conveyed the general perception of the whole group that the distinction is very marginal:

> *"There is a thin line between the care [they] get from the public facilities and the care they can get here such that on referral a parent can say 'I am coming from the clinic because I was told to come', then we ask them, 'do you understand why you are here?' and they respond to say , 'No'. Until you get them to understand that this is a research institution and not like the other clinics"*

Given the respondents' doubts regarding parental understanding of the distinction between research and treatment, we wanted to know how trial staff ascertained whether or not parents understood the information that was provided. It was revealed by all the respondents that the study team is tasked with developing a tool called *"Assessment of Understanding"* which trial staff administer verbally or in writing on every parent who must score above a given minimum mark for their child to be enrolled in the study. One respondent said a parent *"must score 7 out of 10; if lower I re-book them for another session";* but another respondent was less objective and said *"judge from facial expression and gestures"*.

Respondents were asked during the in-depth interviews whether parents asked any questions during the consenting process, and if they did, what the parents' main concerns were; and if they did not ask questions what were the reasons. Six respondents reported that some parents *"especially the educated"* asked questions mostly about the safety of the child, and the benefits, and about the frequency of the visits to the research center. A few asked about compensation for transport, and according to one respondent:

> *"some come when they have made up their mind, they will not even care much about risks. Some do not even consider risks explained as risks and in such cases we experience difficulties with following them up"*

Opinion was divided regarding why parents do no ask questions. One respondent thought the parents do not ask questions often because *"Batswana are submissive by nature. Initially they are quiet but with time they ease up".* Another reason for parental silence which may be attributed to the view that participation would bring benefits was given by one saying:

> *"for now I have not had many of them asking questions because to them they think we are going to help them by testing the babies. Some just want to have their babies tested they would not be intending to participate in the study".*

One respond mentioned that: *"respect and trust for medical personnel and feeling more at ease with nurses than with doctors"* could be attributed to parents' inability to distinguish between treatment and research. It is perhaps for that reason that *"some are just quiet and you will not know whether they are listening or not".* Another respondent explained that the reasons why parents do not ask questions as follows*:*

> *"with the burden of the responsibility over a sick child, parents perhaps develop fear for their children to be involved in research due to lack of understanding and concern about risks; and may be because they are not ready or not sure which decision to make. You may assume that they have understood so you have to check whether they understand but sometimes it is lack of knowledge".*

During the in-depth interviews respondents' opinions were also sought on how long the consenting sessions should last to enable adequate understanding. It became clear that duration varied case by case. For example one respondent said it *"may be one hour but for those who need more time we book them to come another day".* Another respondent reported that:

> *"some come ready to consent or not to consent, so we give them the form to take home and read and give them a time frame when they should come back with an answer".*

However, some respondents reported that the process should be conducted a few times before the parent makes a final decision. For example one respondent said:

> *"at least two to three encounters, usually I try not to make the participant sign at the first encounter. I allow them time to think about the request* [child enrolment] *and consulting with family".*

Two other respondents expressed similar views about the length of the sessions; one of them specifically said that *"depending on the study, I give them choice to come again if they are tired".*

The next section reports findings from in-depth interviews and focus group discussions in response to questions that assessed parental understanding of selected elements of the informed consent process.

4.5 Trial staffs' perceptions about parent's motivation and decision making

In order to understand what motivated parents to make a decision to enrol their children in HIV clinical trials, trial staff opinions were sought on the importance of consulting both parents and relatives of the child even after the person who has brought the child to the clinic has agreed.

All respondents agreed that it was important to consult both parents and other family members, because most parents insist on going back to consult especially for studies that involve drugs. One respondent elaborated that consulting was important for purposes of retaining children in the study. On who exactly the respondents the parents consulted, majority of respondents reported that it was either the grandmother or the spouse or both. Another respondent added that other relatives could also be consulted. However, on whether the outcome of the consultation influences the consenting process, one respondent could not hide her unhappiness and said:

> *"it delays the process but there is nothing you can do. If someone requests I just let them. Another one requested to go back and consult but I had to push because the condition of the child was bad and it needed emergency treatment".*

Another respondent shared similar sentiments echoing the tension that sometimes occurs:

> *"but it delays the process because there might be disagreement on the decision. Some do agree to participate while at the clinic but later come back and refuse to enrol the child".*

Consultation is however beneficial because *"after consulting they come back more relaxed, relieved and comfortable to enrol the children in the study"*.

On how agreement to child enrolment by parents was being indicated, all the respondents said that this is done by signing the consent form. When the respondents were asked about parents' attitude to the signing of the consent form after the lengthy discussion process, one of the respondents said *"parents are happy to sign but some do not want to take a copy of the form with them"*. Several respondents expressed similar sentiments and one respondent

specifically saw the signing as bringing relief to the parent, saying the parent is *"relieved that they will get into the study"*. However, one with long consenting experience noted that:

> *"Sometimes we can tell that the parent is not comfortable with the signing so we can involve a counselor or a senior nurse or doctor to help. Young mothers prefer trial staff of relatively the same age as they are and vice versa"*.

To conclude the interview sessions, trial staff were asked if they had anything they had to say regarding the consenting process. It was interesting to hear them voice their experiences as trial staff in the search for a cure for the disease. For example one of the respondents said:

> *"Some people have realized the importance of doing something about the disease; they see the difference in those who participate. They are hopeful that a cure might come, a benefit that might help other children"*.

Another respondent spoke at length about the cultural practice called 'confinement' which sees a mother having to move to back to her parent's home for more than three months soon after delivery resulting in 'loss to follow-up' and retention in a study. She also spoke about how poverty makes it *"difficult for the parents to afford transport to come for appointments"* and, as also noted by another respondent who spoke about how some parents, due to poverty, spend the transport money given by the centre on other pressing needs and having spent the money, they are unable to show up for follow-ups.

Respondents also spoke about what attracts parents to the research centres and named the good care they receive at the research centre. According to one respondent:

> *"our clients say they get the best care while on study than in public clinics and complain about inadequate public services like shortage of health personnel at the public clinics"*.

Another respondent said *"they* [the parents] *have so much trust in the research centre"*. One attraction for parents that was mentioned is the re-imbursement of transport money which makes the consenting a tactful process for trial staff where for instance, one respondent suggested that *"providing transport money should be mentioned at the very end or after a parent has expressed the need"*. One respondent took the opportunity to speak about the challenge of over-enthusiasm that trial staff sometimes face and said, *"some parents just want to enrol their children without discussion, they already know from friends or recruiters. Some of them will tell you 'You know what I came here for', but we insist on discussing and test for understanding"*. Other challenges were summed up by one respondent:

> *"low literacy levels, too much trust put into health workers, the nature of HIV disease being chronic and with no cure, research not being well*

understood and the implications of signing for research when normal treatment is not signed for".

Another respondent raised the challenges of *"limited understanding of research and science"* and the inadequate *"compensation money* [which] *is too little but the cost of transport has gone up".* Language barrier was also raised as a challenge by another participant saying that *"Setswana is difficult to read even for the Setswana speakers. Also many of the English scientific terms are not in Setswana".* Respondents made a number of recommendations regarding the challenges raised; on delays arising from the parent consulting with other family members, one respondent recommended that:

"Uh!.. I do not know but during the screening the regulations could make it a requirement for the parent to come with a partner or caregiver. Involve everyone who has been in contact with the potential participant in facilitation of understanding and decision making".

This would minimize delays arising from consultations with spouse and relatives. One respondent recommended public education, not just for concerned parents, saying *"sensitize the public about research and its importance".* Many respondents wished to have the consent form shortened and simplified but without omitting vital details and one elaborated thus:

"the consent form should not be too long, it makes the patients stay at the centre for a long time and they get tired or they think about is to be finished with the process and go home. This causes lack of concentration during the consenting process. The patient should be given the summary to take home and read then the trial staff can elaborate during the consenting process".

4.6 Conclusion

Respondents expressed their concern that a lot of legal, ethical and practical challenges still exist, especially therapeutic misconceptions which hinder valid parental consent. However they noted that some parents are getting to understand the importance of pediatric research. They also felt that the care rendered to the parents during the research should be extended to the public facilities to avoid suspicion of undue influence.

The next chapter presents results from the parents' semi-structured interviews.

CHAPTER FIVE

RESULTS FROM SEMI-STRUCTURED INTERVIEWS WITH PARENTS

5.0 Introduction

One hundred and fifty-one (151) parents responded to a semi-structured interview administered by two research assistants over a period of one year. Methodologically, the information gathered from parents through interviews with parents was compared to the information from trial staff during the in-depth interviews and focus group discussions. The presentation of results is according to the five thematic areas of the informed consent process, namely: communication, comprehension, motivation, decision making and voluntariness. The chapter begins with a presentation of the summary of the summary of the descriptive statistics of the parents' and their children's demographic characteristics (Tables 5.1).

5.1 Summary of demographic characteristics of the parents and their children

As shown in Table 5.1, the majority of the interviewees 142(94%) were females aged between 31-49 years. More than 60% lived in rural areas. A great proportion of the parents were single (76%) while only a few of them were married (21%). Most parents, 99 (65.6%), had only completed primary and junior school i.e. 9 years of basic education and were able to read and write131 (87%) compared to only a few 20 (13%) who reported being unable to read and write. Almost all136 (90.7%) the parents preferred Setswana as the language of communication followed by those who 11 (7.3%) preferred English and very few 3 (2%) preferred to communicate in both Setswana and English.

The majority of parents141 (94%) indicated that they were head of household compared to 6 % who reported 'other' as heads of household. A greater proportion of mothers were single parents 113 (76%). About three quarters 79 (58%) of the parents reported that they had paid employment, however most of the jobs cited on probing were in the low-income bracket (e.g. cleaner, farm worker or shop attendant) and so, many of them appreciated the money (Pula.30.00, approximately $5.00) given as compensation for transport. These two comments convey this appreciation:

"*The study was very good because most of the time when coming here I was borrowing money from somewhere"*

"The study was very good because people used to [lend us] money easily while we were on the study but nowadays it is difficult"

Table 5.1 also shows the demographic characteristics of their children. The majority of children who were enrolled in the HIV clinical trials were in the age range of 6 to 15 years 110 (83%) while those who were less than or equal to five years were very few 8 (6.1%). A greater proportion (70%) indicated that they were the biological parents of the enrolled children. Slightly more than half of the children 77 (51%) had previously been enrolled in other clinical trials and about 134 (89%) had been seen in the clinic many times.

Table 5.1: Parents and Children Characteristics who participated in the study (n=151)

Parent Characteristics				
Gender	**Values**	**n**	**%**	**Cumulative %**
	Female	142	94%	94
	Male	9	6%	100
Age (years)	≤=30	25	16.6	16.5
	31-49	98	64.9	81.5
	≥=50	28	18.5	100
Place of Residence	Rural	94	62	62
	Urban	57	38	100
	**Marital status			
*Marital status	Married	32	21	21
	Single	113	76	97
	Widowed	5	3	100
Education	None	13	8.6	8.6
	Primary& Junior School	99	65.6	74.2
	High school	34	22.5	96.7
	Tertiary	5	3.3	100
Ability to read and write	Yes	131	87	87
	No	20	13	100
*Preferred language	Setswana	136	90.7	90.6
	English	11	7.3	98
	Both Setswana & English	3	2	100
Head of household	Self	141	94	94
	Other	10	6	100
Employment	Employed	79	52	52
	Not employed	73	48	100
Children Characteristics				
*Age	≤ 5	8	6.2	6.2
	6-10	56	42.7	48.9
	11-15	54	41.2	90.1
	16-20	13	9.9	100
Relationship to parent	Biological parent	106	70	70
	Other	44	30	100
Previous participation in research	Yes	77	51	51
	No	74	49	100
No. of times child was brought to the clinic previously	Many times	134	89	89
	Few times	17	11	100

*missing data n≤ than 151

5.2 Communication

Parents were asked a range of questions pertaining to communication and the findings are reported under the four sections below.

5.2.1 Parents' awareness of seven basic elements of informed consent

The first element in the informed consent process is disclosure of information about the study so that participants can use this information to make informed decisions. This process provides knowledge or awareness about the study to facilitate understanding. According to Pickard (2007) this knowledge is applied when people remember relevant information. So, parents were asked if they were aware or could recall being told about seven key selected trial elements during the informed consent sessions with trial staff. As shown in Figure 5.1, only129 (85%) of the parents indicated they could remember the purpose of the study while 22 (14.6%) were not aware of the purpose of the study. A higher proportion (95.3%) of parents interviewed indicated that they could remember being told about the risks associated with their child's participation in the clinical trial. Nearly all the parents 148(99%) affirmed they could remember being told about the number of study visits they would have to make during the duration of the study. A large proportion (86.4%) of the parents was aware of the number of times the child would receive medication. Regarding receiving of payment for child enrolment into the study, only 125 parents out of 151 responded to this question, a few, 39 (31.2%) parents could remember being told about a payment while a higher proportion (n=86, 68.8%) indicated that they could not remember.

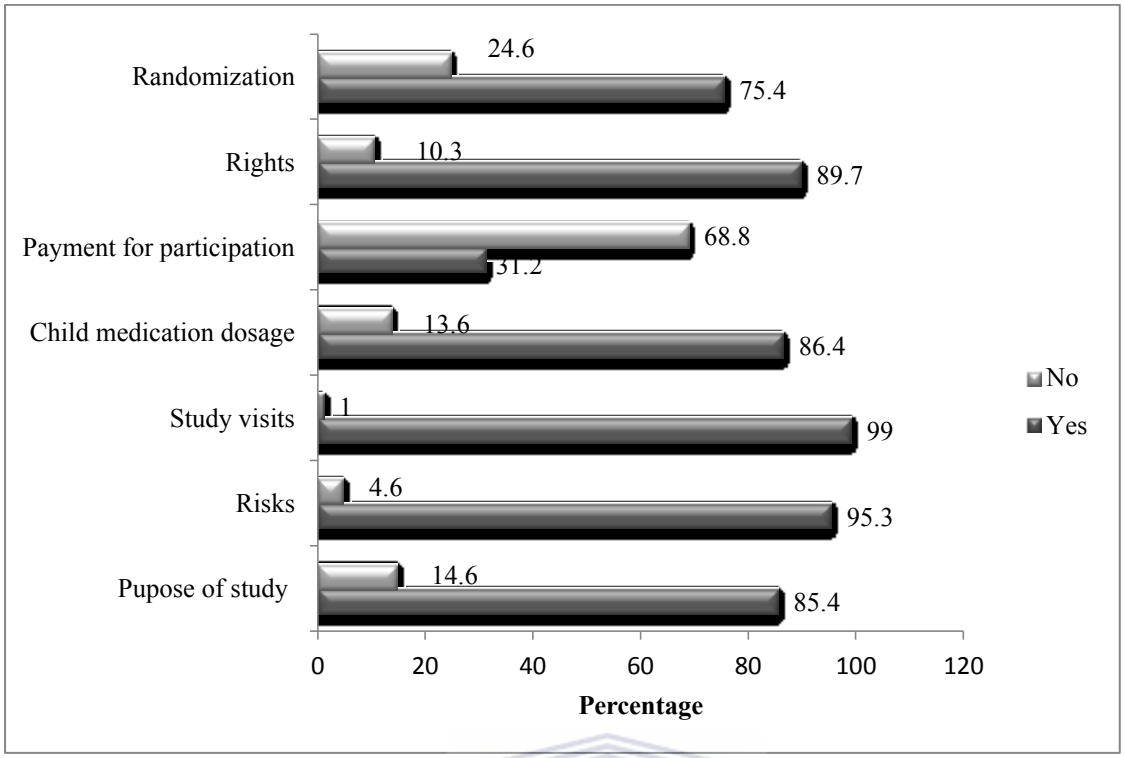

Figure 5.1: Parents' awareness/recall of seven key selected elements of informed consent covered in the studies (n=151)

The number of parents that were aware that they were free to withdraw from the study at any time was high, 122 (81.3%) among the parents interviewed. Out of 140 parents who answered the question about knowing that the doctor would decide which medication would be given to the child, over 75% affirmed that they were told as contrasted with 27 (24.6%) who indicated lack of knowledge of this aspect of the consent form. Although the percentage of those who responded positively to this question was higher it is worth noting that this question was skipped by many parents.

Bivariate analyses showed that age was significantly associated with the parents' ability to remember having been given information about the elements shown in Table 5.2.These included the number of study visits (Fischer's exact; p =0.0248), number of times the child would receive medication (Fischer's exact; p = 0.0470) and that the doctor would decide which medicines to give to the child (p=0.0132). About 98 (75%) of the parents of middle age (31-49 years) remembered most of the elements followed by those who were 30 years and younger (n=25, 61%) while those older than 50 years, 28 (63%) could not remember much.

Parent's previous experience in research was also highly associated with the parent's ability to remember having been told about the risks of child enrolment into the study (Fischer's exact; $p<0.0050$) and how the doctor would decide which medication to give the child ($p< 0.001$). Relationship of parent to the child was also associated with the parent's ability to remember being told about the risks of child participation in the study (Fischer's exact; $p< 0.0490$) and the number of study visits (Fischer's exact; $p< 0.0250$).

5.2.2 Parents' rating of importance of information disclosed

Parents' perceptions were sought regarding how important the information that had been disclosed to them was for decision-making either as '*Important', and 'Not Important'*. Figure 5.2 shows the results. A total of 147 parents responded to this question. The elements that parents considered as '*Important'* for decision-making were knowing why the child had to be enrolled in a study, 132 (89.8%), knowing the risks of enrolling the child in a clinical trial, 141 (96.0%), the number of clinic visits during the study, 142 (96.6%), the number of times the child would be receiving medications135 (92.0%) and that the doctor would decide which medications to give the child 111 (75.5%). Surprisingly being told about whether the parent would receive compensation for child enrolment into the study (n=49, 33.0%) and freedom to withdraw child from the study any time (n=88, 60%) were not considered as important by quite a number of parents.

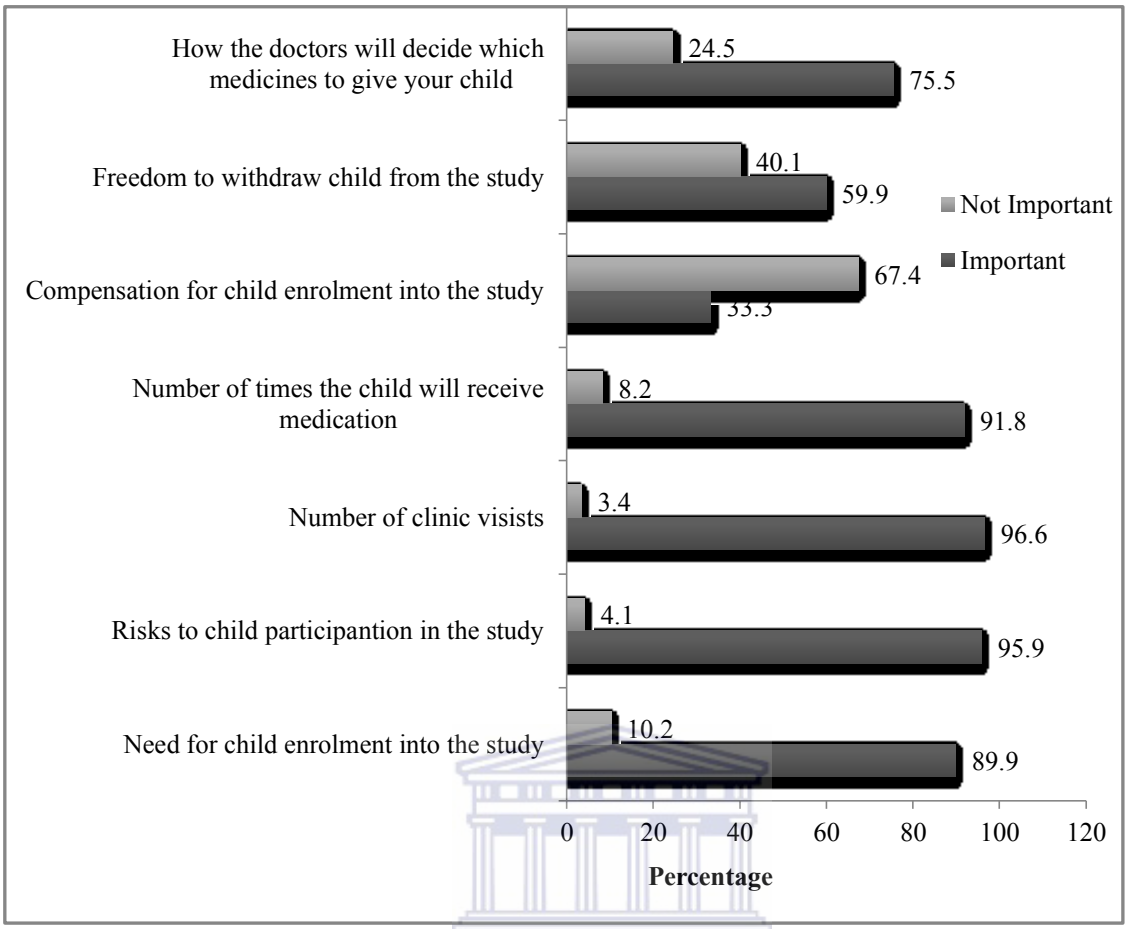

Figure 5.2 Parental rating of importance of information provided for decision making (n=147)

In a separate set of questions, 151 parents were asked whether the information disclosed to them had influenced their decision making as to whether to participate in the study or not. Overall all 148(98%) of the parents felt that the information disclosed had been very important for decision-making and majority of them 149 (99%) reported that they had been satisfied with the information that was provided. Furthermore, overall all 149 (99%) the parents reported that during the consenting sessions, they felt the trial staff were very honest, caring and sympathetic 149 (99%) and were knowledgeable about the study 148 (98%). However, quite a number 83 (55%) also felt the trial staff were being persuasive.

5.2.3 How well-informed parents were about the seven key selected trial elements

It is important that research subjects are well-informed before undertaking important decisions concerning their lives or those they legally represent. In order to assess how well-

informed the parents were about seven key selected trial elements parents were asked using a "yes"-or-"no "responses. The findings are shown in Figure 5.3.

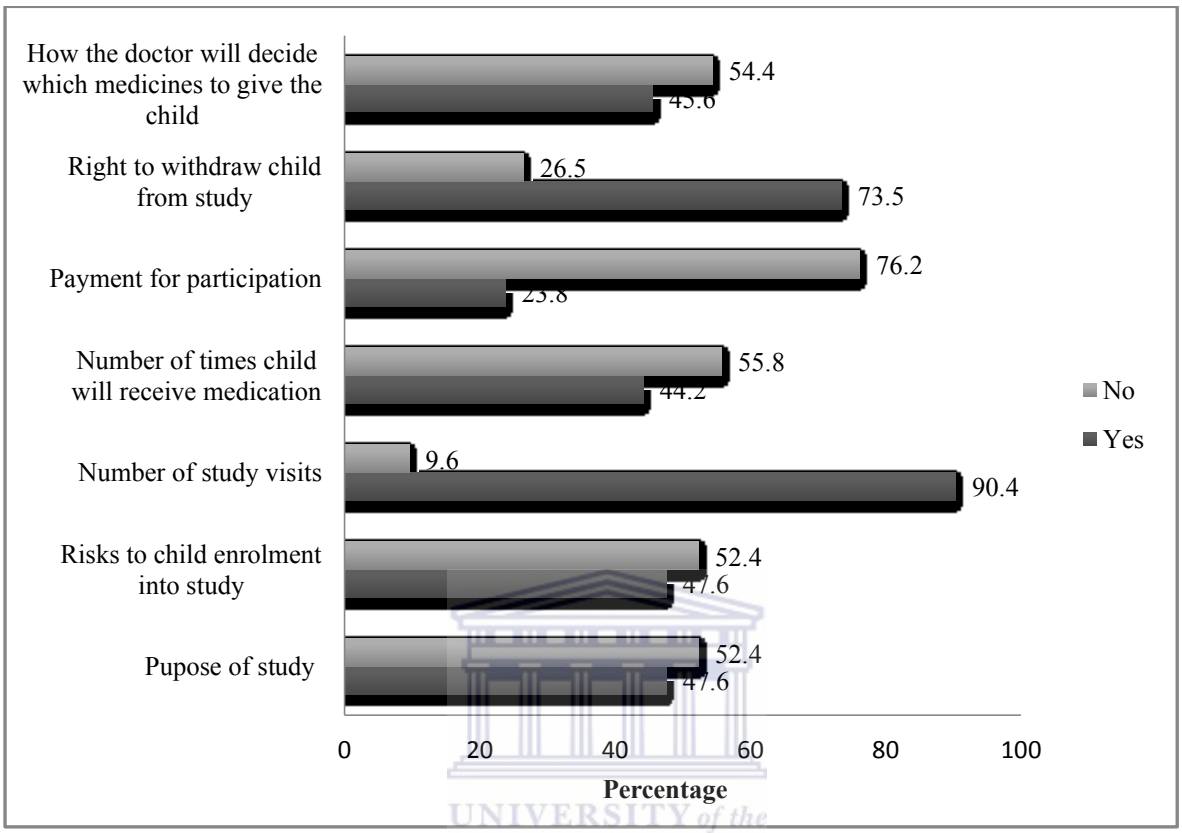

Figure 5.3: Responses from parents about how well informed they felt about seven key selected trial elements (n=147)

Overall the results in Figure 5.3 showed that slightly more than 50% of the parents did not have a full recall of most elements. For example, 52.4% of the parents reported that they were not well-informed about the purpose of study, while 55.8% reported that they were not well-informed about the risks of enrolling the child into the study, the number of times the child would have medication. Another 54.4% reported that they were not well-informed about how the doctor would decide which medications to give the child. However a larger percentage of the parents reported that they were well-informed about the following elements; the number of study visits they would need to make to the clinic during the duration of the study (90%); not being compensated for child enrolment onto the study 62% and 73.5% reported they were well-informed about their right to withdraw the child from the study anytime.

5.2.4 Parent-Trial staff interaction process

Parents' perceptions about how the trial staff conducted the information disclosure process were sought from the parents. Results showed that the majority136 (92.5%) of parents preferred to communicate in the local official language Setswana. The parents were also asked about the first contact person who talked to them about the study. Out of a total of 151 parents, 138 (91.4%) said 'nurses' while 12 (7.9%) said 'doctors' and 1(0.7%) said 'friend'. Regarding the reading of the consent form, parents were asked whether they had read the forms by themselves or someone read it to them. A majority, 71(47.6%) indicated that they had read it by themselves, followed by 43 (28.9%) who responded that they had read some sections on their own and were helped by others to read some of the sections. Some of the parents 31 (20.8%) indicated the form was read to them by the trial staff while very few 4 (2.7%) indicated the form had been read to them by a family member. Unfortunately details of when and where the reading occurred were not asked for. When asked how much time they had taken to decide on child enrolment, majority 126 (84.5%) reported that they had agreed the same day that they were approached for consent, while a few23 (15.5%) reported that they had taken some days to decide. Some of the parents did not answer this question.

Using a format of "yes"-or-"no" response questions, parents were also asked for their opinions about how the consent process was conducted. Overall the results in Figure 5.4 show that the majority of parents were happy with the way the informed consent process was conducted. The majority 124 (91.1%) felt the explanation about the medicines the child would receive was clear. Quite a number 109 (73.2%) were of the opinion that the information provided had difficult medical terms but they were clearly explained. Regarding testing for understanding, almost all the parents agreed that they had been tested for understanding 148, (98%), were given an opportunity to ask questions 148 (96.7%) and they did ask questions 146 (96.7%). Overall almost all the parents 149 (98.7%) reported that they were satisfied with the interaction process and many of the parents 148 (98.7%) were of the opinion that that the information provided had been very important for deciding on child enrolment into the trial.

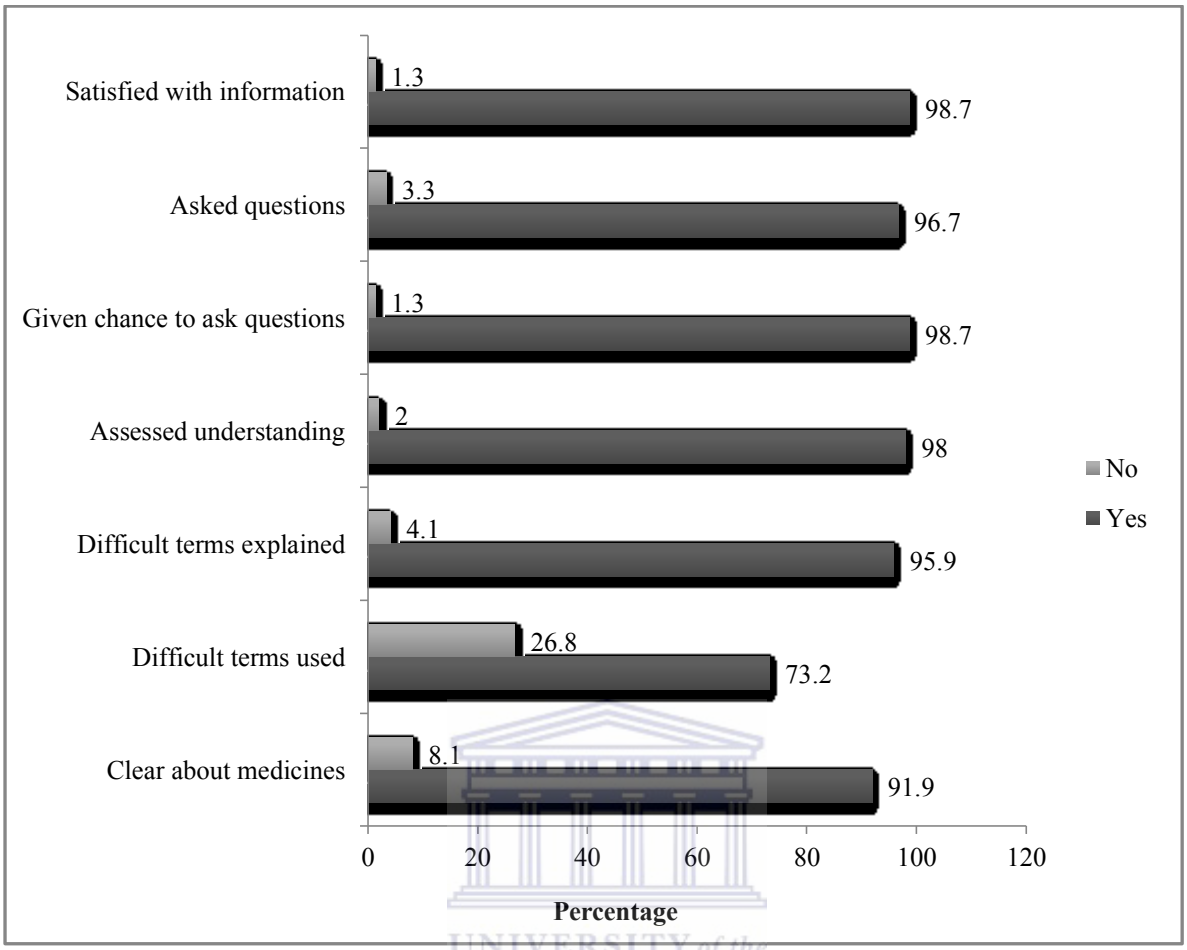

Figure 5.4: Parents' self-report of how the information was disclosed (n=149)

It appears that the information disclosure process went well if the responses from the majority of the parents are to be believed. To verify the extent to which the responses were credible, the study further investigated parents' comprehension as reported below.

5.3 Comprehension

Parents' retained comprehension of the information disclosed was assessed using a set of "true/false" statements about each of the key elements of the informed consent process namely; purpose of the study, study procedures, alternatives to not enrolling child in the study, study risks, randomization and confidentiality. The process involved reading to the parents a set of statements about each of the key selected elements of the informed consent process to ascertain whether they could recognize if a statement was "True" or "False".

5.3.1 Parents' retained comprehension of the information disclosed

Figure 5.5a shows the results from 5 statements describing the purpose of that study in which the parent enrolled the child. Overall a great proportion of the parents correctly recognized that the main reason for their child's enrolment into the study was not to receive treatment (86%), find out which drugs were cheapest (65%) or improve the treatment of future HIV patients (97%) but to test the safety of a new HIV drug (77%) and to find out which medicine works best in order to help future HIV positive children (58%). Overall three out of the five questions (60%) were answered correctly.

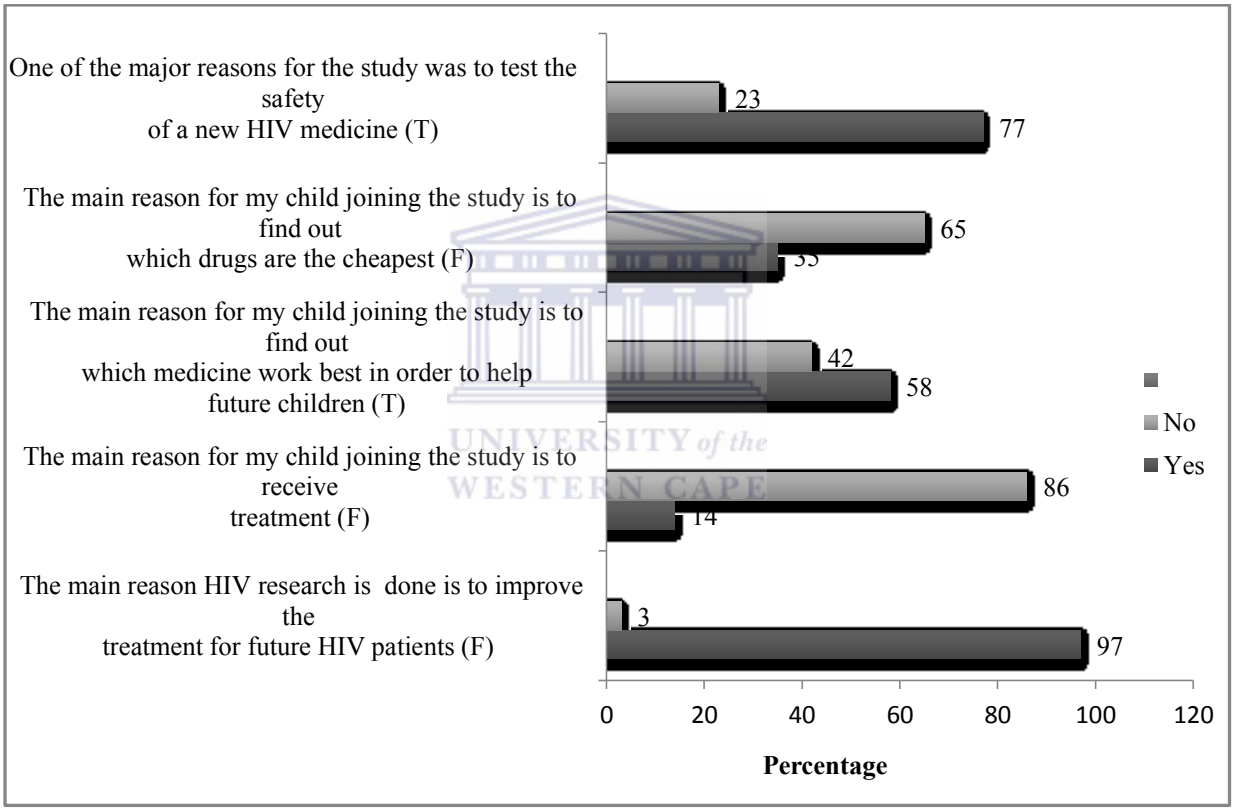

Figure 5.5a: Parents' comprehension of purpose of the study (n=149)

Questions were asked about the non-scientific methodology procedures namely; withdrawal of child from study any time by the doctors, number of study visits and the duration of the study (Figure 5.5b). Out of the 148 parents who answered the questions, the majority 137 (92.6%) could recall that the child could have been withdrawn from the study anytime and the number of times they would bring the child to the clinic 135 (91.8%). However many parents 115 (77%) were not sure of how long the child's participation in the study would last.

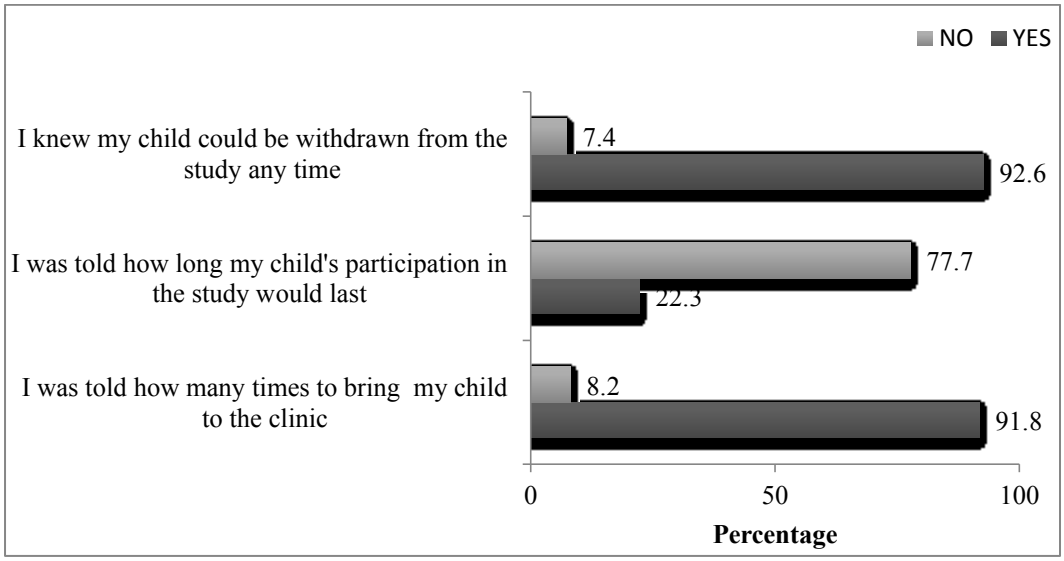

Figure 5.5b: Parents' comprehension of information about non-scientific methodology study procedures (n=149)

Comprehension of scientific methodology procedures like randomization process and placebo use were also assessed (Figure 5.5c). These included how the doctors decided which medicines to give each child and which type of medicines children had received.

Regarding how the doctors decided which medicines to give each child, responses from a good proportion of parents (79.1%) indicated that parents could recall and had understood that the doctors decided which medicines to give their child based on chance while 81.8% could recall that the medicines given to according to the choice of the parent. However more than 50% indicated that the choice of medicines was based on what was best for the child.

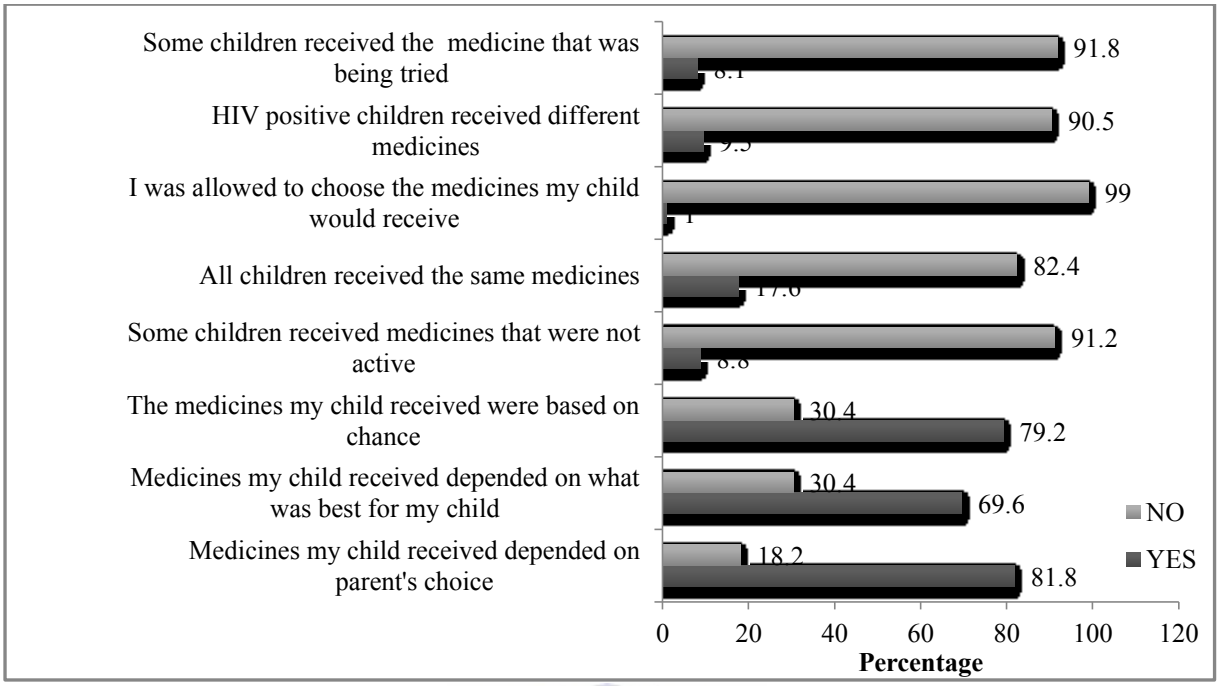

Figure 5.5c: Parents' comprehension of randomization to interventions (n=149)

A large proportion of parents (90%) affirmed that the doctors did not allow them to choose which medicines were to be given to their child. Although most parents 122 (82.4%) understood that all the children had not received the same medicine, and 134 (90.5%) parents knew that HIV positive children had not received different medicines as all the children were HIV positive, results showed that most parents had a poor understanding of how the medicines were allocated to the children. For example, 135 (91.2%) parents did not correctly indicate that some children were supposed to receive medicines that were not active and 137 (91.8%) could not recall that some children were to receive medicines that were being tried. However, of concern was the large proportion (69.9%) of the parents who responded that the choice of medicines was based on what the doctors thought was best for the child.

Parents' retention of comprehension was also assessed regarding their rights to child's enrolment into the study using a set of five "True or False" statements. Results showed that majority of parents could recall their rights regarding child enrolment into the study. For example Figure 5.5d shows that a large proportion of the parents could recall that:

- child enrolment was voluntary (88.1%),

- they could not have enrolled the child into the study without signing or putting a thumb on the consent form (88.5%),
- they could have withdrawn the child from the study anytime (92.5%), and that
- their child could have still been treated at the clinic even if they had refused to enrol the child into the study (91.2%).

However, only 12 (8.1%) parents could recall who would be responsible for payment of research related injuries as opposed to 136 (91.9%) who indicated that they had not been told about this and 54 (36.5%) who indicated that they did not know.

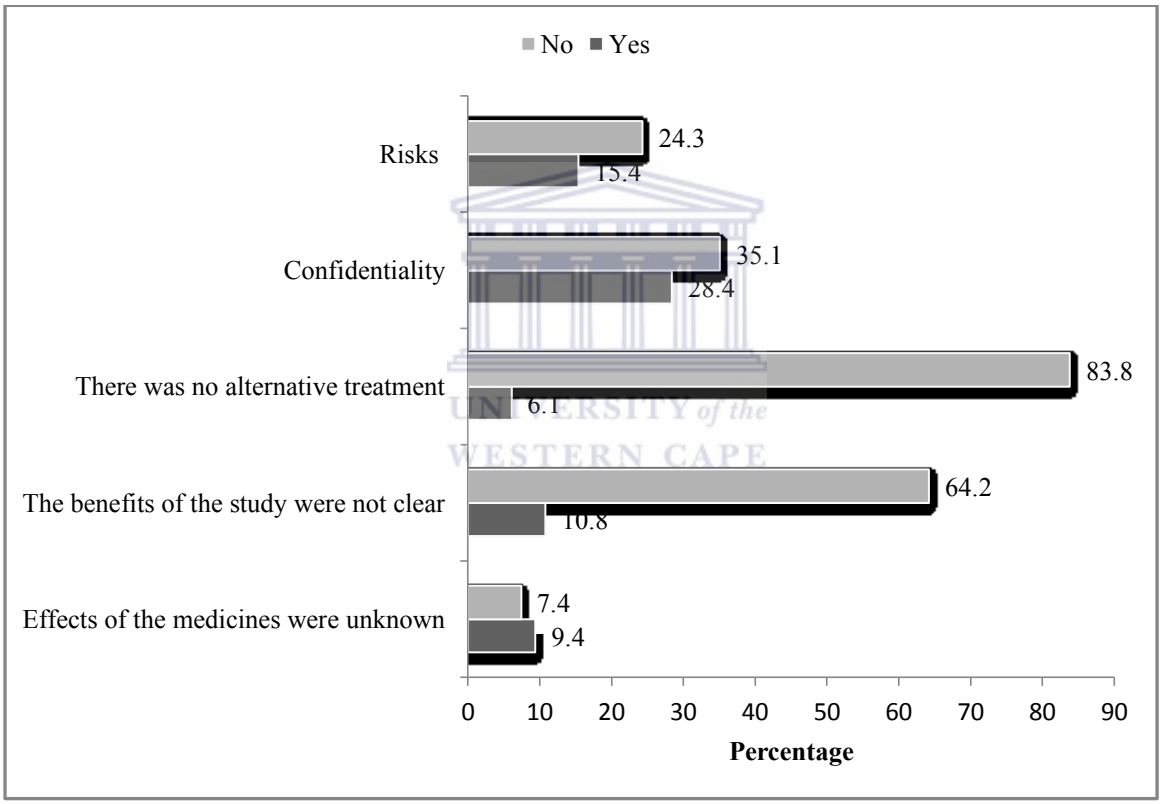

Figure 5.5d: Parents' of comprehension of their rights (n=149)

Parents' retention of comprehension of the elements of confidentiality, risks, benefits and alternative to not participating in the study were also assessed. Figure 5.5e shows that parents overall only a few parents 41 (28%) could recall that other trial staff not involved in the study might be allowed to look at their records and there was a risk that the medicines given to the child having life-threatening effects on the child 22 (15%). However, 95 (63%) of the parents retained an understanding that the benefits to the child of participation were

uncertain and 124(82%) could recall that there were no alternative drugs available to their child other than through participation in the study.

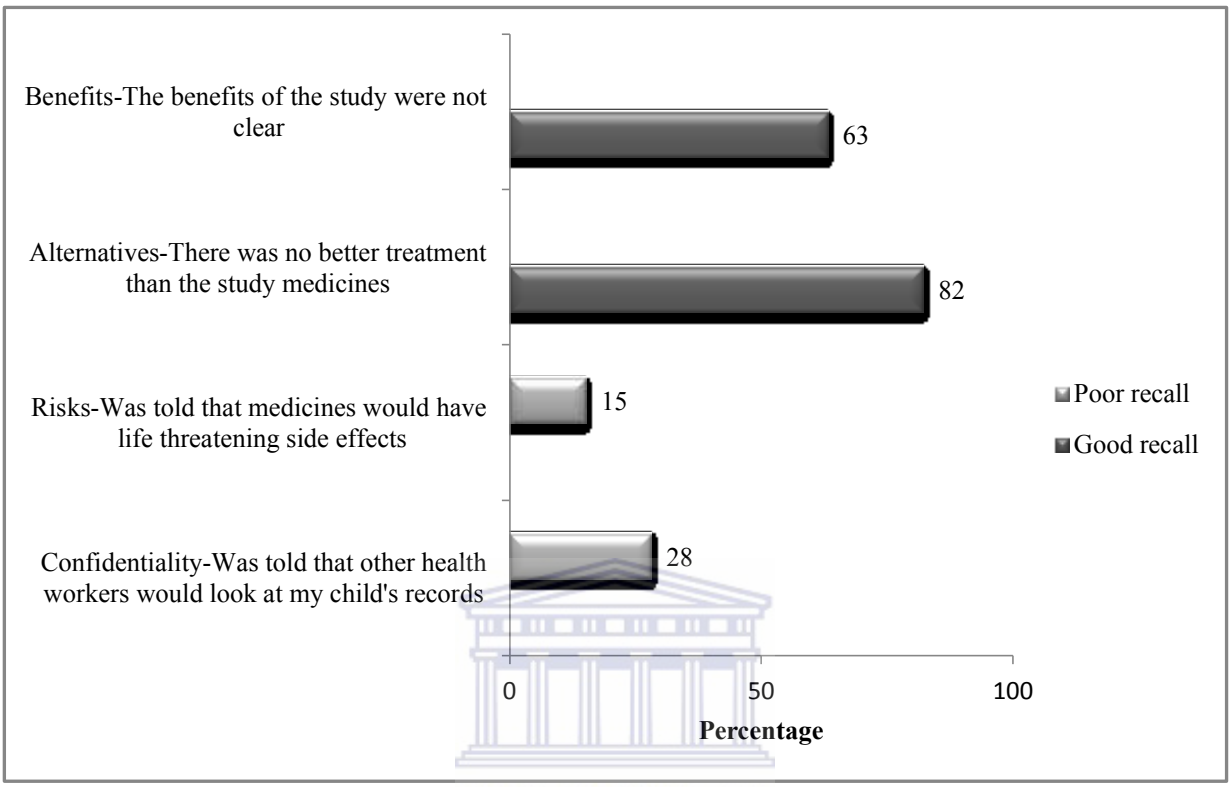

Figure 5.5e: Parents' overall compression of the elements of confidentiality, risks, benefits and alternatives (n=149)

A summary of overall understanding of the groups of questions that were asked about each element is represented in Figure 5.5f below.

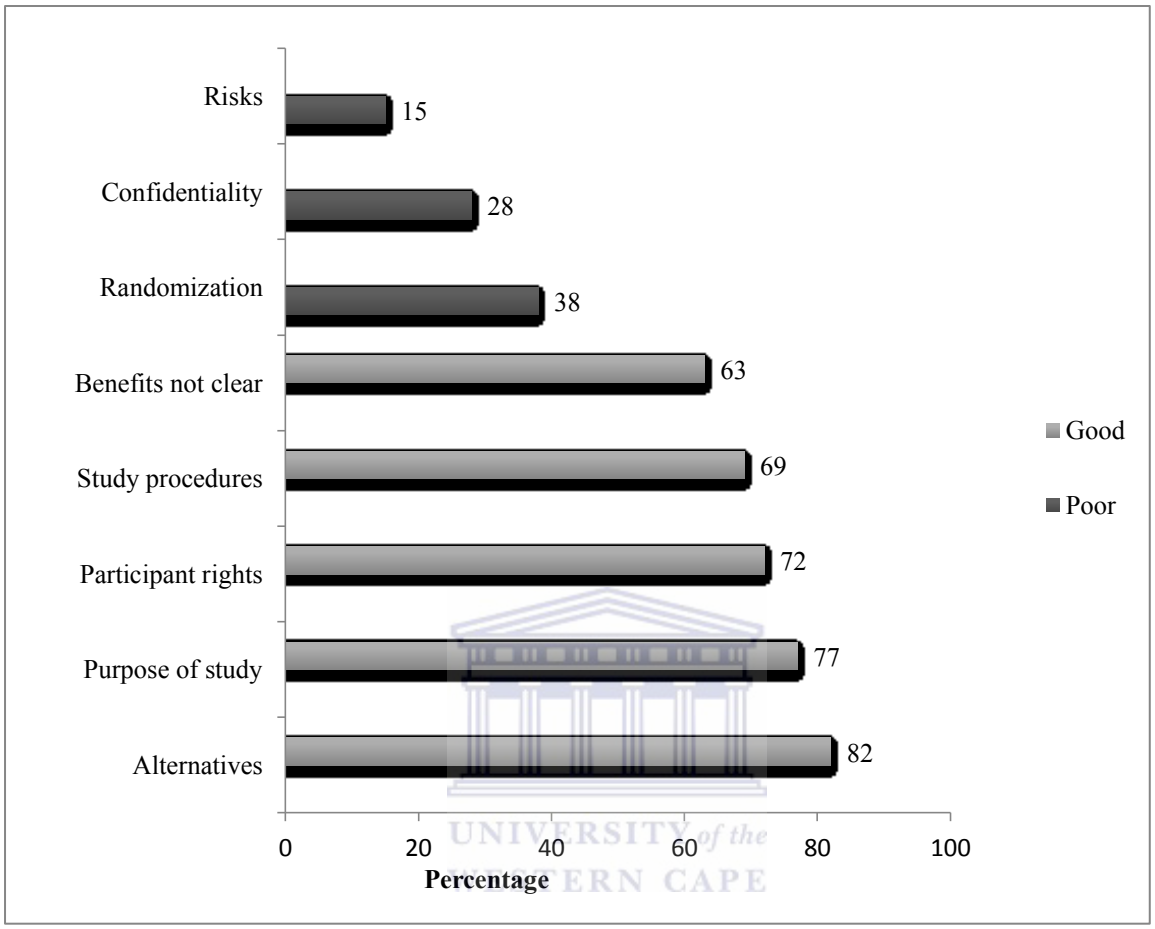

Figure 5.5f: Parents' overall retention of comprehension of selected elements (n=149)

Overall the majority (82%) of the parents had a good retention of comprehension of the fact that there were no alternative treatments for their children's condition other than participation in the study. Likewise, a majority (77%) of the parents had a good retention of comprehension of the purpose of the study, their rights (72%) and the fact that benefits of the study were uncertain (63%). However, fewer parents were able to recall the randomization process (38%), confidentiality of records (28%) and the risks of enrolling the child (15%).

5.4 Parents' motivation to enrol child into the study

In order to examine the motivation to enrol their children in the HIV clinical trials, parents were asked to name the most important reason behind their decision to enrol their child into

the study. Over 65% of the parents indicated that they had been motivated by the 'illnesses of the child, while 32.9% were motivated to *'help'* future HIV infected children. Asked whether they would have joined the study if they had not been paid Pula 30.00 (approximately $4.00), majority, 129 (85%) said that they would still have enrolled their child.

In order to double check the answers that had been given for motivation, parents were also asked whether or not they had been pressured by any other person to enrol the child into the clinical trial. Majority, 147 (97%) responded that they had not been pressured by anyone. Even when they were directly asked who put pressure on them to enrol their children into the study, a large proportion (98%) said that they had not been pressured either by the doctors, trial staff, health facility workers, spouse, family or anyone else. However, when asked about how much pressure they felt themselves to join the study because of their child's illness, more than 65% indicated that this had been a major consideration.

5.5 Parents' decision making and voluntariness

The majority (n=136, 91%) of the parents reported that they had made the final decision to enrol the child into the trial by themselves. The rest of the parents, 13 (9%) reported having been assisted in the decision-making process by the spouse, trial staff, or doctor. Bivariate analyses showed that decision making was significantly associated with the numbers of clinic visits (p= 0.0400), previous experience in research (p=0.002), being a biological parent (p=0.0599) and being paid for participation in the study (p= 0.011).

Regarding voluntariness, parents were asked whether they could have refused to enrol the child in the study if they had wanted to. Majority of parents (n=107, 70%) responded they could not have refused mainly because of their child's illness and because they had been told that they had a right to enrol or not to enroll the child. Some of the comments by the parents at the end of the interviews indicated that they had decided to enrol the child even before they were talked to by the trial staff also some comments indicated an obligation to help future children and others explained that it was because they had understood the study purpose. There were also reasons given by individual parents like "wanting *to know the results from the tests that were done"; 'guilt'* (my child would have seen clearly that I have refused); one

parent said *'they' were not allowing that*" and another said it was because of *"the trust they had in trial staff"*.

On a scale of *'very easy', fairly easy', fairly difficult' and 'very difficult',* respondents were asked to rate the ease with which it would have been difficult to refuse. Out of 151 parents, 147 responded to this question. Only a small proportion (37%) felt it would have been very easy, while 35% felt it would have been fairly difficult, 28% felt it would have been fairly easy while another 8% felt it would have been very difficult.

Regarding how the parents indicated agreement to child enrolment into the clinical trial, a large proportion 89%) did so by signing of the consent form, while 11% put a thumb print on the form. Asked whether they would have preferred to consent by just talking to the doctor or signing on the form, a large proportion (98%) preferred signing the form rather than agreeing verbally. Unfortunately the reasons for this were not asked. Finally the parents were asked how much time it had taken them to decide to enrol the child into the study. The majority 126 (83%) of the parents reported that they had decided the same day while a few, 23 (15%) indicated they had decided a few days after being talked to by the trial staff.

At the end of the interview parents were given an opportunity to comment on the entire informed consent process. Table 5.2 shows the comments that were made by the parents. These comments seem to suggest that parents of children with threatening chronic diseases may view research as a form of treatment. For example a number of parents reported that they wished the study that their child was enrolled in could be repeated as their child had improved a lot during the study, received better drugs than what is offered by the public clinics and some reported that they did not notice any drug side-effects.

Table 5.2: Some of the comments made by parents at the end of each interview

Comments from some parents about the trials
"I joined the study because they had better drugs than the national program. For example the tablet … was only given to children on the study"
"I wish it can repeat again our children are always asking that"
The study was very good, I wish they can repeat"
"I want the study to repeat because we were treated special and the child was seen by the doctor every month to see progress
"The study was very good I wish they can repeat it again"
"I think this study could continue again
"The study was very good even the side effects that were mentioned are not there"
The study was very good because my child did not experience any side effects which I was scared of from the beginning
"My child did not have any side effects she was as normal as everyday"
"Since joining the study my child' health improved a lot"
"When I joined the study my child was very sick but afterwards she improved"
"The study was very good it helped the child a lot
"I managed to learn more about HIV when I was on the study"
"We ended up knowing a lot about ARVs since joining the study"
"The study was very good because they were teaching us everything"
"Because I had already decided to join"
"I think there is hope that medicines will be seen soon"
"The study was very important to the nation"
"If that study was there in 2001, my child would not have died"

These statements raise questions regarding understanding of the information disclosed during the informed consent process, the difference between research and treatment and the voluntariness of informed consent by such parents.

In summary the findings seem to show that despite the high recall of most of the information disclosed to parents, retention of comprehension of information is mainly focused on the benefits linked to care the child would receive from participation in the study.

CHAPTER SIX

DISCUSSION

6.0 Introduction

The purpose of this study was to conduct a holistic analysis of the parental informed consent process for child enrolment in HIV clinical trials in order to develop a model that could be used to guide the consenting process in Botswana. The study was accomplished by (i) analyzing the readability of the consent forms (ii) examining trial staff communication methods and perceptions and (iii) assessing parents' experiences of the consenting process. The discussion is formatted around themes that emerged from the findings.

6.1 Trial staff training

Since skills are central to the consenting process, this section discusses the training of trial staff. All trial staff who participated in this study had adequate and relevant tertiary education mainly in the nursing field. They also had informal basic training in human subjects' protection which was either in the form of online GCP, CITI, short workshops or seminars. Despite this training, trial staff seemed to lack theoretical background knowledge in one critical area, namely the clinical trial phases and their risk categories. It was quite clear that trial staff did not apply this knowledge during the informed consent process which was unexpected. It is well documented that clinical research carries significant risks in hopes of yielding important benefits, thus posing the most complex ethical dilemmas (Slack et. al., 2000, p.291). Most importantly, international research guidelines recognize that clinical research is ethical only when the risks to participants are reasonable (CIOMS, 2002) Appropriate implementation of this requirement is vital to protecting research participants and allowing research to proceed when it poses acceptable risks. Therefore, this study argues that clarity on risk categories of clinical trials according to their phases is important in communication of risks to potential participants and risk/benefit analysis by the trial staff.

This would require comprehensive training that offers intensive curricula and practical skills which are universally recognized. An important finding that emerged about the occupations of trial staff was that conducting the consent process was not a specific job; all trial staff had other full time roles and responsibilities to perform. Multiple roles could imply unspecified job descriptions, resulting into inconsistency in matching job titles with responsibilities, authority, as well as lack of clarity in the professional career position. Performance of multiple roles could also imply additional constraints of long working hours, multi-tasking, split attention and job burnout. Meyer & Partners, (2009) also argue that vague or ambiguous job titles can result into lack of confidence, authority, recognition, motivation, commitment and specific job satisfaction. It is important for an employee's job title to reflect their responsibilities and scope of authority. Adopting a common job title would help in role classification and maximization of potential. This study recommends that research organizations consider having a position and job title like 'Research Consenter' for trial staff who deal specifically with conducting the consenting process. The responsibility of such a person would include the adhoc job titles reported by trial staff in this study such as recruiter, research nurse, and study coordinator. This approach would substantially improve knowledge in clinical trials, research ethics and communication skills which were identified as challenges for trial staff in chapter four.

6.2 Communication

Studies of consent form readability (LoVerde, Prochazka & Byny, 1989; Johnson, 1998) have shown that when this information is disclosed using a written informed consent document, the readability and comprehension of the text is very critical for conveying study information to enable a potential participant to arrive at a decision concerning their willingness to participate in research studies. A valid informed consent process requires effective communication between the trial staff and the potential participant. The potential participant must be given adequate information concerning the study. This provides adequate opportunity for the subject to consider all options, and for the trial staff to respond to the subject's questions and ensure that the subject has comprehended this information.

The main finding of the readability analysis confirmed that the forms were written at a grade level (mean FKRE=50.29 and mean FKGL=11.5) far higher than the average grade level of

the parents who were asked to read them and the levels recommended by research regulations. Results of similar difficulty were indicated in a study of a larger sample (n=2380) of pediatric biomedical research informed consent forms (Tarnowski, Allen, Maryhall et al. (1990). Although this evaluation was based on the English version of the informed consent standards using US metrics which might not equate to the readability in Setswana, in general, it's pretty clear the levels of readability are far too high. Some studies have revealed the same concern (Hochhauser, 2004; Kithinji and Kass, 2010). However readability scores are not without criticism. Valentini, D'Alonzo, Pirozolli et al. (2013), rightly cautioned about basing comprehension of consent form information on readability scores since readability scores work only for certain languages mainly English and that readability is not equated to understanding because not everything readable is understandable. Writing about a topic like clinical trial information is difficult in itself. Readability scores do not consider test description like the lists of side effects of a drug or descriptions of disease complications. Readability only evaluates the syntax of a document without evaluating other parameters like flow of information. Additionally, the score does not reflect level of understanding which depends on intrinsic factors such as proficiency in a language, motivation, culture and education levels. However, since these reader characteristics and textual features lend themselves to subjectivity, subjecting the ten consent forms to the readability tests yielded a very objective basis of analysis.

Of concern is the level of assessment of readability of the consent forms by the national research ethics committee. Informed consent forms used in all clinical trials must be reviewed and approved by an independent ethics committee before practical use in the trials (Directive/2001/20/EC). The fact such difficult informed consent forms were allowed by the review process, means that Botswana Research Ethics Committee does not assess readability during the reviews sessions. Efforts need to be made by the investigators and the research ethics committee to devise ways of simplifying the consent forms without compromising the intensions of valid informed consent. One of the trial staff cautioned that there is need to be aware of the possibility of functionally illiterate participants, unable to read who may try to conceal the difficulty because there is a social stigma attached to not being able to read.

Regarding the drafting of the consent form, trial staff complained about their minimal involvement. Without tapping on the knowledge of culture, language and the setting that trial staff possesses, the consent form becomes too decontextualized. Their main involvement is

only in translation and even this responsibility is the reserve of selected senior staff members at the institutions. Some trial staff rightly suggested that if they got the opportunity, there were a lot of things they could change in the form and the research setting particularly regarding the cultural and social-economic conditions of the parents. Many of the trial staff were critical of the excessive length of the consent forms used. The lengthy forms meant that too much information was provided and thus overloaded potential participants with information to be communicated in the short time available whether at the clinic or at home. Even then, significant questions remain about how to deliver the right amount of information to parents with different backgrounds and needs to facilitate their decision making. Gikoyo, Bejon, Marsh et al. (2008) observed that much of the detail currently prescribed in consent forms is designed to protect the investigators and their institutions rather than the participants. Dresden & Levitt (2001) noted that it is no surprise that in studies done on the informed consent form have found that patients prefer simpler and easier to read; forms that can provide them the necessary information to make a decision regarding participation in the trial. Shorter versions covering the crucial points only with information sheets covering more detailed information that might be relevant were also recommended by the trial staff in this study. Use of short video capsules in waiting areas in the hospital may also serve as a useful tool. Some trial staff mentioned that they use illustrations. The National Cancer Institute (2013) recommended involving all stake holders namely; the investigators, participants and research ethics regulators in the drafting of the consent form document. In addition, outlining, use of bullet points and diagrams have been recommended in order to reduce bulk.

Some trial staff though felt the information was adequate both for their legal protection and for the participants to read or be read to at home. However, while some trial staff felt a summarized version could be used, the question that arises is "who should decide what is important?" The fact that informed consent forms are becoming too lengthy and complex and that it is essential that they are written in clear, direct language and be administered in small proportions to ensure comprehension, are issues that have been raised elsewhere (see Elcoat, 1986; Kass *et al*. 2010, To support this the issue further, other studies have shown that even long forms that use simple clear language can pose challenges for comprehension, retention of information, and recognition of the important points as individuals often skim over texts that are longer than a 1000 words (Sharp, 2004; Rugege-Hakiza, Glynn, Hutching, *et al*., 2003). A study that aimed at simplifying consent forms for biobanking studies found that a 2-page form contains the information that most prospective participants identify as important

(Beskow et. al., 2010), although another study (Stunkel *et al*, 2010) concluded that comprehension was not affected either by the length or complexity of the consent form. Indeed the trial staff were of the opinion that the issue of determining the length of the consent form is very difficult to resolve. It is recommended that the form be written while bearing in mind the people who are going to read it. For example, a predominantly rural sample with barely any reading skill or experience, such as this study interviewed, would require a much simplified version perhaps even accompanied by pictures. Unfortunately, the trial staff reported that they are minimally involved in drafting the consent forms despite their experience and familiarity with the culture of the study participants.

Regarding the complexity of the information provided both the trial staff and the parents confirmed that the medical language used made consent forms difficult to read. Results showed that difficulty resulted partly from the unfamiliar medical vocabulary used and the syntactic complexity as ascertained by the readability formulas. Graesser et al., (2004) observed that sentences with difficult syntactic composition are structurally dense, syntactically ambiguous, or ungrammatical. Many reading theorists have also affirmed the importance of sentence length in text readability and recommend that strategies to simplify readability should include using short, familiar words or simple synonyms; limiting the use of polysyllabic words; and keeping sentence length less than 12 words and paragraph length less than 7 lines (Bormuth, 1969; Chall & Dale, 1995; Kintsch, 1979). Pandiya (2010 p.90) recommended that wherever possible, technical terms should be replaced with common terms; that outlining, bulleting points, using a large typeface and diagrams help the reader to follow complex concepts; and that texts become simple when active verbs rather than the passive voice, short sentences, and frequent paragraphing are used. These challenges are not only unique to consent forms written in English; similar challenges have been identified in a study where assessment of readability of non-English-language consent forms was conducted (Kithinji and Kass, 2010).

6.3 Models of the consent process that promote autonomy

Many models have been proposed for describing the patient/doctor communication process (Emanuel & Emanuel, 1992; Wear, 1998; Brody, 1989; Charles, 1997) cited in Delany, (2005). These models capture the key elements of the communication process. The trial staff

in this study seem to apply in the research setting the Emanuel & Emanuel (1992) paternalistic models described in chapter two as a one-way communication process not guided by participant's rights or autonomy. This prevails in situations where trial staff would be following the legal professional practice by disclosing all information irrespective of whether the person recruited understands or not. Using this model, information disclosed is intended to encourage/coerce the patient to consent to the intervention which undermines individual autonomy. Some trial staff for example reported that they preferred to extract only certain information especially about drugs because they felt the parents would not memorize drug names. Such decisions raise questions about who decides which information needs to be extracted without being paternalistic. Three standards of disclosing information were described in chapter two. Results showed that most of the trial staff use the professional standard as they reported that they disclose all the information in the consent form to the parents. This is a one-way paternalistic interaction which does not promote autonomy. Regarding the standard used to communicate information. A few of the trial staff reported that they extract only important information to disclose to the parents. This would be similar to applying the reasonable person standard where adequacy of disclosure is determined by what information is material to the decision that a reasonable or competent person would want to understand. The subjective standard would also apply where adequacy of disclosure is determined by information a particular person would want to understand. The reasonable standard and subjective standards of interaction have been found to be good options (Baruch, 2001; Guarino, Lamping & Elbourne, 2006) for shared decision making and respecting individual autonomy. These standards are also in line with Emanuel & Emanuel's (1992) three physician/parent interaction models namely; the informative; interpretative and deliberative models which promote autonomy by providing choice control, self-determination and moral-self-development (see Chapter Two). It is difficult to decide which standard is favorable to use across different research contexts. Argard (2005) proposes that the subjective standard could be the best as it acknowledges that information provided should be tailored to match the specific information needs of the potential participants taking into account things like culture, values, beliefs and health status. However, Pedroni and Pimple (2001) argue that none of the three standards discussed above articulates a notion of *full* or complete information, since this is considered unattainable and perhaps even undesirable goal. Therefore, they recommended that the best way to facilitate informed consent may be to design consent forms and other informational materials to satisfy a reasonable person standard, supplemented by conversations intended to elicit and answer any questions that are

not otherwise addressed. Information methods that require trial-staffs' dialogue are unlikely to be successfully implemented in the current Botswana setting where the traditional paternalistic methods are still common practice, and participants are submissive and trust that the doctor acts in the best interest of the patient.

Overall, results in this study showed that trial staff are legally and ethically bound to disclose all the information in the informed consent document as stated in various research regulations (CIOMs, 2002, ICH-GCP, 2002. Some trial staff however indicated during the in-depth interviews that they would have preferred extracting only certain information due to large quantity and complexity of information in the consent form document. Disclosing all information without much interaction with the potential participant in form giving them an opportunity to ask questions, answering them promptly and completely would tantamount to the trial staff being paternalistic. However, we have to acknowledge that trial staff do not have the authority to alter or control the consent process. Trial staff confirmed during the in-depth interviews and focus group discussions that parents did not ask many questions during the discussions although the parents themselves claimed that they asked questions mainly about the safety of the child. With this evidence, one can conclude that the communication or interaction method mainly used by the trial staff is the paternalistic one which does not promote autonomy. Through training, it is possible however for trial staff to learn to use methods like those described in chapter two that promote participant autonomy.

Four other informed consent models cited in Delany (2005) that exist assist in the interaction process. Three of these models namely; the 'Event Model' (Wear, 1998), the 'Transparency Standard Model' (Brody, 1989), and the 'Shared Decision Making Model' (Charles, 1997), apply the paternalistic practice , therefore are not applicable to promotion autonomy as they are essentially prescriptive, describing what the physician should say in communication encounters and dictate the elements to be complied with. For trial staff who extract only certain information for disclosure they apply the 'Process Model' which recognizes the patient's/participant's expert knowledge of the history and context of their problem and regarded the patient/participant as part of the treatment or research team. This model would be ideal to apply when communicating parental informed consent information as it promotes mutual sharing of information, calls for respect for autonomy and allows time to reflect on proposed options, risks, and benefits during the informed consent process. The 'Conversation Model of Interaction' can be used where only certain information is extracted from the form for disclosure. This model marks a shift from the traditional paternalistic prescriptive models

as it involves active reflection on the values, motivations, expectations and interests that may influence implementation of the informed consent process (Delany, 2005). The above models have been recommended as favorable because of their capacity to recognize that meaningful interaction is based on understanding and assumption of participant autonomy and right to self-determination (Katz, 2000)

This study would recommend the application of models that promote autonomy as they acknowledge the role of each stakeholder in the process and recognizes the important role of significant others such as the spouse, community/family elders, and the chief. However, this would require a change in the regulatory requirements by which trial staff are currently bound as part of their jobs and would further require assigning them greater latitude in how they engage with individual parents.

6.4 Parental consent and the law

Parental consenting requires clear legislation, research ethics regulations and guidelines to protect the rights and welfare of both the parent and the child. As explained in chapter two, in Botswana legislation about the age of consent to participate in research is ambiguous because the legal age of majority is 21 while the Children's Act (Cap 28: 04) defines a child as any person below the age of 14 years. However, the government reduced the age of consent to HIV testing from 21 to 16 (Ministry of Health HIV & AIDS National Treatment Guidelines, 2012 section 2.3). Hence the current Botswana HIV Testing and Treatment guidelines (2007) provide that children at the age of 16 may consent independently to HIV testing and treatment but this is not extended to research. This lack of clarity creates an ethical dilemma for the trial staff and parents who wish to enrol children into HIV clinical trials. Specifically, this denies such mothers the opportunity to enrol their children in HIV clinical trials even if they would have wanted to. Furthermore, the Botswana National Co-ordinating Agency BIAS III, a Sentinel Surveillance Survey (2011) showed that in 2011, 10% of pregnant women aged 15-19 year old and 19% of the 20-24 year old mothers were HIV positive. It means this group cannot benefit from the services offered to HIV positive children despite the lack of a vaccine or cure for HIV. In the absence of clear legislation to age of consent to participation in research, the legal age of consent to medical treatment of 18 years is applied.

There is need for research stakeholders, government and the public to initiate dialogue on age of consent to HIV research and research in general.

In addition to legislations, many research regulations prescribe that informed consent forms used in all clinical trials must be reviewed and approved by an independent ethics committee before practical use in the trials (Directive/2001/20/EC; Declaration of Helsinki, 1964). These however are only guidelines and not rules which are interpreted differently by different ethics committees and reviewers.

6.5 Parental vulnerability

Results from perceptions of trial staff background of parents who agree to child enrolment into HIV clinical trials in Botswana and cross-checked against the demographic characteristics of the parents confirmed that most parents who agreed to participation in research had low levels of education and came from low social-economic backgrounds. This situation is likely to render the parents vulnerable. Trial staff also found the parents in this category submissive to health personnel so cannot say 'no' to enrolment of their children and did not even know their rights. This is a common trend that has been observed in other studies where people from communities in the developing world believe the doctor/health personnel 'knows it all' and have their best interest at heart (Makgoba, 2002). Similar findings have been reported in a number of studies conducted in Africa (Bhutta, 2004; Dawson & Kass, 2005). One trial staff showed preference for working with parents with low education levels as they showed a lot of interest in the education that was provided and were very good with adherence. However, parents with high education levels and social-economic status were perceived by trial staff not to be interested in participating in research and many of them did not visit the public health clinics where most recruitment occurs. However, this is unlikely to change unless such populations are educated more about the importance of research.

Interviews with parents revealed that a rural location, poverty, low education levels, and the inability to distinguish between research and treatment combine to make parents vulnerable to consenting without fully understanding the process due to low levels of both general literacy and health literacy. The Institute of Medicine (IOM, 2004) defines health literacy as

the degree to which individuals have the capacity to obtain, process and understand basic health information and services required to make appropriate health decisions. The report further goes on to explain that in order for an individual to read and understand a text, they must have prior knowledge about the topic to be discussed including reading fluency, the vocabulary used, familiarity with health concepts presented in materials or discussed, and the complexity and difficulty of the printed and spoken messages that a person encounters in the healthcare environment. To some extent a few parents who had participated in more than one HIV clinical trial seemed to display good health literacy levels about research, HIV and ARVs. Previous research experience and familiarity with health care settings were found to be highly associated with the parent's ability to remember having been told about the risks of child enrolment into the study and the number of study visits a child would make to the clinic. Trial staff also noted these two variables as important for the success or failure of the informed consent process because they enabled to the acquisition of new knowledge (health literacy) as trial staff reported that parents who had previously enrolled a child in a study easily agreed to child enrolment. A similar observation was made by Baker (2007 p.879) who noted that prior vocabulary and background knowledge about the disease from written documents are likely to improve an individual's comprehension. For example, some parents during the interviews expressed the wish that studies like the ones in which they had enrolled their child in should be repeated while some came back to the clinics to inquire whether there were any studies they could enrol their children into. However some trial staff cautioned that this could have been due to lack of understanding of the difference between research and treatment (therapeutic misconception). It is wrong though to dismiss all rural folk, such as those in this study, as lacking in health literacy levels. Indeed Miller, DeWitt, McLeay & O'Keefe (2009) showed that even highly educated people did not understand health information educational materials.

In this study, all the trial staff agreed that it was very important for people that implement the consenting process to have some background knowledge of the culture of potential participants as this would foster understanding of the parents' behavior and reactions to child enrolment in a clinical trial. For example most parents who requested to go back home and consult before agreeing to child enrolment, it was a polite way of declining or silent refusal. This was also another way of showing respect to the health personnel, spouse or elders. Trial staff themselves having been socialized in the same cultural setting had the same cultural beliefs so respected the parents' wishes. Such factors were likely to pose challenges if the

western conceptualization of bioethics was rigidly adhered to. For this reason many scholars (Faden and Kass, 1998; Ggadegesin, 1988; IJsselmuiden and Faden, 1992) express doubt about the successful implementation of individualized informed consent in non-western settings. Because informed consent is based on the western belief of individualism, it is not understood in communities where the norms of decision-making are collective. They go further to argue that informed consent is not appropriate for Africa because culturally, individuals are not autonomous; the potential subjects are not "competent" or the communication difficulties are insurmountable; and urgency makes informed consent requirements unreasonable (i.e., informed consent slows down the search for solutions to urgent health problems. For example in many sub-Saharan countries, the spirit of 'Ubuntu' which refers to interdependence, communalism, sensitivity towards others and caring for others are all part of people's lives (Turaki, 2006). Shaibu (2007) reached a similar conclusion that in Botswana, implementation of informed consent was influenced by family, cultural dynamics relating to gender, respect for older persons and care giving arrangements; and that there was a need for research investigators to be culturally sensitive, exercise discretionary judgment guided by respect for culture and decision-making protocols applicable to a particular setting. In Botswana preservation of cultural values and collective identity is recognized in the National Vision 2016 (http://www.vision2016.co.bw/). Communities in Botswana have great respect for authority (elders, spouse, and health professionals). Individualized consent processes may therefore be inappropriate. These considerations also confirm the requirement that clinical research should not violate the Kantian principle (cited in van der Graaf R & van Delden, 2012) that "people must not be used merely as a means for the purposes of others".

However, the trial staff clarified that encouraging participants to consult with family and relatives did not mean informed consent was collective but that it was necessary as a way of being culturally sensitive. In Botswana involvement of community leaders like the chief ('Kgosi') was reported by the trial staff as important because even participants asked whether permission had been sought from the chief before the research was initiated.

Knowing the language of potential participants was also recognized as important for the success of the informed consent process. It was found that that the trial staff interacted with the parents in Setswana the national language and most parents preferred to be talked to in this language. Botswana is multilingual. Hence some trial staff were rightly concerned about

the translation of the English informed consent forms only into Setswana and not any other languages. Failure to translate sometimes compromises comprehension for those individuals whose mother tongue is not Setswana. This is a highly political issue as the current language policy in Botswana does not provide room for the use of other indigenous languages in conveying information (Nyathi-Ramahobo, 1999) which can deny many people access to crucial information (Batibo and Mosaka, 2006). This however does not mean that the use of Setswana itself is without problems. Some trial staff indicated that they find written Setswana difficult to read and communicate especially interpreting the difficult English technical medical terms that do not exist in Setswana. Trial staff rightly recommended that the language issue needed to be taken up by the National Research Ethics Committee. Challenges of language barrier in full comprehension of study information have also been recognized elsewhere (see Bhutta, 2004; Dawson & Kass, 2005).

6.6 The parent dilemmas of proxy consenting

When parents are asked for permission for a child to participate in clinical research, it is often a time of great stress and pressure. Molyneux et al. (2013) attribute this to a therapeutic misconception a key ethical tension of clinical research whereby many parents who enrol their child in a study will think that the research intervention is designed to provide a therapeutic benefit, when in actuality the intention is to gather data for the purpose of contributing to medical knowledge. In the current study results showed that the major motivating factor for parental child enrolment was the illness of the child. This could have been the reason why the elements of number of visits and the fact that doctors could withdraw the child from the study any time were well recalled and understood. The number of times the child would be brought to the clinic could have been understood by the parents as regular care for the child. On the other hand, a doctor withdrawing the child from the study was also well understood as it is worrisome to the parents. The sense of responsibility that accompanies parents' decision making about trials may paradoxically render them more vulnerable, especially to the anticipation of regret. These are dilemmas that have made parental consent a complex area in research that has attracted wide scholarship (see Kyriaki, Panagiotou, Katsaragakis, and Tsilika, & Parpa, 2009; Zikmund-Fisher, Sarr, Fagerlin & Ubel, 2006; Stevens & Pletsch, 2002; Eiser, Davies, Jenney & Glaser, 2005; Canvin & Jacoby, 2006; Gilovich & Medvec, 1995). Zawistowski (2003 p.408) distinguished between a

parent deciding to give proxy consent for a child to participate in a trial and an adult deciding about their own participation in a trial. In the case of proxy consent, the primary responsibility is the best interest of their child while for an adult the role is exercising individual autonomy. Because all parents want to do the best for their children, their role is to care for and protect them. When a child is sick, parents rely on professionals (including traditional medicine men) to decide what is best for the child. When the same professionals request to enrol the child in research, it is normal for a parent to fear making the 'wrong' decision about their child. In non-western setting, parents are socialized to trust medical experts who are expected to know and act in the best interest of the child. In this current study, the validity of the decision has been observed to differ by parent according to age, level of education, personal experiences, values, and the medical situation the child. There was also the satisfaction that they acted as good parents to their child whatever decision they made. For example one parent when asked whether she would refuse to enrol the child said "my child would have seen clearly that I have refused". Cohen (1993) rightly notes that for parents the diagnosis of serious illness in a child can be a shattering experience. Additionally, when consent is sought soon after diagnosis of a life threatening disease without cure like HIV, parents will be making decisions when they are distressed and vulnerable (Levi, Marsick & Kodish, 2000). Being approached about a trial confronts parents with large volumes and complex sets of new information well beyond their everyday experience and they can never be certain about what is the 'right' decision. However, whilst they may be vulnerable, protecting their child is fundamental to the parental role and this will shape how they think about trials. Caldwell, Butow & Craig (2003) report parents who felt personally and directly accountable for their child's outcome on a trial and thought that giving consent for a child would be much more difficult than deciding to take part in a trial themselves. Survey evidence confirms that the responsibility to act in the best interests of one's child is keenly felt, with one third of parents in one study reporting that while they might accept certain research risks for themselves they were much less certain about accepting the same risks for their baby (Singhal, Oberle, Burgess & Huber-Okrainec 2002). Surprisingly, during the parents' interviews in the current study, the question that was asked to rate the ease with which a parent would have refused to enrol a child if they had wanted to, slightly more than half (55%) of the parents said it would have been very easy and the remainder (45%) said it would have been difficult. Considering the fact that most parents were desperate because of the child's illness it is unlikely that they were providing a genuine answer or were trying to say what the researcher wanted to hear.

6.7 Parents' recall, importance of information disclosed and knowledge of trial elements

Results showed that despite the trial staffs' perceptions that the low education and social economic-status would compromise recall or awareness of the key elements disclosed, most parents had a high level of awareness on the seven key selected elements discussed. This could be an indication of the importance attached to these elements. In addition, over 85% of the parents could recall being told about the purpose of study (85%), the number of times the child would take medications (86%) and their rights (89%). The only element most parents could not recall being told about was payment for child enrolment into the study (69%). This was because most trial staff reported that they did not mention payment beforehand to avoid being accused of undue influence. Surprisingly, the high level of awareness did not exactly match with the importance the parents attached to getting information about each of the elements for decision making. For decision making, most parents mainly attached a lot of importance to elements like number of study visits they would have to make to the clinic, the number of times the child would receive medicines and payment for child enrolment into the trial, more than on understanding details of purpose of study and randomization. This could possibly be an indication that the motive parents had for enrolling the child into the trial was to receive care considering the lack of standard treatment for pediatric HIV and the possibility of therapeutic benefit. It could have also been a retrospective reconstruction of priorities especially about compensation for child enrolment into the study as most trial staff indicated that it was not mentioned until the end of the discussions or if a parent hinted that they would not afford to come to the clinic regularly due to lack of transport money. However, the majority of parents agreed that they had been given a chance to ask questions and they did ask questions and were satisfied with the answers provided.

Findings in this study seem to suggest retention of comprehension was based on the health status of the child. Therefore the trend in elements most recalled seemed to show selective recall. Most parents seem to have recalled information that they regarded as important to the welfare of the child. This could be explained in terms of the role parents have to play in caring and protecting their children (natural parental instinct). The roles and responsibilities of the parents to the child were explained in chapter two. Naturally all parents want to act in

the ‘best interest’ of the child; and socially and legally their role is to care for and protect them. However in non-western settings where culture dictates collective decision making, this role could be reversed when it comes to a sick child. In this situation, parents have to depend on the health professionals, spouse, family or relatives to exercise their responsibility of deciding what is best for the child. This can be challenging as the parent have to make judgments about the threat of the child's condition as well as the risks of the trial and judgments from others. Therefore they have to do everything that they can to get as much information as possible about what s/he is being requested to do in order not to make a wrong decision that would result into regret and blame for others in case something wrong happens to the child. Survey evidence on studies that examined parental informed consent confirmed that the responsibility to act in the best interests of one's child is keenly felt, with one third of parents in one study reporting that while they might accept certain research risks for themselves they were much less certain about accepting the same risks for their baby (Singhal, Oberle, Burgess & Huber-Okrainec (2002). Mothers whose children were enrolled into a bone marrow transplant trial, for example, dreaded the possibility that they might have to live with the knowledge that they had made the 'wrong' decision and this was intensified when things did not go well for the child (Stevens & Pletsch, 2002).

Regarding parents opinions about how the interaction or communication process was conducted, parents expressed their satisfaction with the process. As results showed in chapter five, most parents reported that the process had facilitated their decision making as information was clearly explained to them, they were given the opportunity to ask questions and when they did ask questions the explanations given were satisfactory. All the parents agreed that they were tested for understanding which encouraged learning. Overall almost all the parents reported that they were happy with the way the information was disclosed to them and felt the trial staff were honest, caring and showed empathy. However, there were quite a number who felt the trial staff were being coercive. It is difficult to judge the genuineness of these opinions as most trial staff reported that interactivity was very low during the trials with parents not asking questions. The trial staff indicated that this could be attributed to culture e.g., fear of questioning authority and trust for medical personnel making the parents submissive. Trial staff also mentioned the possibility of therapeutic misconception as well as the stress and desperation about a sick child. The duration between a parent being approached and consenting was also regarded as important as most parents agreed to child enrolment the same day because the decision is made even before the consenting process and do not pay

much attention to the information being disclosed. The difference in care given at the research centre and the public facilities also contributed to the parents opinions as shown by some of the comments made by the parents in Figure 5.6. Regarding researcher-participant interactivity, Shilling, Williamson, Hickey et al., (2011) noted that parents said little during the trial process and responded to chunks of information interrupted by closed questions such as *alright?* and *ok*? posed by the researcher using brief affirmation of *'okay', 'right' or 'yeah'*. The same authors also noted that when parents are asked about the interaction process they do not focus on the information provided but more on their experiences with the researcher. For example, the sense of security and comfort during the discussion, liking the researcher and the confidence that the trial was safe thereby expressing the confidence and trust in the researcher.

6.8 Comprehension

Information given to research subjects requires a level of understanding and appreciation for meaningful deliberation about a decision. Beauchamp and Childress, (1994) observed that understanding on the part of the research participants is not necessarily the same as *'true'* understanding because sometimes participants fail to understand the underlying scientific methodology of the studies. In such cases, what the subjects *actually* authorize differs substantially from what they *intend* to authorize, and thus informed consent is unfulfilled (Meisel & Roth, 1983). Other literature shows that despite the efforts by research investigators and Institutional Review Boards (IRBs) to design carefully worded consent forms, the informed consent process seems to be misunderstood and therapeutic misconception is common (Ness, Keiling & Lidz, 2009). Results in the current study showed that trial staff did not want to commit themselves to confirming that parents did not understand the difference between research and treatment judging from the vague explanations given regarding this question and the reluctance with which the question was answered. Other factors like age, severity of illness and need, educational level, cognitive capacity, familiarity with research, language, values and culture as well as literacy have also been found to affect understanding of disclosed information (Pace, 2005). In the case of parents who participated in this study comprehension may be compromised by the stress and anxiety over a child with a chronic illness that has no cure or a vaccine.

The challenge of measuring understanding in the informed consent process is well recognized elsewhere. For example, Lindegger et al. (2006 p. 561) tested understanding using four different methods of assessment on the same individuals and the results showed different levels of understanding. In this study, results showed that trial staff were doubtful about parents' understanding of most of the information disclosed to them despite their facilitation of the process using institutional assessment tools, going over the information, asking questions and encouraging parents to take the consent form to read or be read to. This could be attributed to three factors (1) as already established by readability scores, the forms were written at a grade level far higher than the average grade level of the parents who were asked to read them; (2) report by trial staff of the anxiety and stress observed among some parents when the option of enrolling a child in a trial was presented to them. Some studies (Ruccione, Kramer, Moore and Perin, 1991; Levi, Marsick; Drotar and Kodish, 2000) have reported similar findings and explained that the anxieties associated with making decisions on behalf of one's sick child may put particular stress on an adult's comprehension, reasoning, and decision-making capacities. (3) '*Selective denial'*, a protective mechanism against hopelessness explained by Daughterly, Ratin et al. (1994) cited in Tomamichel, Sessa, Hertzig et al (1995 p.367) as the hope of a patient or one's child being among the small sub-group of patients who will respond to the therapy and beat all odds. This was indicated by some trial staff who noted that some parents looked happy and hopeful when they were approached with the option of enrolling a child in a trial.

The trial staff also identified a number of factors that could undermine comprehension. For example, the age and social economic status of the parents, their lack of health literacy and lack of cultural background especially language by trial staff. Furthermore, trial staff expressed concern of how Botswana legislation and research ethics committee requirements of drafting consent form documents and disclosing information pose a threat to comprehension and can turn off parents from listening or reading the document. However despite all this criticism, the trial staff acknowledged the necessity and value of detailed informed consent documents in achieving an adequate understanding of what is proposed, why that is the preferred action among alternatives, and authorization without coercion.

Although results of communication process showed that recall of information was very good, and parents felt well-informed and rated the information provided as very important to them for decision making, comprehension assessment of some of the elements of informed consent

did not reflect this finding. The results of comprehension assessment showed understanding of mainly those that do not involve scientific methodology. For example overall analysis of comprehension of all key selected elements showed that alternatives, purpose of study, benefits being uncertain, parents' rights as well as non-scientific methodology study procedures (like number of study visits and doctors withdrawing the child from the study anytime) were quite well understood. Of note, the most highly recalled element, most well informed about, rated as most important and highly understood was the number of study visits the child would have to make to the clinic. This showed that the concept of the child's access to sustained care was very important to majority of parents. In this case, one could speculate that the real reason for enrolling the child was the anticipated benefit that the child and the parent get out of the trial. This was further confirmed by the trial staffs' reports that some parents did not pay much attention to the information provided during the interaction process because they came with their minds made up to enrol the child in the trial. Similar observations have been made elsewhere (Daughterly et al., 1995) cited in Itoh, Sasaki, Fujii (1997 p. 110).

The results also showed some confusion about understanding elements that involved scientific methodology such as the trial design procedures, the basis of the choice of medicines given to the child, and understanding that some children were given medicines that were not active (see Figure 5.5c). Although almost all the parents (99%) knew that they were not allowed to choose which medicine the child would receive and that the doctor's choice of medicines depended on chance and not what was best for the child, less that 10% of the parents identified correctly that some medicines given to the children were not active and some children received medicines that were being tried. This observation could suggest that some parents may not have understood these components of trial design despite the high levels of recall and being well-informed. In the literature, this is referred to as *'therapeutic misconception'* where the research subjects transfer to the research setting the assumption that the physician always acts only in the best interest of the patient (Appelbaum, Roth, Benson et al., 1987 cited in Mfutso-Bengo, Ndebele, Jumbe et al (2008 p. 41). The element of risk was also found to have been poorly understood. One could argue that the parents were not so concerned about the possible risks but the opportunity of the child accessing care. This is expected in situations where there is no alternative to participation in research like the case of life threatening diseases like HIV with no cure or vaccine. Generally issues of randomization and placebo use have been found difficult to understand by research

participants in many African countries (Appelbaum, 2002; Molyneux, Wassenaar, Peshu, Marsh, 2005; Tindana, Kass, Akweongo, 2006) cited in Mfutso-Bengo, Ndebele, Jumbe et al., 2008 p. 38; Chaisson, Kass, Chengeta et al. 2011) although they are important for valid informed consent.

Another significant finding was the low levels of perceived risk as illustrated by only 15% of the parents who answered correctly that the medicines could have life-threatening effects. Comments made by parents also indicated that the parents did not understand the risks of the trial. For example a number of parents reported that they were very happy with the study because their children did not have any side effects. This shows that parents might have underestimated the risks of enrolling their children in HIV trials and were more concerned about the child accessing care or it could have been a case of selective denial described earlier. The element of confidentiality was also poorly understood. It has been observed that maintaining confidentiality during research conducted in developing countries is a major challenge. Botswana culture encourages the traditional practice of discussing issues of importance in familial and communal settings. Shaibu (2007) observed that participants enrolled in research can freely share their private information among neighbors who happen to drop by during the interviews. Secondly the family settings or even clinic settings do not offer privacy.

Certain gaps have been identified elsewhere regarding comprehension of information. In a multi-center study that asked research investigators about information they had disclosed to potential participants, 58% indicated having disclosed full information, 42% only gave information on the proposed treatment, while 12% had not informed patients about the trial prior to randomization and 38% did not tell the patients about randomization while 5% did not seek consent at all (Williams & Zwitter, 1994). In the same study, however at least more than 90% of the investigators had provided the participant with a copy of the consent form, an opportunity to read before coming for the next visit and information about risks but less than 56% of the investigators had emphasized randomization and only 8.5% had made a formal assessment of understanding. This shows that some elements of the consent form may not be communicated effectively

Despite all the above identified challenges to comprehension, parents were confident that they were well-informed about pediatric HIV trials and had learned a lot about HIV and ARVs. This could be attributed to the intensive education given by trial staff. Furthermore

parents echoed the good care, honesty and empathy received from the trial staff that facilitated understanding (Figure 5.6).

The next section discusses the perceptions of the parents about the informed consent communication process.

6.9 Motivation and decision –making to enrol child in HIV clinical trials

As indicated in chapter one, the fourth objective of this study was to identify and describe the reasons for parental approval to enrol their children in HIV clinical trial studies. The study also aimed to assess the extent to which parents understand the information provided during the communication processes. Understanding what motivates parents to agree to child enrolment into HIV clinical trials is an important issue in informed consent process. Considering the inherent complexity of most real life problems, giving informed consent requires both 'rational' and 'emotional' capacity. According to Arnold and Feldman (1986) an individual's choice is influenced not only by the perceptions of his/her goals but the anxiety and confusion experienced while making the decision. This is likely to happen to mothers of HIV positive children.

As shown in chapter five, parents cited two important reasons for child enrolment into HIV clinical trials namely; *'illness'* of the child (67.1%) and to '*help*' (altruism) future HIV positive children (32.9%). Over 85% of the parents confirmed that their motivation was without any pressure from spouse, health trial staff or family or by anyone. Quite a number of parents reported that before reaching the final decision, they had consulted with their spouses, family and close relatives. However, consultation was more of a cultural issue of collectivism, respect and trust or fear of blame in case anything went wrong. All trial staff felt that encouraging parents to consult with close family members or friends was important as a form of social network support. Although requesting to go home and consult with family by some parents was reported by some trial staff as a polite refusal, some trial staff reported that some parents actually went back and consulted others and such parents seemed more relaxed, relieved and comfortable to agree to child enrolment. Over 70% of the parents reported that they had been under so much pressure from others to agree to child enrolment. This could have been due to the hopelessness of lack of alternatives and selective denial.

Although the results indicated that the parents had understood that the benefits of the study were uncertain, having been motivated by the illness of the child could be interpreted to mean that parents expected direct benefit from the study which was not a rational decision but based on desperation. The rational decision should have been the one of helping future HIV positive children. This finding is contrary to what motivates parents from western settings (Zupancic, et al, 1997) where altruism is priority.

Some parents gave reasons other than child's illness and altruism. For example some said they had made the decision to enrol the child even before they were talked to by the trial staff, others explained that it was because they had understood the study purpose. There were also reasons such as the parent wanting *to know the results from the tests that were done;* the parent's fear of guilt ("*my child would have seen clearly that I have refused"*); and the *"trust* [parent's] *put into the trial staff".* Studies on adult informed consent have found that the doctor is very influential in decision-making (Jenkins & Fallowfield, 2000). This difference could be due to the parental protection responsibilities towards the child.

Regarding decision-making, results showed that for majority of parents, parental consent was solely individual. This finding could have been influenced by the fact that most parents were single or by the illness of the child. The few parents who indicated that their decision was motivated by the social obligation to help could have been a recall of what they had been told during the discussions. It seems doubtful that the decision made by most parents was valid and whether altruism could have been a genuine motivator. Parental decision was significantly associated with relationship to the child (being a biological parent), number of clinic visits, previous experience in research and payment or compensation for child enrolment. Other studies have found that a valid decision can be compromised by the trust put into medical experts on the principle that "the doctor knows it all and acts in the best interest of the child". In addition the parental decisions have been observed to differ according to age, level of education, personal experiences, values, and the medical situation the child as well as the fear of guilt and being able to feel confident that they have acted as good parents to their child whatever decision they make (Mkgoba, 2002; Marley, Lau, Davies, 2005).

The case of HIV which is a life threatening disease a child being diagnosed HIV positive can be a shattering experience to the parent. So when consent is sought soon after diagnosis,

parents will be making decisions when they are distressed and vulnerable. These responses show the parental commitment to the child's interests, emotional instability and inability to make rational decisions because of the vulnerability caused by this kind of illness. Parents that are approached about a trial like the one investigated in this study are confronted with new and complex information and so they may not be immediately certain about what is the 'right' decision. Despite being vulnerable, protecting a child is fundamental to the parental role and this shapes the decision made.

According to the results about parental motivation to child enrolment, the voluntariness may be questionable. Although almost all the parents were well informed about the element of voluntariness, about 70% parents indicated that they could not have refused to enrol their children even if they had wanted to because of the child's illness and confessed that refusing would have been very difficult. This confirms the element of desperation of the parents. Although trial staff felt consultation with spouse and family was important, this study indicated the opposite. This could have been explained by the secrecy and stigma still attached to the HIV disease in Botswana. Mystakidou, Panagiotou et al., (2009 p.49) observed that the HIV epidemic had pushed infected individuals of the developing world to the margins of their societies. Almost 90 % of parents confirmed their agreement to child enrolment into HIV clinical trials by signing on the consent form but very few (9%) acknowledged agreement by putting a thumb print on the consent form and almost all the parents preferred signing than agreeing verbally. Unfortunately the reasons for this were not probed. However, being happy with the signing could have been from the relief that finally the child will be helped but without understanding of the legal implications. Of concern, most parents reported that they made the decision to enrol the child the same day. It is questionable whether this was valid consent or the decision was made because of the pressure parents were under to access help for the sick child. The trial staff however contradicted the parents saying that the consenting sessions could last more than an hour while some trial staff said they did not encourage parents signing the consent form the same day. Such contradiction raises doubt as to who was telling the truth and further confirms what the study suspected all along that the consenting was not absolutely voluntary.

At the end of the interview parents were given an opportunity to comment on the informed consent process. The general comments that they made could be interpreted in two ways either some of the parents who commented that the study was very good and they wished it

could be repeated did not understand that the child was in an experimental study or those who reported that the child had improved were allocated into the arm using an intervention drug that was possibly efficacious. Furthermore, parents who appreciated the care given at the research center being better than that at the public clinics did not understand the children were in an experimental study and needed close observation. The disparities between the care given at the research center and that at the public clinics could raise questions about parents' voluntariness or could be interpreted as undue inducement. For example some parents commented that the tablet that the child was receiving was only given to children that were on the trial; some said if the study could be repeated they would enrol their child; some said they were treated special and the child was seen by the doctor on every clinic visit; some reported that the child had improved and had not experienced any of the side-effects that they were warned about.

Many parents also appreciated the constant education they received about HIV and ARVs and felt the trials were very important for the nation and were hopeful a drug would be found very soon. The observation of disparity in care and benefits among children on-trial and those not on-trial has been observed in a study by Molyneux et al. (2013) where the parents and children on-trial were not paying for hospital stay and were seen by the doctor every time they needed to which did not happen for non-participating parents. Considering that all parents whose children are admitted for whatever reason love and care for their children dearly this preferential treatment extended to research participants would cause resentment. For the ethicist this preferencial treatment could be interpreted as undue inducement. There is need for governments and sponsors to devise strategies to reduce the disparity between the two groups.

6.10 Results conclusions

Chapters 4 and 5 enabled the researcher to identify some of the challenges and gaps in the current practices of conducting parental informed consent process for pediatric HIV clinical trials in Botswana. The results showed that the consent forms used to seek consent from parents who're to enrollment of their children into HIV clinical trials in Botswana are generally difficult to read and written at a higher level than that of most participants. The process of seeking consent is a female dominated area and all trial staff have the relevant

qualifications in various medical disciplines and multiple tasks but need more specialized knowing in areas like research ethics, clinical trials research and communication skills which could be an added advantage to their role. Results also showed that trial staff were of the opinion that the information disclosed to the parents was too much and complex for their comprehension and valid decision making. Trial staff mainly used the paternalistic method of disclosing information mainly because they have to legally protect themselves. Trial staff were also doubtful about parental understanding of the scientific procedures of the trial studies. Results showed that mostly women are involved in the care of their children and these women have low education levels, social economic status and mainly from the rural areas. It was also evident from the results that age, previous experience in research and relationship of parent to the child played a major role in the parents' ability to recall disclosed information. Motivation by most parents to child enrolment was mainly associated with the numbers of clinic visits promised, parents' previous experience in research, being a biological parent and being paid for participation in the study. Overall, findings seemed to suggest that the main motivation factor for child enrolment into HIV clinical trials by parents was the illness of the child and accessing health care for the child rather than altruism. This raises questions about the autonomy, voluntariness of the parents and the validity of the consent obtained. The study also demonstrated the importance of knowledge of culture of participants by the trial staff and the researchers as well the unavailability of standard guidelines and laws to guide researchers and to assess the quality of parental informed consent forms. Therefore these findings informed the practice model that was developed in the next chapter.

6.10 Limitations of the study and recommended future research

The study would specifically like to note the limitations relating to the use of readability formulas in contexts where scores originally based on American school grade levels are transferred without question to predict reading ease elsewhere. Additionally, in this study FKRE and FKGL were applied to the English version of the informed consent form only. Ideally, the same measure should have been applied to the Setswana version also which is the one the participants actually signed. Both these limitations are attributed to the fact that there are no existing readability formulas on the market that measure texts written in Setswana. The readability scores that the study reports are however useful since they predict the readability challenges faced by those who translated the consent form from English to

Setswana; challenges that may have affected the Setswana version participants signed. Future research using a larger sample and readability tools that measure readability for texts written in language like the cloze procedure would improve on these flows. Future research also needs to take into account other factors that affect readability mentioned earlier such as text organization and reader characteristics.

Another limitation pertains to the small number of institutions that conduct pediatric HIV research in and around Gaborone. This resulted in the scarcity of suitable participants and difficulty of obtaining permission to sample participants. Due to this the trial staff population for this study was not randomly drawn but instead, convenience sampling was used. This limitation was overcome by using qualitative approaches that enabled the documenting of individual participant's experiences. The findings may therefore not be generalizable. Future research could include trial staff from other sites outside Gaborone.

Thirdly, the researcher suspects that certain factors in the design of the study must have introduced the Hawthorne effect. For example, because the trial staff interviews were not conducted at the same time as the actual observation of the consenting process, interview responses may have been biased since trial staff were unlikely to criticize their performance or that of the institution. Another design factor that may have introduced the Hawthorne effect relates to having the parents as participants - parents could not criticize the trial staff due to the vulnerability created by the patient/doctor relationship and the nature of HIV disease having no satisfactory standard treatment. It was naturally that they do not jeopardize their children's chances of accessing care. However, as with the original Hawthorne studies, these factors may not have had a role in the findings; but it would help if further studies minimize bias resulting from these design factors.

Another limitation of this study was the use of TRUE/FALSE closed-ended question to measure parental retention of recall of information and comprehension. This method is imperfect as it allows participants to guess or just say what they heard whether it was understood or not. However, future research like collecting data from on-going studies and using open-ended questions would improve on these limitations.

Finally, the data obtained about perceptions of trial staff on information disclosure and comprehension excluded clinicians who play a key role in explaining to the parents the scientific procedures of the study.

CHAPTER SEVEN

A MODEL FOR OBTAINING PARENTAL INFORMED

7.0 Introduction

The aim of this thesis was to conduct a situational analysis of the current methods and practices of obtaining parental informed consent for HIV clinical trials with pediatric patients conducted in Botswana in order to use the findings to develop a model that can guide the parental informed consent process in future. Models are often used in public health research to explain research questions under investigation and various meanings and uses of the term exist. In this study, a model is defined according to Earp & Ennett (1991, pg 163) as a diagram of proposed causal linkages among a set of the concepts believed to be related to the process of obtaining valid informed consent. The model developed in this study addresses the research questions set out in chapter one, section 1.5 namely: (i) how readable and understandable the consent forms used to obtain parental informed consent are; (ii) how effective the trial staff-parent communication methods and practices were according to the trial staff and parents perspective; (iii) the extent to which parents recall and understand the information provided during the communication processes; (iv) the parental perceptions of, and levels of satisfaction with, the informed consent process; (v) what motivates parents to enrol their children in HIV clinical trials; and (vi) the extent to which the parental decision to enrol a child in HIV clinical trials was voluntary.

These questions were answered using the methods described in Chapter three, Sections 3.7 and 3.9; and were reported in chapters 4 and 5; and discussed in chapter 6. The model development process was also informed by theories and existing models from literature review reported in chapter 2. The main ethical theories applied to the model are Kant's non-consequentialists ethical theory and Mill's consequentialist ethical theory. In addition, the

many existing informed consent models were scanned to identify the missing links in obtaining valid parental informed consent in the Botswana setting. The need to develop a model that can guide researchers in future arose from the problems stated as a statement of the problem in chapter one, section 1.2 regarding the process of obtaining valid parental informed consent.

7.2 The Model

The model is illustrated by boxes which represent the concepts while the arrows indicate the interrelated nature of the causal linkages in the process. Triangulation methods were applied in form of document analysis, in-depth interviews, focus group discussions and semi-structured questionnaire to verify the needs of trial staff for obtaining valid parental informed consent and parents' perceptions regarding the informed consent process. The results presented in chapters 4 and 5 identify the needs and expectations on both the part of the trial staff and parents in obtaining valid informed consent. The interpretation of the results in chapter six assisted in identifying the problem areas in obtaining parental informed consent and the identified problems were used to develop a model (Figure 7.1) tailored to respond to them.

7.2.1 Steps followed in the development of the model

The following steps adapted from Earp &Ennett (1991) were used in developing the model.

Step 1: Identification of the specific end point of interest which is valid parental informed consent.

Step 2: A situational analysis of the current practices and perceptions of the trial staff and parents was conducted to generate concepts that were used in model development.

Step 3: Analysis and interpretation of data from the mixed methods applied in chapter 6 to generate the concepts used to build the framework.

Step 4: Relationships among concepts based on empirical and theoretical evidence as well as available knowledge from literature about the problem of obtaining valid parental informed consent were used to determine the causal relationships.

Step 5: Only concepts that can be realistically addressed for intervention strategies were retained on the basis of practical considerations, importance of various concepts, relationships, literature and scientific merit, and theoretical considerations.

The model (Figure 7.1) identifies trial staff as one of the two key components of the process of obtaining parental informed consent. As indicated in the illustration, in-depth interviews with trial staff revealed some of the vital competencies that trial staff require to be able to facilitate obtaining a valid informed consent from the parents. For example as shown in box one, knowledge, attitudes and skills of research governance framework, clinical trials research and research ethics were identified as vital elements to successful information disclosure. As noted in the findings the listed elements were found to be lacking. Possession of the knowledge and skills would enable good practices that promote autonomy during the information disclosure process. The second box from the right illustrates vital competencies that individuals conducting the informed consent process require for proper disclosure of information that can promote autonomy and facilitate understanding. Furthermore, in order for the trial staff to facilitate understanding they should be able to use appropriate methods shown in the third box. These methods would lead to a shared decision which is not based on therapeutic misconception, coercion or undue influence. In this way the parent would be assisted by the trial staff to make an autonomous valid informed consent.

The second key component of the developed model is that of the parents shown in the lower section of the model. The lower first box from the right shows that some of the predisposing factors that were identified in this study like gender, low education levels, low socio-economic class, residing in the rural areas and being a single head of a household could have an influence on the achieving an autonomous decision by the parents. Such attributes can increase a parent's vulnerability to coercion and undue influence. These attributes have also been identified elsewhere (Kyriaki, Panagiotou, Katsaragakis, Tsilika, & Parpa, 2009).

Results in chapter five also showed that some of the factors like parent's previous experience in research, and therefore familiar with clinic settings and being a biological parent were enabling factors that provided skills, experience, higher health literacy levels and experiences which had exerted an influence on recall of information and comprehension of some of the elements of the informed consent process. These are shown in the second box from the right in the parent component e.g. good health literacy, life experiences and previous experience in

research. Therefore trial staff should be cognizant of these factors that can promote autonomous decision-making. However, there are other factors that were identified in the study that could be reinforcing factors to a parent's agreement to child enrolment into clinical trials. For example the social-structure of the parents (culture, beliefs, values and attitudes) and strong cues like the illness of the child, and need to access health care services. These factors are likely to exert an influence on the parent's decision-making capacity by increasing their motivation to agree to child enrolment into HIV clinical trials. This effect may imply that the decision by a parent to child enrolment in trial studies may not have been absolutely voluntary. Therefore trial staff need to recognize that these factors are likely to be coercive and can result in undue influence as far as a parent giving a valid informed consent is concerned. Generally the reinforcing factors raise questions about the validity and voluntariness of the parent's consent. Overall, the model also captures the consenting process as a continuous process with the general socio-economic, cultural and environmental factors encompassing the trial staff and parental factors.

In conclusion, although obtaining valid informed consent may seem impossible, the model can minimize the challenges encountered by both the trial staff and the parent if the trial staff can possess that factors identified in each of their component concepts as well as recognize and respect the parents' concepts showed in Figure 7.1.

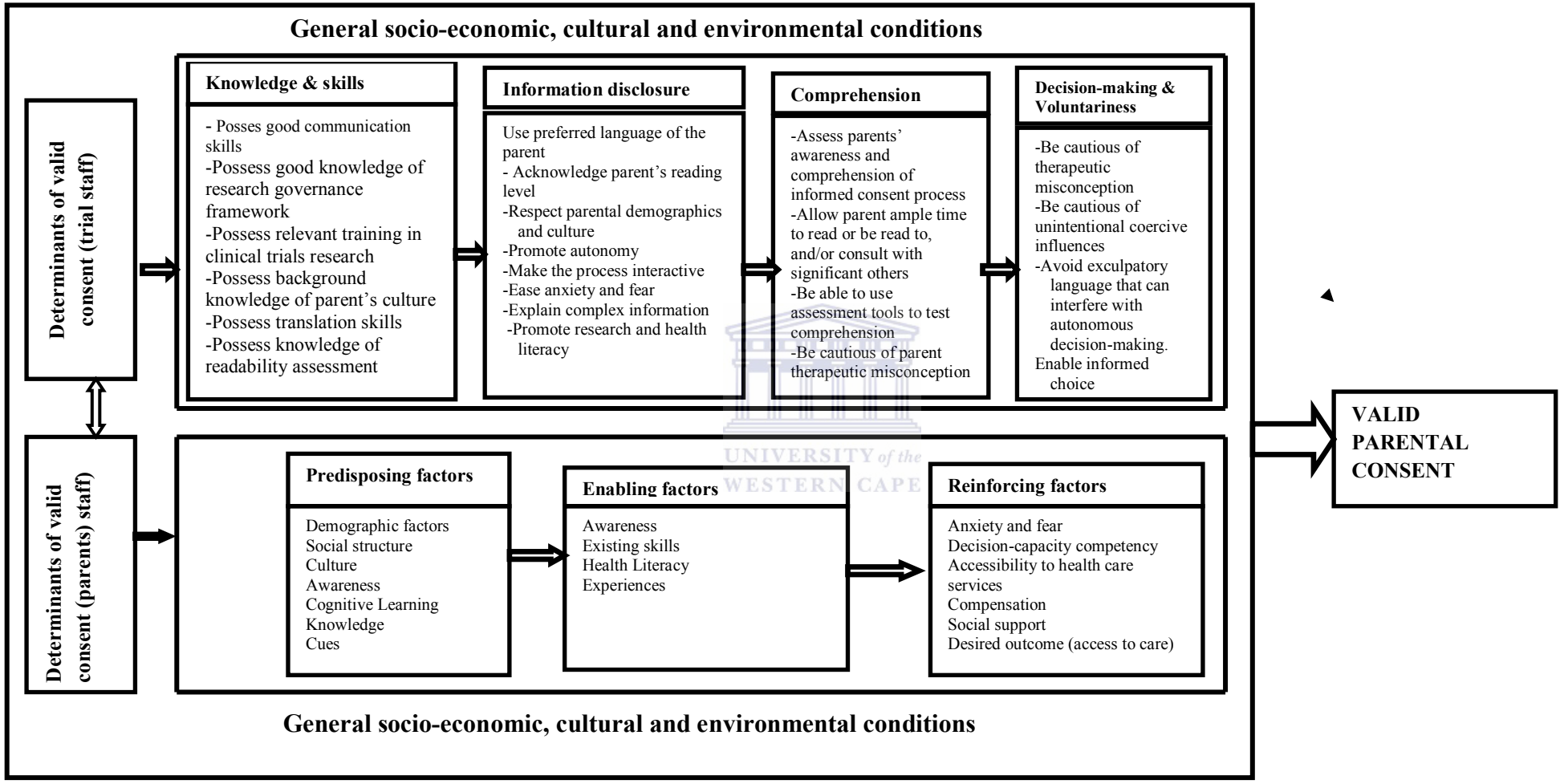

Figure 7.1: A model for obtaining parental informed consent for HIV clinical trials research with pediatric patients

CHAPTER EIGHT

GENERAL CONCLUSIONS AND RECOMMENDATIONS

8.0 Introduction

Chapter one outlined the statement of the problem regarding the process of obtaining valid parental informed consent. One of the major problems is the current increase in volume and complexity of pediatric HIV clinical trials conducted in Botswana due to the HIV pandemic, the government commitment to combating the disease and recommendations by WHO and FDA and other organizations to promote pediatric research into childhood diseases. However, the increase has not been accompanied by corresponding strength in the capacity of the country's research governance framework. There is a need to be mindful of the fact that the urgency and importance of the goals of HIV preventive (in this case vaccine) and treatment should not overshadow the need to protect the well-being and human rights of vulnerable trial participants like children.

The lack of background knowledge of the culture of Botswana by research institutions that draft the consent form raises challenges of comprehension due to language and cultural differences. Another challenge noted was the fact that most of the clinical trials conducted in Botswana are multisite studies where the consent forms are developed by sponsors and institutions outside Botswana. This raises problems of lack of sensitivity on the part of the researchers to the values and culture of Botswana and failure to contextualize the information provided to participants as reported in chapter five. Furthermore, differences in socio-economic status, authority/power, and health care systems between the trial staff and parents were identified to have an influence on the voluntariness with which decisions are made by the parents (Maruatona & Cervero, 2004; Botswana/ United Nations report, 2004) and confirmed in the results in chapters four and five. Additionally, it is doubtful that parents with chronically sick children asked to enrol their children in clinical trials would be expected to decline such participation.

Thirdly, at the moment Botswana lacks a standardized consent guide form to guide researchers who conduct trials involving children. The consent form guide that exists does

not comprehensively cover issues relevant to child participation in research but instead caters for all types of research. Chapter one also outlined the lack of translation into law and policies of children's rights charters like the United Nations Convention for Children's Rights, Convention on the Rights of the Child (United Nations General Assembly, 1989) and the African Charter on the Rights and Welfare of the Child (1990) which compels countries to respect and protect children's rights regarding participation of children in research (Fombad, 2005).

In addition, Chapter one outlined the lack of a clear legislation regarding age of consent to participation in research or dealing with the capacity of children to make medical decisions as well as the conflict between Botswana culture and the international instruments. The instruments emphasize that "the best interest of the child must be the primary consideration and children are rights holders" while Botswana culture as cited in Fombad (2005) like many other African cultures, believes that adults know what is best for the children and they are in a position to articulate the views of the children. Furthermore, considering the burden of nursing a chronically ill child, poverty, cultural differences and the low literacy levels might influence decision making of parents to child enrolment into research. Currently there is a paucity of literature in Botswana about the adequacy of obtaining parental informed consent and the factors that influence parents' decision making. Studies conducted thus far have mainly concentrated on adult informed consent (Shaibu, 2007; 2006).

This study therefore aimed to conduct a situational analysis of the current methods and practices of obtaining parental consent for pediatric HIV clinical trials conducted in Botswana in order to determine the readability and comprehension of the consent forms used to obtain consent from parents; to identify the communication methods, practices and perceptions of the trial staff regarding informed consent information disclosure; assess the extent to which parents are able to recall and understand the information disclosed to them and their satisfaction with the informed consent process; to identify and describe the reasons for parental approval to child enrolment into trial studies and use the findings to develop a model that can be used as a framework to guide the parental consent process in future. From the aims and objectives mentioned above, conclusions are made about each of the objectives.

8.1 Readability of the consent forms

When the information about the study is disclosed using a written informed consent document, the readability and comprehension of the text is very critical for conveying study information to enable a potential participant to arrive at a decision concerning their willingness to participate or not (Johnson (2004). It can be concluded from this study that the forms used for obtaining the parental consent process are too lengthy and difficult to be read and understood by the parents who were asked to read them and the levels recommended by research regulations. Results of similar difficulty were indicated in a study of a larger sample of pediatric biomedical research informed consent forms (Tarnowski, Allen, Maryhall et al. (1990). Although this evaluation was based on the English version of the informed consent standards using US metrics which might not equate to the readability in Setswana, in general, it is clear the levels of readability are far too high. Some studies have revealed the same concern (Hochhauser, 2004; Kithinji and Kass, 2010). It can also be concluded that there is minimal involvement of trial staff in drafting of the consent form. This results in missing out on tapping on the knowledge of culture, language and the setting trial staff possess. Another conclusion that can be made on readability is that there is no standardized formal assessment made on the readability of the consent form prior to its use. As a requirement, informed consent forms used in all clinical trials must be reviewed and approved by an independent ethics committee before practical use in the trials (Directive/2001/20/EC).

It is essential that consent forms are written in a clear, simple language that the participant understands and be administered in small proportions to ensure comprehension (CIOMS, 2002). In this regard, it can be concluded that the language the consent forms are translated into may not be well understood by all the parents who participate in trials research.

8.2 Communication

Another conclusion that can be drawn from the results is that the lengthy forms provide too much information. They thus overloaded potential participants with information much of which is also very complex. This challenge has been observed elsewhere (Gikoyo, Bejon, Marsh et al., 2008; Dresden & Levitt, 2001; Pace et al., 2005). Significant questions however remain about how to deliver the right amount of information to parents with different

backgrounds and needs to facilitate their decision making. It has been observed that much of the detail currently prescribed in consent forms is designed to protect the investigators and their institutions rather than the participants (Dresden & Levitt, 2001). The complexity of information provided to parents has been observed elsewhere. For example, The South African Department of Health (2006) observed that consent forms often present highly complex information that must be understood by patients and this was a major barrier to comprehension for many research volunteers especially those with low literacy skills.

Results showed in chapter four showed that trial staff disclosed all information without much interaction with the potential participant in form of giving them an opportunity to ask questions, answering them promptly and completely. However, we have to acknowledge that trial staff do not have the authority to alter or control the consent process. In addition trial staff confirmed that parents did not ask many questions during the discussions although the parents themselves claimed that they did. With this evidence, one can conclude that the communication or interaction method mainly used by the trial staff is the paternalistic one which does not promote autonomy. Through comprehensive training in communication skills, it is possible however for trial staff to learn to use methods like those described in chapter two that promote participant autonomy. A great deal of variance in physician-patient communication styles mainly in clinical settings has been observed (Korsch, Freemon, and Negrete (1971) and this can compromise the success of the communication process. The basic principle that governs informed consent is autonomy which have become symbols of integrity (Beauchamp and Childress, 2001).

8.3 Comprehension

It can be concluded from the results that trial staff are doubtful about parents' specific understanding of the difference between research and treatment, randomizations, study risks, confidentiality, and the uncertainty about the benefits of the study to their children. Results from the parents' interviews also showed low recall and comprehension of the above mentioned elements. Therefore one can conclude that there is lack of understanding of some of the elements of the consent form especially those that are not to do with accessing care for the child. This study interpreted this as stemming from therapeutic misconception. The study also concludes that the parents were not so concerned about the possible risks but about the

opportunity of the child accessing care. A number of authors have observed lack of understanding of disclosed information by research participants. For example, Marshall (2006) provided evidence from empirical studies on informed consent which suggest that even when provided with information about the nature of research, participants systematically misinterpreted the risk/benefit ratio of participating in research because they fail to understand the underlying scientific methodology. In such cases, what the participants actually authorize differs substantially from what they intend to authorize, and thus informed consent is frustrated. Pace et al., (2005) found that although most respondents in comprehension of consent to a randomized trial among HIV positive individuals in Thailand said they were well informed, only one third correctly reported that half of the participants would receive the experimental therapy. Such misunderstandings may arise from use of complex epidemiological terms like randomized assignment, placebo control groups, double blinded procedures and fixed treatment protocols. Other barriers to comprehension identified include the form's excessive length, lack of adequate time to read the form, high reading levels, and poor format and layout of the form; barriers which Hochhauser (2004) rightly says increase risks to both the researcher and participants, lead to therapeutic misconceptions, poor enrolment and failure to follow up.

8.4 Motivation, Decision-making and voluntariness

One major conclusion about motivation of parents to child enrolment into HIV clinical trials was self-interest in the form of perceived benefit regardless of the risks to the child. Expecting benefit could be attributed to inadequate information disclosure or understanding because potential participants should be told about uncertainty of benefits and should understand that they should not expect benefits when there is clinical equipoise. Although parental decision-making was purely personal many parents preferred to consult from significant others before making a final decision and trial staff confirmed that this had appositive influence on decision-making. The study concludes that because of the urgent need by the parents to access care for the child parental valid consent could have been compromised, thereby rendering the consent obtained invalid.

The literature reviewed in chapter two showed that in order for individuals to exercise their autonomy they must have the capacity to make free choices without coercion or undue

influence (Schiffman and Kanuk, 1997) which reflects voluntariness. The individual's choice is also influenced by the perceptions of his/her goals, anxiety and confusion experienced while making the decision (Arnold and Feldman, 1986 p. 340). In Botswana like in many developing countries, the health care of children is mostly a woman's responsibility. However, decision-making by women is often compromised by gender bias and power issues (Wassenaar, Bardorf & Richter, 2005). For example, Marshall (2004) found that nearly one-third of more than 400 participants married women interviewed in Nigeria to participate in the hypertension and breast cancer study needed permission from their spouses. Pace, et.al., (2005) also noted that voluntariness can be compromised by the stress caused by the nature of illness of the child as well as other socio-economic factors and these may erode decision making capacity. Decisional capacity is critical in decision-making to participation in research.

8.5 Recommendations

The recommendations listed below were drawn from the conclusions above. Implementing these recommendations would help to improve the process of obtaining parental informed consent for HIV clinical trials pediatric patients. However it worth noting that most of the recommendations will require advocacy from the trial staff, research institutions that conduct pediatric research and the Botswana national research ethics committee because the consent forms are pre-prepared and the trial staff have no authority to alter them as their role is to implement.

The first set of recommendations collectively lists all the strategies that can be put in place to improve the research governance framework regarding participation of children in trial studies:

- Botswana National REC should draft clear guidelines on clinical trials research involving children to guide researchers.
- Botswana National REC should draft a local standard template of the consent form that guides researchers designing parental consent forms. This requires provision of regulations and guidelines for seeking parental consent by the research ethics authorities.

- Botswana government should review some of the laws or include them into the legal system for example developing the human research bill.

The second set of recommendations focuses on improving the readability of consent forms:

- Research institutions should tap on the experience and cultural expertise of the trial staff, including both English and Setswana specialists, when translating the consent forms so as to make the language of the form clear and plain.
- All pediatric HIV clinical trial research investigators, participants and research ethics regulators should work together to in developing a of the consent form template
- Government, research institutions and other stakeholders should support short-term and long-term training to clinical trials research to enhance their knowledge and skills which could lead to specialization in areas identified as inadequate. This could also change the mind set and attitudes of clinical trial staff towards the consenting process.
- Research ethics training and communication skills should be a job requirement for those seeking to be employed in the area of seeking consent from parents who enroll their children in clinical trials.
- Research sponsors, investigators and research ethics committees should devise ways of simplifying consent forms readability without compromising the intensions of valid informed consent.
- Trial staff should be aware of the possibility of functionally illiterate participants, unable to read who may try to conceal the difficulty because there is a social stigma attached to not being able to read.
- Research sponsors, investigators and the research ethics committees should assess the readability of the English consent forms to get a general picture of the readability and understandability of the consent form submitted for review. They should also engage local language specialists to ensure that the translated versions are readable.
- Research sponsors, investigators and the research ethics committees should draft shorter versions of informed consent forms covering the crucial points only with information sheets covering more detailed information that might be relevant should be considered.
- Trial staff should diversify methods of disclosing information instead of focusing only on written documents. For example, the use multimedia for improving research

literacy by using options such as videos in the clinic waiting areas, illustrations in the consent form document, outlining, use of bullet points and diagrams should be considered.

The third set of recommendations centers around communication

- All research institutions involved in conducting pediatric HIV clinical trials should provide comprehensive and intensive prior health information (health literacy) about the study to all parents about their child's disease and the study procedures before the informed consent encounter in order for them to have good background knowledge. This knowledge would enhance familiarity with health concepts presented in the informed consent form.
- The trial staff should differentiate between general literacy and health literacy because low education levels do not necessarily translate into low health literacy levels. This would minimize the paternalism noted above.
- The trial staff should have some background knowledge of the culture of the potential participants in order to disclose information in a culturally appropriate and sensitive way.
- Research Institutions should offer training opportunities in communication skills, clinical trials research, pediatrics and research ethics to trial staff at different levels to improve their communication practices and methods as well as understand the principles and judgments that direct ethical actions. Health training institutions should introduce the necessary courses in their curriculum.

The fourth set of recommendations is directed towards comprehension of information disclosed:

- Clinical trial research staff should assess the decision-competency capacity of potential participants prior and during the screening process;
- Research staff should use familiar examples to explain some of the complex information; or engage specialists in health education and promotion
- Researchers should involve senior research team members like the clinicians in the consent process since the consent process is continuous.

- Governments should empower the research ethics committee members through providing resources human and financial, which can enable the members to monitor the consenting process regularly.

The fifth set of recommendations is centred around motivation, decision-making and voluntariness of participants:

- Trial staff must be cautious of unintentional coercive influences and avoid giving excessive incentives that can interfere with autonomous decision –making.
- The consent form should clearly explain the participant right of freedom to withdraw from the study and assurances that refusal to enrol a child in the study would not in any way interfere with the child getting standard care normally provided.
- Investigators should ensure that auxiliary care is provided to participants during research and is relatively similar to what is provided in the public facilities.

In summary this study contributed to an understanding of the legal, ethical and practical challenges faced by the trial staff and parents in achieving valid informed consent for pediatric HIV clinical trials. This information can be applied to other clinical research settings. Although it was clear from the findings that obtaining valid parental informed consent is almost impossible due to the vulnerability of the parent created by the child's illness and need to access care, parents had high regard for research, research institutions and the trial staff because of their satisfaction with the consent process, the care and education as well as the compassionate nature of the trial staff unlike what happens in public facilities.

The model developed can be used to minimize some the challenges that were identified. The recommendations suggested could contribute to the improvement of the parental informed consent process in Botswana. The model will be presented to the Ministry of Health, National Research Ethics Committee responsible for oversight of all research involving human subjects and to research institutions that conduct trials with pediatric patients. The information will also be disseminated in form of journal articles and at relevant conferences.

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LIST OF APPENDICES

APPENDIX 1: TRIAL STAFF CONSENT FORM

Title: A Model for Obtaining Parental Informed Consent for HIV Clinical Trials Research with Pediatric Patients
What is this study about?

This is a research project being conducted by **Mary Kasule, for a Ph D study**. I am inviting you to participate in this research project because you're conducting an HIV clinical trial that involves children as participants. As an Investigator involved in HIV clinical trials involving children, you might be in a position to provide me with the information that I can use to answer some of my research questions. The purpose of this research project is to identify the challenges encountered by research investigators who conduct clinical trials involving children when seeking informed consent from parents/guardians who enrol their children in HIV clinical trials. It is hoped that the recommendations from this study will help in addressing these challenges therefore improve the informed consent process for children participation in clinical trials in Botswana.

What will I be asked to do if I agree to participate?
You will be asked to answer questions by filling out a form, someone will interview you and you may also be asked to participate in a focus group discussion. The interviews will be conducted in a private room at the site where you conduct the clinical trial. The interview should take less than an hour. The research assistant will audiotape the session because we don't want to miss any of your comments. The questions that you will answer by filling in a form will include questions on personal information, the second section will have questions on the pre-enrolment stage of the consent process and the last section will include questions on the enrolment stage of the consent process. The interview will last about an hour.

Would my participation in this study be kept confidential?
We will do our best to keep your personal information confidential. To help protect your confidentiality, all effort will be made to ensure that the forms that you fill in and the recorded tapes will be kept in lockable filling cabinets and these will remain locked at all times. Identification codes will be used on the forms and no other forms of identifiers will be requested from you. The Principal Investigator will be the only one with access to the key. Data that will be entered in the computer will be protected with a password only accessible to the Principal Investigator. The transcribing of the recorded information will be done by an independent researcher to avoid identification of individuals by voice. In case of any publications, or report about this research project, your identity will be protected to the maximum extent possible.

What are the risks of this research?
Some of the questions asked in this study might make you uncomfortable and you are free not to answer any such questions if you do not wish to.

What are the benefits of this research?
This study might identify the challenges encountered by investigators when seeking informed consent and the findings will be used to develop a model that can help solve or improve identified challenges. The findings will also contribute evidence that can used to inform policy and other stakeholders regarding the protection of the rights and welfare of children and caregivers who participate in clinical trials.

Do I have to be in this research and may I stop participating at any time?
Your participation in this research is completely voluntary. You may choose not to take part at all. If you

decide to participate in this research, you may stop participating at any time. If you decide not to participate in this study or if you stop participating at any time, you will not be penalized or lose any benefits to which you otherwise qualify.

What if I have questions?

This research is being conducted by *Mary Kasule at the Ministry of Health.* If you have any questions about the research study itself, please contact Mary Kasule, Ministry of Health, and P/Bag 0038 Gaborone. Tel: +267-363-2466. E-mail address: mkasule@gov.b. Should you have any questions regarding this study and your rights as a research participant or if you wish to report any problems you have experienced related to the study, please contact:

Head of Department: Mr. P. Khulumani, Ministry of Health, Health Research Division, P/Bag 0038, GaboroneTel: 3632018E-mail: pkhulumani@gov.bw

Audio taping/Videotaping/Photographs/Digital Recordings

This research project involves making audiotapes to allow data to come out in its detailed richness and allow research assistants to observe the participants and make notes. These tapes will be locked up in filling cupboards and only the research team will have access to the key. The tapes will be destroyed three years after close-out of the study.

Please indicate below whether you agree to be audio taped.

___ I agree to be audio taped during my participation in this study.

Signature……

Date……

___ I do not agree to be audio taped during my participation in this study.

Signature……..

Date……..

Declaration by researcher/research assistant

I_____ declare that:

- I explained the information in this document to the participant.
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understood all aspects of the proposed study

Signature of researcher/research assistant_____

Date_____

.**Audio taping/Videotaping/Photographs/Digital Recordings**

This research project involves making audiotapes to allow data to come out in its detailed richness and allow research assistants to observe the participants and make notes. These tapes will be locked up in filling cupboards and only the Principal Investigator will have access to the key. The tapes will be destroyed three years after close-out of the study.

Please indicate below whether you agree to be audio taped.

___ I agree to be audio taped during my participation in this study.

___ I do not agree to be audio taped during my participation in this study.

Signature of participant_____

Date_____2009

Declaration by researcher/research assistant

I_____ declare that:

- I explained the information in this document to the participant.
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understood all aspects of the proposed study

Signature of researcher/research assistant_____

Date_____

APPENDIX 2: TRIAL STAFF IN-DEPTH INTERVIEW GUIDE

Title: A Model for Obtaining Parental Informed Consent for HIV Clinical Trials Research with Pediatric Patients

Start Time……

This study is aimed to identify challenges encountered by investigators who conduct children HIV clinical Trials regarding seeking informed consent from parents/guardians who agreed to enrolment of their children into HIV clinical trials. Your participation in this study is voluntary and you have the liberty not to answer any of the questions; however I hope you will participate in this study, as your input will help us to enhance the informed consent process in studies where children are enrolled as research subjects. All of your responses will be confidential and will not in any way be used to identify you!

QUESTIONNAIRE IDENTIFICATION:

INTERVIEWER: …….. QUESTIONNAIRE NUMBER | | | | |

DATE: | D | D | M | M | Y | Y | Y | Y |

Instructions: Please answer the following questions by filling out this form.

PERSONAL INFORMATION		
No	**QUESTION**	**ANSWER**
Q1	Gender	O M O F
Q2	Age	O 20-30 yrs. O 30-40 yrs. O 40-50 yrs. O over 50 yrs.
Q3	Highest academic degree awarded	
Q4	Occupation	
*Q 5	Have you had any specialized training in ethics of conducting clinical trials research?	O None O Research courses at Tertiary level O Good Clinical Practice(GCP) O Basic Bioethics O Advanced Bioethics O Clinical trials O Advanced Bioethics O Ethics seminars or workshops O Other _____ Please Specify
Q6	Do you have any specializations in pediatrics? and how long have you been involved in recruitment/conducting pediatric HIV clinical trial	
Q7	Citizenship.	
Q8	Place of residence	
PRE-ENROLLMENT STAGE		

*Q 9	Which Phase of clinical trial have you been involved in?	**Phase I**= first introduction into man, healthy volunteers, usually single dose, preliminary safety & pharmacokinetic/dynamic profile(blood& urine) **Phase II** = therapeutic exploratory studies, small sample size of patient groups, efficacy & safety, double-blinded studies, dose range and regimen and common side effects **Phase III**= therapeutic confirmatory studies, double-blinded, large sample size of patient groups, long term studies, efficacy and safety, side effect profile and pre-registration. **Phase IV**=therapeutic use or post marketing surveillance, limited to approved indications, differentiate drug from others, dose-response, general safety.
Q10	What was the risk category of the clinical trial you recently conducted?	O Less than minimal risk to the human subject O Greater than minimal risk but presents a prospect of direct benefit to the human subject O Greater than minimal risk with no prospect of direct benefits to the human subject but likely to yield generalizable knowledge about the human subjects' disorder or condition.
Q 11	On average, what generally is the highest level of education attained by the majority of the parents/guardian who give consent for their children's participation in clinical trials?	O No education O Primary O Secondary O Tertiary O Don't know
Q12	On average, what is the average age of the parents/guardians whom you have obtained consent from for their children's participation in clinical research?	O 15- 25 O 26-30 O 31-35 O 36-40 O 41-45 O > 45
Q13	On average how many of your participants have previous experience with research on HIV disease?	O Majority O Few O Very few
Q14	What generally is social economic status of the majority of the parents/guardians who participate in your studies?	O High O Medium O Low O Very low
Q 15	How do you rate the importance of prior of knowledge of a research investigator about Botswana culture, values and beliefs before the start of the study?	O Very important O Important O Fairly important O Not important Give a reason for your answer_____

	Do you think this knowledge plays any role in the success or failure of a consenting process? (Please explain)	
Q16	Who prepares the consent form that you use in the clinical trial?	O Sponsor O Institution O Principal Investigator O Research Team O Other _____ Please specify
Q17	On average how many pages is your consent document?	1-5 pages 6-10 pages 11-15 pages >15 pages
Q 18	Which of the following research guidelines are you familiar with regarding the protection of research participants and how helpful they are to the consenting process?	O Botswana laws O The Belmont Report O The Declaration of Helsinki O The CFR O The CIMOS O The ICH(GCP) O Botswana Guidelines on conduction of Clinical trials Version 2008 O The Botswana Consent form Guide O The Nuremberg Code O Other _____ Please specify Answer
*Q 18 b	GCP guidelines recommend that both the informed consent discussion and the informed consent form should include the twenty elements. Do your consent forms include all these elements and are you able to go through all these during your sessions?	(Please explain)
Q 19	What challenges do you encounter from the **sponsors** regarding the requirements for preparation of the informed consent document for the clinical trial if applicable?	Please briefly explain (translating into language(s) understood by participants)
Q20	What challenges do you encounter from the **ethics committees** that review your consent form if applicable?	Please briefly explain
INFORMATION DISCLOSURE		
Q 21	What recruitment methods do you use to let parents/guardians know about this study? *(Check all that apply.)*	O Radio announcement O Posters/billboards O Circulation of flyers w/in local NGO/Church O Circulation of flyers w/in specific communities O In-clinic contact

		O Referrals from other clinics or medical professionals O Other _____ (Please Specify)
Q22	Who talks to the parents/guardians/children about the clinical trial when they came to the hospital/clinic?	O Self O Co-investigator O Study Nurse O Study recruiter O Research assistant O Other _____ (Please specify)
Q 23	In what language are the discussions of the information about the study held?	O English O Setswana O Other_____ Please specify
Q24	How is the information about the clinical trial communicated to the parent/guardian/child (verbally/read to the participants/asked participants to read)	O Verbally by reading the consent form to the respondent in English O Verbally by reading the questionnaire to the O respondent in Setswana O English written consent is given to the parent/guardian to go home and read O Setswana written consent is given to the parent/guardian to go home and read O English written consent is given to the parent/guardian to read during the consent session O Setswana written consent is given to the parent/guardian to read during the consent session O Other _____ Please specify
Q25	From your experience, which of the following elements of the consent form do find difficult to communicate to participants and why?	O Purpose of study O Procedures to be performed on the child O Risks of the study O Unforeseen risks O Benefits of the study O Right to withdraw without reproach O Consent for transfer of samples O Consenting for use of stored samples for future use O Possible alternatives O Payment for participation O Responsibility for care in case of injury while on the study O Confidentiality and privacy O How the doctor will decide which treatment to give your child O The number of times your child will receive the treatment O The possibility of quitting the study

		O Placebo use O Randomization O Control group Other _____ Please specify
Q26	How would you rate the amount of information provided to the parents/guardians in the studies you have conducted? Do you consider all the information relevant for the participant to make an autonomous decision?	O Too much O A lot O Average O Too little O Other _____ Please specify
Q27	Considering the risks involved in clinical trials, when disclosing information to participants, which criteria do you use?	O Reasonable-doctor standard (doctor may use a reasonable skill and may withhold information) O Reasonable-patient standard (doctor has the duty to disclose all the information necessary to making an intelligent and rational choice) O Disclose all the information
Q28	How would rate the complexity of the technical language used in the consent document and how do enhance understanding of such language?	O Too complex O Fairly complex O Understandable O Other _____ Please specify and give reasons
	UNDERSTANDING	
Q29	How do majority of participants initially react to experimentation on their children? Do the parents understand the difference between research and treatment?	O Extremely frightened O Very frightened O Fairy frightened O Anxious O More anxious than when they came in O Pleased O Satisfied O Pleased O Sad O Other _____ Please specify
Q 30	Do the parents/guardians ask any questions?	O Yes O No
Q31	If yes what are usually their main concerns? Briefly explain	O Safety of the child O Payment for participation O Risks O Benefits O Difference between research and treatment O Why was the child chosen to participate O What happens in case of refusal to participate regarding future treatment Other _____ Please specify
Q32	If no questions are asked do you find out why?	O Yes O No
Q33	What do you think is the most common reason for the parents/guardians not asking questions?	Please specify_____

Q34	According to your observation, what is usually the general emotional state of the parents/guardians during the consenting process?	O Calm O Anxious O Distraught/upset O Other _____ Please explain
Q35	How do you test the level of understanding of the information provided about the trial?	O Verbally O Written test of understanding Pictures & stories Other_____ Please specify
Q36	How would you rate the level of attentiveness of the parent/guardian during the consent process?	O Very high O High O Fair O Low O Very Low
Q37	How much time do you think is appropriate for the informed consent process to enable understanding?	Please indicate and give reasons
DECISION MAKING		

Q39	Is it important to you to always consult the two parents or the **relative(s)** of the participants even if the person who has brought the child to the clinic agrees to participate? Do all the parents insist on consulting with the spouse or family before making a decision?	O Yes O No
Q40	Who do you mainly consult before enrollment of the child into the study?	O Spouse O Grandmother O Grandfather O Uncle O Auntie O Other_____ Please specify
Q41	Does the involvement of a participant's **spouse or relative(s) influence** the **time** necessary to obtain informed consent?	O Yes O No Please give a reason for your answer
Q42	How do majority of the parents/guardians indicate their agreement to their children's participation clinical research?	O By signing on the consent form O By putting a thumb on the consent form O Verbally
Q43	How do the parent(s)/guardian(s) react to being asked to sign a consent form?	Did not seem to mind Were reluctant to sign Other_____ Please specify
Q44	How do you facilitate the decision-making process?	Please briefly explain
Q45	From your interaction can you identify any social, cultural, economic or any other factors that you think might influence the parents/guardians to agree to enroll their children in the study?	Please briefly explain

Q46	Describe any measures you put in place to ensure that participants and the consenting parents/guardians do not feel coerced or pressured to join the study as well as continued consent during the study.	Please briefly explain
Q47	Please describe any general challenges you sometimes encounter in the process of seeking informed consent from parents/guardians/child	Please briefly explain
Q48	Please give any recommendations that would help in enhancing the informed consent process for child participation in clinical Trials.	Please briefly explain
Q49	Do you involve competent children in the consent process?	Please state
Q 50	Children of what age do you engage in the consent process	O 3-8 years O 9-15 years O 16-21 years
THANK YOU FOR YOUR TIME AND COOPERATION END OF QUETIONNAIRE Time……..		

APPENDIX 3: FOCUS GROUP DISCUSSION GUIDE

Title: A Model for Obtaining Parental Informed Consent for HIV Clinical Trials Research with Pediatric Patients

Informed consent is recognized as the patient /participant safety mechanism for clinical research. Obtaining informed consent embodies challenges and complexities deeper than may be immediately determined.

Participant Background Information

1. Can we start by introducing ourselves? Briefly tell us about your educational background and what you do regarding the consenting process of potential study participants?
2. How many of you have been involved in pediatric HIV clinical trials/studies?
3. How do you rate the importance of prior of knowledge of a research investigator about Botswana culture, values and beliefs before the start of the study?
4. Do you think this knowledge plays any role in the success or failure of a consenting process?
5. On average, what is the highest level of education attained by the majority of the parents/guardian who give consent for their children's participation in clinical trials?
6. Which Phase pediatric clinical trial have you been involved in (Phase I , II, III or IV)?
7. How would you rate the risk category of the clinical trials you have been involved in?(Less than minimal risk to the human subject, greater than minimal risk but presents a prospect of direct benefit to the human subject, greater than minimal risk with no prospect of direct benefits to the human subject but likely to yield generalizable knowledge about the human subjects' disorder or condition)
8. What does the term informed consent mean to you?
9. From your experience, can you briefly explain what the informed consent means to potential participants or parents who enroll their children in clinical trials?
10. Can you briefly carry us through a typical a typical consenting session?

Consent form documentation

1. Please tell us about your role in the documentation of consent forms.
2. On average how long are the consent forms that you use?
3. What are some of the challenges you encounter in documentation process? (Language complexity, translation, sponsors, ethics committee).
4. Several international and national guidelines have been developed to guide the preparation of the consent form. How strictly are these guidelines followed and applied in the preparation process (including all elements)?
5. Can you suggest some recommendations as to how to design a consent form that would be contextualized to Botswana's context regarding, readability and understanding; quantity and quality of information to be included, clarity and simplicity in order to enhance recruitment and adherence to procedure?
6. Any other comments you would like to share about the consent form?

Information disclosure

1. What recruitment methods do you use to let parents/guardians know about research studies?

2. Who talks to the parents/guardians/children about the clinical trial when they came to the hospital/clinic? (First contact person)

3. To what extent are the clinicians/doctors/physicians involved in the information disclosure process?
4. One of the requirements of a valid informed disclosure is "full disclosure" of information. What is your opinion about the feasibility of

achieving this requirement and what methods do you use to achieve this?

5. How would you rate the amount of information provided to the parents/guardians in the studies you have conducted? Do you consider all the information relevant for the participant to make an autonomous decision?
6. What is your opinion about the quantity and quality of information usually disclosed to participants?
7. Do parents ask questions during the information disclosure sessions and what type of questions do they usually ask?
8. How do ensure that parents understand the difference between treatment and research to avoid therapeutic misconceptions.

Understanding

What is your opinion about this statement "Information disclosure should mainly aims at fulfilling legal requirements than facilitating autonomous decision"?

1. Can we briefly talk about the challenges you encounter in facilitating understanding (i) the procedures, (ii) risks and benefits, (iii) voluntariness, (iv) scientific and epidemiological research terminologies and information explained in statistical terms?
2. Can you suggest any possible solutions to these challenges?
3. Regarding time constraints and sponsor requirements how you determine how much time is needed for the participant to respond to the request of participation.
4. Can we talk about some of the different methods you use to test participant understanding and suggest what has worked best?

Voluntariness

1. What are some of the factors you have observed to influence the decision to enroll children in HIV clinical trials.
2. In cases where children are above 7 years of age, to what extent do you involve them in the informed consent process and what methods do you commonly use to facilitate their understanding of what is being suggested to them?
3. Can tell us about the positive things parents say about their children's participation in HIV clinical trials.
4. Can you tell us the negative things parents say about their children's participation in HIV clinical trials?
5. Generally how satisfied are you with the current practices of the consenting process in the studies you have been involved in?

THANK YOU FOR YOUR TIME AND COOPERATION

END OF DISCUSSION END TIME……A.M/P.M

APPENDIX 4: FOCUS GROUP PARTICIPANT CONSENT FORM (INDIVIDUAL)

Title: A Model for Obtaining Parental Informed Consent for HIV Clinical Trials Research with Pediatric Patients

What is this study about?

This study is being conducted by **Mary Kasule, for a Ph D study**. I am inviting you to participate in this study because you are involved in the consenting process of parents/guardians who enrol their children in HIV clinical trials conducted in Botswana. *As a research investigator who seeks informed consent from parent/guardians who agree to enrol their children in HIV clinical trials conducted in Botswana to find out about more about the HIV disease prevention, treatment and care among children, you might be in a position to provide me with the information that I can use to answer some of my research questions.* The purpose of this study is to conduct a situational analysis of the current practices of obtaining parental consent for pediatric HIV clinical trials conducted in Botswana in order to evaluate the quality of the process and use the findings to develop a conceptual model that can be used as a framework to guide the parental consent process. Specifically the study aims to assess the documentation of consent forms and other participant information, information disclosure, comprehension of disclosed information and voluntariness of parents to enrol their children n HIV clinical trials. It is hoped that the recommendations from this study will help in addressing these challenges therefore improve the informed consent process for child participation in HIV clinical trials.

Do I have to take part in the focus group discussions and if I do can I stop participating in the focus group discussions at any time?

Your participation in this research is completely voluntary. You may choose not to take part at all. If you decide to participate in this research, you may stop participating at any time. If you decide not to participate in this study or if you stop participating at any time, this will not affect your ongoing research studies in any way.

What will I be asked to do if I agree to participate?

You will be asked to participate in a focus group discussion comprising of researchers involved in the consenting of parents/guardians of children who are enrolled in HIV clinical trials. Guiding questions will be asked by a trained moderator. The discussions will be held at a selected site in a room that can afford a maximum degree of privacy and individual participants will be not be identified by their names but will be assigned a number which will be displayed on a nametag. The focus group discussions should take a maximum of ninety (90) minutes. The moderator and note-taker will be audio taping the session as well as taking notes so that we don't miss any of your important comments and contributions. The questions that you will answer will include questions on consent form and participant information documentation, information disclosure and parental understanding of provided information as well as parental voluntariness.

Would my participation in this study be kept confidential?

We will do our best to keep the information you provide during the discussions confidential. Your identity as well as that of all team members involved in the focus group discussions will remain confidential. The moderator and note-maker will not use names or personal identifying information in anything written about this focus group discussion. To help protect your confidentiality, all effort will be made to ensure that the tapes with the answers to your questions and any notes which will be made during the group discussion will kept in lockable filling cabinets which will remain locked at all times. The research investigator for this study will be the only one with access to the key. Data that will be entered in the computer will be protected with a password only accessible to the research team. In case of any publications, or reports about this research project, your identity will be protected to the maximum extent possible. Your identity as well as that of the focus group team members will remain confidential.

What are the risks of this research?

Some of the questions asked in this study might make you uncomfortable; however you are free not to answer any such questions if you do not wish to.

What are the benefits of this research?

This study might identify some of the challenges encountered by research investigators when seeking parental informed consent as well as gaps in the process. Findings will be used to develop a model that can address the

identified challenges and gaps. The findings will also contribute evidence that can be used to inform policy, develop research guidelines and standard operating procedures that may help to standardize the consenting process.

What if I have questions?

This research is being conducted by *Mary Kasule at the Ministry of Health.* If you have any questions about the research study itself, please contact Mary Kasule, Ministry of Health, and P/Bag 0038 Gaborone. Tel: +267-363-2466. E-mail address: mkasule@gov.bw. Should you have any questions regarding this study and your rights as a participant or if you wish to report any problems you have experienced related to the study, please contact:

Head of Department: Mr. P. Khulumani, Ministry of Health, Health Research Division, P/Bag 0038, Gaborone; Tel: 3632018; E-mail: pkhulumani@gov.bw

Declaration by participant

I have read or has been explained the information above, and I have had all my questions answered to my satisfaction. I voluntarily agree to participate in this focus group discussion Please indicate below whether you agree to participate in the focus group discussion

___ I agree to be audio taped during my participation in this study.

Signature……

Date……

___ I do not agree to be audio taped during my participation in this study.

Signature……..

Date

Audio taping/Videotaping/Photographs/Digital Recordings

This research study involves making audiotapes to allow data to come out in its detailed richness and allow research assistants to observe the participants and make notes. These tapes will be locked up in filling cupboards and only the research team will have access to the key. The tapes will be destroyed three years after close-out of the study.

Please indicate below whether you agree to be audio taped.

___ I agree to be audio taped during my participation in this study.

Signature……

Date……

___ I do not agree to be audio taped during my participation in this study.

Signature……..

Date

Declaration by researcher/research assistant

I_____ declare that:

- I explained the information in this document to the participant.
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understood all aspects of the proposed study

Signature of researcher/research assistant_____

Date_____

APPENDIX 5: FOCUS GROUP TEAM CONFIDENTIALITY BINDING FORM

Title: A Model for Obtaining Parental Informed Consent for HIV Clinical Trials Research with Pediatric Patients

To ensure clear professional boundaries and protect the privacy of individuals participating in the focus groups, the focus group team agrees to the following:

1. The information collected during the focus groups is strictly intended only for academic purposes.
2. The focus group team agrees that it will not speculate about the identity of any particular focus group participant.
3. Team members who observe a focus group will not record any personal identifying information in their notes or disclose any personal information in the debriefing sessions.
4. Team members will maintain the confidentiality of each person and situation they may come in contact with.
5. The facilitator (s) and note-taker(s) will obtain consent to the discussion and note taking from all focus group participants prior to the start of the discussion.

_____

Signature of Focus Group Team Member

_____

Date

APPENDIX 6: PARENTS/GUARDIAN CONSENT FORM

Title: A Model for Obtaining Parental Informed Consent for HIV Clinical Trials Research with Pediatric Patients

What is this study about?

This is a research project being conducted by **Mary Kasule, for a Ph D study**. I am inviting you to participate in this research project because your child is enrolled in a study that I have selected to use for my study. *As a parent who agreed to enrol your child in a study about finding out more about the HIV disease treatment among children, you might be in a position to provide me with the information that I can use to answer some of my research questions.* The purpose of this research project is to identify the challenges faced by parents/guardians who agree to have their children participate in studies that aim to find out about causes of HIV disease, and how it can be prevented and treated during the process of giving research investigators permission (informed consent) to enrol their children in the studies. It is hoped that the recommendations from this study will help in addressing these challenges therefore improve the informed consent process for child participation in HIV clinical trials.

What will I be asked to do if I agree to participate?

You will be asked to answer questions asked by a trained research assistant. The interviews will be conducted in a private room at one of the sites where HIV clinical trials involving children are conducted or any place that you find convenient. The interview should take less than an hour. The interviewer will be audio taping the session because we don't want to miss any of your important comments. The questions that you will answer will include questions on personal information, how the information about the study is given, your understanding of the information that you are given and how you decide to agree to enrol your child in the study.

Would my participation in this study be kept confidential?

We will do our best to keep your personal information confidential. To help protect your confidentiality, all effort will be made to ensure that the tape recorders with the answers to your questions and any notes that will be made during the interview will kept in lockable filling cabinets which will remain locked at all times. The research investigator will be the only one with access to the key. Data that will be entered in the computer will be protected with a password only accessible to the research team. In case of any publications, or report about this research project, your identity will be protected to the maximum extent possible.

What are the risks of this research?

Some of the questions asked in this study might make you uncomfortable and you are free not to answer any such questions if you do not wish to.

What are the benefits of this research?

This study might identify the challenges encountered by parents/guardians when giving informed consent and the findings will be used to develop a model that can address the identified challenges. The findings will also

contribute evidence that can used to inform the authorities to set rules that may help to conduct the process of informed consent better.

Do I have to be in this research and may I stop participating at any time?

Your participation in this research is completely voluntary. You may choose not to take part at all. If you decide to participate in this research, you may stop participating at any time. If you decide not to participate in this study or if you stop participating at any time, you will not be penalized and your child will continue to be treated for any illness each time you go to any health facility.

What if I have questions?

This research is being conducted by *Mary Kasule at the Ministry of Health.* If you have any questions about the research study itself, please contact Mary Kasule, Ministry of Health, P/Bag 0038 Gaborone. Tel: +267-363-2466. E-mail address: mkasule@gov.b. Should you have any questions regarding this study and your rights as a research participant or if you wish to report any problems you have experienced related to the study, please contact:

Head of Department:

Mr. P. Khulumani, Ministry of Health, Health Research Division, P/Bag 0038, Gaborone

Tel: 3632018

E-mail: pkhulumani@gov.bw

Audio taping/Videotaping/Photographs/Digital Recordings

This research project involves making audiotapes to allow data to come out in its detailed richness and allow research assistants to observe the participants and make notes. These tapes will be locked up in filling cupboards and only the research team will have access to the key. The tapes will be destroyed three years after close-out of the study.

Please indicate below whether you agree to be audio taped.

___ I agree to be audio taped during my participation in this study.

Signature…… Date……

___ I do not agree to be audio taped during my participation in this study.

Signature…….. Date

Declaration by researcher/research assistant

I_____ declare that:

- I explained the information in this document to the participant.
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understood all aspects of the proposed study

Signature of researcher/research assistant_____

Date_____

APPENDIX 7: TETLA YA MOTSADI/MOTLHOKOMEDI WA NGWANA YA GO KA TSAYA KAROLO MO PUISANONG

Setlhogo: Tsela ya go tsaya tetla mo motsading go akaretsa bana mo ditshekatshekong tsa HIV

Patlisiso e ke ka ga eng?

Patlisiso e diriwa ke **Mme Mary Kasule, yo e leng moithuti.** O kopiwa go tsaya karolo mo patlisisong e ka gore ngwana wag ago o tseneletse tshekatsheko e mmatlisisi a tlhopileng go e dirisa mo tshekatshekong ya gagwe. *O le motsadi wa ngwana o ne wa dumela gore ngwana wa gago a tsenelele tshekatsheko e o go yone go sekasekiwang go itse dintlha tsa botlhokwa ka kalafi ya mogare wa HIV mo baneng. Mosekaseki o ne a lemoga fa o ka tswa o na le kitsiso e e ka mo thusang go ka araba dipotso dingwe tsa patlisiso ya gagwe.*

Maikaelelo a patlisiso e ke go leka go tlhaloganya ka dikgwetlho tse batsadi kgotsa batlhokomedi ba bana ba dumetseng gore bana ba bone ba tsenelele patliso ya go leka go itse ka mogare wa HIV ba lebaganeng le tsone. Mmatlisisi o leka go itse gore dikgwetho tse di ka emisiwa jang kgotsa di ka kganelwa jang fa motsadi/motlhokomedi a letlelela gore ngwana wa gagwe a tseye karolo mo ditshekatshekong tse. Re solofela fa dintlha tse mmatlisisi a tla di lemogang ka dikgwetlho di tla thusa basekaseki go tokafatsa tsela ya gore motsadi wa ngwana o ka fa tletla ya gore ngwana wa gagwe a tsenelele tshekatsheko e ya kalafi ya mogare wa HIV.

Ke ya go kopiwa go dira eng fa nka dumela go tsaya karolo mo patlisisong e?

O tla kopiwa go araba dipotso tse o tla di bodiwang ke mothusa mmatlisisi yo o rutetsweng tiro e. Potsoloso ya patlisiso e e tla tshwarelwa mo ntlong ee faphegeling, o tla bo o nale mmatlisisi fela. Dipotsolotso tse di tla tshwarelwa kwa lifelong le ngwana wa gago a tseneletseng ditshekatshekong teng kana ko wena o bonang go ka tshwanela kana fa go go siametseng teng. Potsolotso e e tla tsaya metsotso e sa feteng masome a marataro (oura). O tla botswa dipotsa ka botshelo jwa gago le ba lelwapa la gago, dipotso ka fa ba bongaka ba go fang kitso ya tshekatsheko e ngwana wa gago a e tseneletseng, dipotso ka fa o tlhaloganyang kitso e o e filweng le ka fa o dumelanang le ba bongaka ka go letlelela gore ngwana wag ago go ka tsenelela tshekatsheko.

A go tsenelela patlisiso e go tla nna sephiri sa me le mmatlisisi

Re tla dira ka fa re kgonang ka teng gore kitso ka gago le botshelo jwa gago e itsiwe ke mmatlisisi fela. Sengwe le sengwe se re tla se dirang mo potsolosong ya patlisiso e se tla nna mo lifelong le le babalesegileng e bile le tla lotlelwa ka nako tsotlhe. Mmatlisisi ke ene fela a tla nna le selotlelo sa lefelo leo. Fa patlisiso e e ka tsengwa mo computareng go tla tsengwa dinomoro tsa sephiri go itsa o pe yo o senang tlela go ka bula mekwalo ya patlisiso e. Fa go ka dirigala gore patlisiso e e go ka kwalwa ka yo ne kgotsa go ka amoganwa kitso ka yone re tla netefatsa gore kitso epe ka ga wena ga e itsewe ke ope, le gore o mang go tla nna sephiri, e bile ga go kitla go itse ope gore o kile wa tsenelela patlisiso e.

A go na le ditlamorago tsa go tsenelela patlisiso e?

Dipotso dingwe tse o tla di botswang gongwe ga di na go go tsaya sentle mme o letlelesega gore o seka wa di araba fa o sa tseege sentle.

Mosola wa patlisiso e ke eng?

Patlisiso e e leka go tlhaloganya ka dikgwetlho tse batsadi kgotsa batlhokomedi ba bana ba dumetseng gore bana ba bone ba tsenelele ditshekatsheko. Re solofela fa dintlha tse mmatlisisi a tla di lemogang ka dikgwetlho di tla thusa basekaseki go tokafatsa tsela ya gore motsadi wa ngwana o ka fa tletla ya gore ngwana wa gagwe a tsenelele tshekatsheko e ya kalafi ya mogare wa HIV.

A ke a patelesegang go tsenelela patlisiso e e bi le a ke kgona go emisa go tsaya karolo mo patlisisong e? Go tsaya karolo mo patlisong e ke boithaopo. O kgona go emisa go tsaya karolo o gololesegile. Fa o eletsa go tsaya karolo o ka dira jalo mme o letlelesega go emisa go tsaya karolo nako ngwe le ngwe. Fa o dumelane le go tsaya karolo mo patlisisong e, go o na go otlhaiwa e bile ngwana wag a go o tla tswelela ka go nna le seabe mo tshekatshekong ea a e tseneletseng.

Fa ke na le dipotso?

Patlisiso e key a ga mme *Mary Kasule go tswa kwa lephatla la botsogo.* Fa o na le dipotso ka ga patlisiso e oka ikopanya le Mary Kasule, Lephatla la Botsogo, P/Bag 0038, Gaborone. Mogala ke + 267 363 2466. E-mail address: mkasule@gov.bw.

Fa o na le dipotso dingwe mabapi le patlisiso e kana mabapi le ditshwanelo tsa gago le go tseneleng patlisiso e ka na o batla go ikuela o na le di ngongorego mabapi le patlisiso e, o ka ikopanya le

Mogolwane wa Lephatla la Botsogo

Mr P. Khulumani, Lephatla la Botsogo, Lakalana la Dipatlasiso tas Botsogo, P/Bag 0038, Gaborone

Mogala: 3632018

E-mail: pkhulumani@gov.bw

O kopiwa go supa fa o dumelana kgotsa o sa dumelane le go nna le seabe mo patlisisong ee.

_____ Ke a dumela go tsenelela patlisiso ee.
Saena fa/ Baa monwana fa ……. Letsatsi ……
_____Ga ke dumelane go tsenelela patlisiso ee.
Saena fa/ Baa monwana fa, fa o sa dumelane …….. Letsatsi …….

Netefatso ya mmatlisisi/ kgotsa mothusa mmatlisisi

Ke le _____
ke netefatsa gore:

- Ke tlhaloseditse mongwe le mongwe yo o tsayang karolo mo patlisisong gore patlisiso e ke ya eng le gore ke eng ba kopiwa go tsaya karolo mo go yone.
- Ke mo kgotlhaditse gore fa a na le dipotso a ka botsa e bile ke mo file sebaka ka araba dipotso.
- Ke kgotsofalela gore o tlhalogantse sengwe le sengwe ka patlisiso e.

Saena fa/ baa monwana (Mmatlisis/ mothusa mmatlisisi)
…….

Letsatsi
……

APPENDIX 8: PARENT SEMI-STRUCTURED INTERVIEW GUIDE (ENGLISH)

Title: A Model for Obtaining Parental Informed Consent for HIV Clinical Trials Research with Pediatric Patients

Questionnaire #__ __ __

Date: __ __/__ __/__ _

Thank you for agreeing to participate. Your participation in this study is voluntary and you have the liberty not to answer any of the questions. The information gathered will allow the authorities to improve the process of talking to parents of children enrolled in studies such as the one your child was in. The information you give will remain confidential and will not in any way be used to identify you.

Please remember that if you do not want to answer any specific questions, you are free to skip them.

SECTION A: We would like to know about you, your child and your family

1	Gender	Male	Female				
2	What is your age in years?						
3	Where do you live?	Town/city	Village	Ward			
4	What is your highest level of education?	Tertiary	Senior school	Junior school	Primary School	Non-formal education	None
5	Do you know how to read and write	Yes	No				
6	In which language can you read fluently and write well?	English	Setswana	Other (specify)			
7	Are you the mother (father, parents/guardians) of this child?	Yes	No				
8	How old is your child?						
9	If you are the guardian to this child, what is your relationship to this child?	Grandmother	Grandfather	Auntie	Uncle	Other	
10	Has your child ever been in other research studies?	Yes	No				
11	How many research studies has your child been in?						
12	Have any of your other children been in any research studies?	Yes	No				
13	How many times have you brought your child to see doctors in the last year?	Very few times	Few times	Many times	Probe for frequency		
14	How many people live in your house?						
15	Who is the head of the house?						
16	What is your marital status?	Co-habiting	Married	Single	Divorced	Other	
17	Are you working?						
18	If you are working were do you work?						
19	What is the job of the child's father (mother)?						
20	The house where you live, is it for…?	My Land Lord	My Relative	My Employer	My Spouse		
21	What type of a house do you live in?	High Cost	Medium Cost	Low cost	SHAA House		
22	Does the house where you live have the following utilities?	Electricity	Running Water	Both (electricity and running water)			

SECTION B: Tick the answer which is correct in your case

1. Who talked to you before you agreed to have your child in the study?
   (i) Doctor (ii) Nurse (iii) Social worker (iv) Friends (v) Other (specify)
2. In which language were spoken to during the consenting process
(i) Setswana (ii) English
3. Were you asked to read and sign the consent form or someone read it to you?
   (i) I read and signed the consent form (ii) the researcher/ nurse read it to me
   (iii) A family member read it to me (iii) I read some sections and was helped to read others
3. Do you remember how long the consent form in your study was?
   (i) Too long (ii) Fairly long (iii) long (iv) short
4. How much time after being told about the study did you take to agree to have your child in the study?
   (i) I agreed the same day (ii) I agreed after a few days (iii) I agreed after some weeks .

5. When you were discussing the study, did the nurse tell you about …?

	QUESTION	**Yes**	**No**	**Don't know**
1.	Why your child needed to be in the study?			
2.	Whether the medicines might have some bad effects on your child's health?			
3.	How many times you and your child will be coming to the clinic during the study?			
4.	How many times your child will receive the medicines?			
5.	If there would be any payment you will receive for agreeing to have your child in the study?			
6.	If you were free to stop your child any time from being in the study?			
7.	How the doctors will decide which medicines to give your child?			

6. As you talked with the nurse about the study

	QUESTION	**Yes**	**No**	**Don't know**
1.	Did he/she speak in a language you understand?			
2.	Did he/she explain clearly about the medicines your child would receive?			
3.	Do you think all the information provided was important for you in deciding whether your child should join the study?			
4.	Did he/she use any difficult medical terms you could not understand?			
5.	Did he/she explain the difficult terms used?			
6.	Did he/she provide you information about your child's disease?			
7.	Did he/she test how well you had understood the information given?			
8.	Were you given a chance to ask questions?			
9.	Did you ask any questions?			
10.	Were you satisfied with the information that was being provided?			

7. How important was it to you to get information about …?

	QUESTION	**Very important**	**Fairly important**	**Not important at all**
1.	Why your child needed to be in the study?			
2.	Whether the medicines might have some bad effects on your child's health?			
4.	How many times you and your child will be coming to the clinic during the study?			
5.	How many times your child will receive the medicines?			
6.	If there would be any payment you will receive for agreeing to have			

	your child in the study?			
7.	If you were free to stop your child any time from being in the study?			
8.	How the doctors will decide which medicines to give your child?			

8. How well informed do you think you are right now about …?

		Very well informed	**Fairly well informed**	**Not well informed**
1.	Why your child needed to be in the study?			
2.	Whether the medicines might have some bad effects on your child's health?			
3.	How many times you and your child will be coming to the clinic during the study?			
4.	How many times your child will receive the medicines?			
5.	If there would be any payment you will receive for agreeing to have your child in the study?			
6.	If you were free to stop your child any time from being in the study?			
7.	How the doctors will decide which medicines to give your child?			

9. As you discussed the information about the study with the nurse, did you feel he/she was being…..?

	QUESTION	**Yes**	**No**	**Don't know**
1.	Honest			
2.	Forcing you to agree			
3.	Truthful			
4.	Caring and sympathetic to your feelings			
5.	Knowledgeable about the study			

SECTION C: Please respond to each statement as best as you can by saying Yes, No, or don't know for any of the studies your child joined

	QUESTION	**Yes**	**No**	**Don't know**
1.	The main reason HIV research is done is to improve the treatment for future HIV patients			
2.	The main reason for my child joining the study is to receive treatment			
3.	The main reason for my child joining the study is to find out which medicine work best in order to help future children			
4.	The main reason for my child joining the study is to find out which drugs are cheapest			
5.	One of the major reasons for the study was to test the safety of a new HIV medicine.			
6.	In this HIV study, each group of children received a different medicine.			
7.	My child received the medicine which was being tried			
8.	The doctors did not know the effect of the medicine used on my child			

9.	It is not clear whether the study will benefit my child			
10.	There is no better way to treat my child's illness than using the medicines in the study.			
11.	I was allowed to choose the medicines my child received			
12.	I knew how long my child's participation in the study was likely to last			
13.	If I had not wanted my child to participate in the study, I could have refused.			
14.	I could have had my child participate in the study without signing or putting a thumb on the consent form			
15.	I could have withdrawn my child from the study at any time			
16.	If I had withdrawn my child from the study he/she could still have been treated at the clinic?			
17.	All the children in my child's study got the same medicines?			
18.	Some children received medicines which were not effective			
19.	The study doctor decided which medicines each child would get based on chance			
20.	The study doctor decided which medicines each child would get based on what he/she thought was best for each child			
21.	The study doctor decided which treatment each child would get based on what each parent wanted			
22.	I am free to take my child could drop out of the study any time.			
23.	I was told how many times I would have to bring my child to the clinic after joining the study			
24.	I was told the medicines my child was getting could have life-threatening side-effects			
25.	I was told that other health workers or other people that are not directly involved in my care could look at my child's medical records			
26.	I was told who will pay for my child's care if he/she was injured or became ill as a result of participating in this study.			
27.	The consent form used in the study listed the names of people I should contact if I had any questions about my child's participation in the study.			

SECTION D: Please respond to each question as best as you can by choosing from the answers given. You can choose more than one answer.

1. What was the most important reason for having child join the study?
   (i) To help future HIV-infected children (ii) To have my child treated
   (iii) To receive the money being paid for participating (iv) My child's illness

2. If the study team was not going to give you P 30.00 each time you brought your child would you still have joined the study?(i)Yes (ii) No (iii) Don't know

3. How much pressure, if any, did you feel from other people to join the study?
(i) A lot of pressure. (ii) A fair amount of pressure (iii) A little pressure (iv) No pressure at all

4. From the following list of people, please pick all the people from whom you felt any pressure to join the study

(i)	Doctor		(vi)	Close friends	
(ii)	Nurses		(vii)	Anyone else? *Who was that person?*	
(iii)	The health center				
(iv)	My spouse				
(v)	My Family				

5. How much pressure, if any, did you feel to join the study because your child is sick?
(i) A lot of pressure (ii) A fair amount of pressure (iii) A little pressure (iv) No pressure

6. Did you personally make the decision to have your child join the study?
(i)Yes (ii) No

7. Did any other person help you make the decision to have your child join the study?
(i) Yes (ii) No
8. Who helped you decide to have your child join?

(i)		The doctors	(v)	My family	
(ii)		The nurses	(vi)	Close friends	
(iii)		The health center staff	(vii)	Anyone else? *Who was that person*	
(iv)		My spouse			

9. Could you have refused to have your child join the study if you had wanted to?
(i)Yes (ii) No
10. Give reasons for your answer above?

11. How easy would it have been for you to refuse to have your child join the study?
(i) Very easy (ii) Fairly easy (iii) Fairly difficult (iv) Very difficult

12. You agreed to join the study either by signing your name or by putting your thumbprint on a form. Which one of the following did you do?
(i) Signed my name on a form (ii) Put my thumbprint on a form
13. Would you have preferred to join the study by telling the doctor, without having to sign your name (put your thumbprint) on the form? (i) Yes
(ii) No

Those are all of our questions—is there anything else you'd like to tell us?

_____
_____
_____

Thank you very much for answering our questions! End time: __ __:__ __ AM/PM

ANNEX 9: PARENT SEMI-STRUCTURED INTERVIEW GUIDE (SETSWANA)

Setlhogo: Tsela ya go tsaya tetla mo motsading go akaretsa bana mo ditshekatshekong tsa HIV

Nomoro patlisiso :____

Letsatsi: __ __/__ __/__ _

Nako ya go simolola: __ __:__ __ AM/PM

Ke lebogela go bo o dumetse go tsenelela puisano e. Go tsaya karolo ga gago ke boithaopo e bile o gololesegile go sa araba dipotso tse o sa batleng go di araba. Le fa go ntse jalo re solofela gore o tla tsaya karolo, ka kitso e re tlaa e bonang fa e ka re thusa go bona gore a go nale sengwe se se tlhokang go tokafadiwa. Dikarabo tsotlhe di tla nna sephiri e bile ga gona yoo tla itseng gore ke tsa gago.

Tsweetswee, gakologelwa gore o ka nkitsise fa go na le potso e o sa batleng go e araba re ka fetela kwa go e nngwe. O kgona go emisa go tsaya karolo nako nngwe le nngwe. Fa o batla go emisa go tsaya karolo, ga gona go ama ngwana wag ago ka gope. O nkitsise fa o batla ke boelela potso nngwe kana o sa tlhaloganye potso nngwe.

KAROLO YA NTLHA

DINTLHA KA GA WENA

Re batla go itse ka wena, ngwana wag ago le lelwapa la gago.

1	Bong	Rre			Mme		
2	O wela fa dingwageng dife?						
3	O nna kae?	Toropo		Motse			
4	O ithutile/tsene sekolo go fitlhelela kae?	Mmadikolo	Sekolo se se golo (Senior)	Sekolo se se golwane (Junior)	Sekolo se se botlana	Thuto ga e golelwe	Ga ke a tsena sekolo
5	A o itse go bala le go kwala?	Ee			Nnyaa		
6	O kgona go bala le go kwala puo efe sentle?	Sekgoa		Setswana		E nngwe (Tlhalosa)	
7	A o mmaagwe, rragwe kgotsa motlhokomedi wa ngwana yo?	Ee			Nnyaa		
8	Ngwana wa gago o dingwaga di le kae?						
9	Fa o le motlhokomedi wa ngwana yo, le sikana jang?	Nkuku	Ntatemogolo	Mmangwane Rakgadi	Malome Rangwane	Ba bangwe	
10	A ngwana wagago o kile a tsenelela dipatlisiso tse dingwe?	Ee			Nnyaa		
11	Di le kae?					Go feta Boraro	
12	A o na le bana bangwe ba ba kileng ba tsenelela dipatlisiso?	Ee			Nnyaa		
13	O tsisitse ngwana wa gago go bona ngaka ga kae ngwaga o o fitileng?	gangwe	gabedi		Gararo	Go feta botlhano	

14	Go nna batho ba le kae mo ntlong ya gago?	Babedi		Bararo		Bane		Go feta Bone	
15	Tlhogo ya lelwapa la gago ke mang?	Nna	Monna wa me		Rre		Mme		Ba bangwe
16	Seemo sagago sa lenyalo ke sefe?	Ke nyetswe/nyetse		Ga ke a nyalwa/nyala		Ke kgaoganye le monna/mosadi		Tse dingwe	
17	A o a bereka?								
18	Fa o bereka o bereka o le eng?								
19	rraagwe/mmaagwe ngwana wag ago o a bereka?								
20	Ntlo e le nnang mo go yone ke ya ga mang?	Yame	Mohirisi	Losika		Motho yo ke mmerekang		Monna/Mosadi wa me	
21	Le nna mo ntlong e e ntseng jang?	Ya madi a a kwa godimo		Ya madi a a fa gare		Ya madi a a fa gare		Tse dingwe	
22	A le na le ditlamelo tse?	Motlakase		Metsi mo ntlong		Motlakase le metsi			

KAROLO YA BOBEDI

Re batla go itse gore go/gone go le botlhokwa go le kae mo go wena go itse dintlha dingwe tsa patlisiso pele o dumela go letlelela ngwana wa gago go tsenelela patlisiso.

1. O itsile jang ka tshekatsheko e pele o tsaya tshwetso ya go tsaya karolo?

(i) Ngaka (ii) Mooki (iii Mmaboipelego (iv) Ditsala (v) Seromamoa/TV (vi) Pampiri tsa dikgang (vii) Dipamprii tsa Ipapatso(viii) tse dingwe (Tlhaloso)

2. O tlhaloseditswe ka tshekatsheko e go dirisiwa puo efe?

3. A o ipaletse pampiri ya go tsaya tetla kana o e baletswe ke mongwe?

(i) ke badile ka ba ka baya monwana pampiri ya go tsaya tetla 1(ii) mmatlisisi o e mpaletse 2 (iii) Ke e baletswe ke mongwe wa lesika 3 (iii) Ke badile bontlha bongwe ke bo ke thusiwa ke ba bangwe 3

4. O tsere nako e e kae o sena go bolelelwa ka tshekatsheko go tsaya tshwetso ya go tsaya karolo

(i) ke tsere tshwetso lone letsatsi leo (ii) Morago ga malatsinyana (iii) Morago ga dibeke

5. Fa o ne o tlhalosetswa ka tshekatsheko, a o ne o tlhaloseditswe tse di latelang?

Potso	Ee	Nyaa	Ke lebetse
Maikaelelo a tshekatsheko e	1	2	98
Ditlamorago	1	2	98
Gore wena le ngwana wag ago le tshwanelwa ke go etela kokelwana ga kae?	1	2	98
Gore ngwana wag ago o tlaa amogela molemo/diritibatsi ga kae?	1	2	98
Gore a le tlaa fiwa phimolo dikeledi kana le duelelwa go tsaya karolo?	1	2	98
Kgonagalo ya go emisa go tsaya karolo o gololesegile?	1	2	98
Gore dingaka di tlaa tsaya tshwetso ya go fa ngwana wa gago molemo/diritibatsi ofe/dife?	1	2	98

EE =1 NNYA =2

6. Fa ngaka/mooki a go tlhalosetsa ka tshekatsheko,

Potso	Ee	Nyaa	Ke lebetse
A o ne a bua ka teme e o e tlhaloganyang?	1	2	98
A o go tlhaloseditse gore ngwana wa gago o tlaa fiwa melemo/diritibatsi efe/dife kana gore ngwana wag ago o tla dirwa eng?	1	2	98
A o go file dintlha tse dintsi thata?	1	2	
A o go file dintlha tse di lekaneng?	1	2	
A dintlha tsotlhe tse o di filweng di go thusitse go tsaya tshwetso ya go letelela ngwana wag ago go tsenelela tshekatsheko e?	1	2	98
A o dirisitse mafoko a a thata bongaka?	1	2	98
A o ne a go tlhalosetsa mafoko a a thata?	1	2	98
A o go boleletse dintlha ka bolwetsi jwa ngwana wagago?	1	2	98
A o ne a rurifatsa gore o tlhalogantse go le kae ka dintlha tse a neng a di go bolelela	1	2	98
A o filwe tshono ya go botsa dipotso?	1	2	98
A o ne wa botsa dipotso?	1	2	98

7. Fa o tsaya tshwetso ya go tsenelela patlisiso, go ne go le botlhokwa go le kae mo go wena go tlhaloganya tse di latelang? Botlhokwa thata (1) , Botlhokwa (2) , Botlhokwanyana (3) Go ne go se botlhokwa(4) ?

Potso				
Maikaelelo a tshekatsheko	1	2	3	4
Ditlamorago	1	2	3	4
Gore wena le ngwana wag ago le tshwanelwa ke go etela kokelwana ga kae?	1	2	3	4
Gore ngwana wag ago o tlaa amogela molemo/kalafi ga kae?	1	2	3	4
Gore a le tlaa fiwa phimolo dikeledi kana le duelelwa go tsaya karolo?	1	2	3	4
Kgonagalo ya go emisa go tsaya karolo o gololesegile?	1	2	3	4
Gore dingaka di tlaa tsaya tshwetso ya go fa ngwana wa gago kalafi efe?	1	2	3	4

Botlhokwa thata (1) , Botlhokwa (2) , Botlhokwanyana (3) Go ne go se botlhokwa(4) ?

8. O kare o itse go le kae ka tse di latelang?

Ke itse thata(1) , ke itse mo go lekanetseng (2), Ke iste go le go nnye (3) Ga ke itse sepe(4)?

Maikaelelo a tshekatsheko	1	2	3	4
Ditlamorago	1	2	3	4
Gore wena le ngwana wag ago le tshwanelwa ke go etela kokelwana ga kae?	1	2	3	4
Gore dingaka di tlaa tsaya tshwetso ya go fa ngwana wa gago kalafi efe?	1	2	3	4
Gore a le tlaa fiwa phimolo dikeledi kana le duelelwa go tsaya karolo?	1	2	3	4
Kgonagalo ya go emisa go tsaya karolo o gololesegile?	1	2	3	4

Kgonagalo ya gore wena kana ngaka a bo a sa iste gore ngwana o fiwa molemo/diritibatsi ofe/dife kana selekanyo sele kae	1	2	3	4

Ke itse thata(1) , ke itse mo go lekanetseng (2), Ke itse go le go nnye (3) Ga ke itse sepe(4)

9. Fa le bua ka tshekatsheko e le babatlisisi, a o ne wa iphetlhelela tse di latelang?

A o ne a lebega a bua boammaaruri	1	2	98
A o ne a dirisa puo e e patleletsang?	1	2	98
A o ne a le boikanyego?	1	2	98
A o ne a rekegela maikutlo a gago?	1	2	98
A o ne a itse tiro ya gagwe?	1	2	98

10. A o kgotsofalela ka fa o tlhaloseditsweng tshekatsheko e ka teng?

AROLO YA BORARO

Re batla go itse gore o tlhalogantseng go le kae ka tshekatsheko e e o e tseneletseng?

		Ee	Nnyaa	Ga ke itse
1	Lebaka la konokono la go dira ditekelesto tsa melemo ya mogare wa HIV go tokafatsa kalafi ya bana ba ba nang le mogare wa HIV	1	2	3
2	Ngwanake o tseneletse tshekatsheko e gore a bone kalafi	1	2	3
3	Ngwanake o tseneletse tshekatsheko e gore go bonwe gore melemo e e tlhwatlhwa tlase go gaisa ke efe?	1	2	3
4	Ngwanake o tseneletse tshekatsheko e gore e re mo isagong go bonwe gore melemo e e thusang bana Botoka ke efe?	1	2	3
5	Maikaelelo a matona a mmatlisisi ke go sekaseka pabalesego ya molemo o mosha wa HIV			
6	Mo tshekatshekong e e ngwanake a leng mo go yone, setlhopha sengwe le sengwe sa bana bat la se tla fiwa selekanyo se setona sa molemo go gaisa ditlhopha tse dingwe go fitlhela balwetsi ba babangwe ba simolola go nna le dikai tsa ditlamorago tse di diphatsa			
7	Melemo ya ga ngwanake e ne e le ya tekeletso fela			
8	Ditlamorago tsa molemo o dirisiwang mo go ngwanake ga di itsiwe.	1	2	3
9	Ga go itlhalose gore a tshekatsheko e e tlaa solofela ngwanake molemo?	1	2	3
10	Ga gona tsela e nngwe e e botoka ya go fodisa bolwetsi jwa ga ngwanake ko ntle ga go dirisa melemo ya patlisiso e	1	2	3
11	Ke kgona go itlhophela gore ngwanake o tsaya molemo ofe	1	2	3
12	Ke itse gore ngwanake o tla tsaka karolo mo patlisisong e go fitlhelela leng			
13	Fa ne ke sa batle ngwanake a tsenelela patlisiso e ke ka bo ke sa dumela gore a e tsenelele			
14	Ke ne ke ka nna ka dumela gore ngwanake a tsenelele patlisiso e ke sa baya monwana mo pampering ya teseletso go tsenelela patlisiso			

15	Ke ne ke itse gore ke kgona go gogela ngwanake morago gore a seka a tsaya karolo nako nngwe nngwe.	1	2	3
16	Ke ne ke itse gore fa ngwanake sa tlhole a tsaya karolo, o tlaa tswelela a bona kalafi ya bolwetsi jwa gagwe mo kokelong e.	1	2	3
17	Bana botlhe ba ba mo tshekatshekong e ba tlaa bona melemo	1	2	3
18	Bana bangwe bane ba tshwaetswe setlhopha se se fiwang molemo o o sa berekeng/fodiseng.	1	2	3
19	Bana botlhe mo tshekatshekong ba filwe molemo o o tshwanang.	1	2	3
20	Ngaka ke ene a neng a tlhopha gore ngwana o tsaya molemo ofe.	1	2	3
21	Ngaka ke a neng a tlhopha gore ngwana o tsaya molemo ofe a lebeletse gore ke eng se se siametseng ngwana	1	2	3
22	Ngaka ke ene a neng tlhopha gore ngwana o tsaya molemo ofe a lebeletse gore batsadi ba batla eng	1	2	3
23	Ke ne ke letlelelwa go tswa mo tshekatshekong nako nngwe le nngwe	1	2	3
24	Ke ne ke tshwanelwa ke go tsisa ngwana wag ago ko kokelong gantsi fa o sena go tsenelela tshekatsheko e?	1	2	3
25	Melemo o ngwanake a neng a tshwanetse go o fiwa o ne o na le o nale ditlamorago tse di tshosetsang matshelo	1	2	3
26	Ke tla a atswiwa ka kalafi ya ga ngwanake fa a ka gobala e le ntateng ya go nna motsaya karolo mo patlisisisong e.			
27	Ke ne ke boletswe batho ba k eke ikopanyang le bone fa ken a le dipotso ka ga ngwanake e le mo tsaya karolo mo patlisisong e			

KAROLO YA BUNE :

Re tlaa batla go itse gore go tsile jang gore o tseye tshwetso ya go tsaya karolo mo tshekatshekong e.

1. Ke lebaka le fe le le dirileng gore o letelele ngwana wag ago go tsaya karolo mo patlisisong e.

_____

2. Fa babatlisi ba ne bas a go fe P30.00 nako nngwe le nngwe fa o tla kokelong, a o ne o tlaa tsenelela tshekatsheko e fela?

i) Ee 1
ii) Nnyaa 2
iii) GA KE ITSE 98
iv)

3. How A Oo neng o patleletswa ke bangwe go tsenelela patlisiso e (TLHOPHA E LE NNGWA)

i) Ke patleleditswe thata 1
ii) ke patleleditswe 2
iii) Ke patleleditswe go le go nnye 3
iv) Ga ke a patleletswa gotlhelele 4

Ngaka	1
Mooki	2
Kokelo	3
Monna/Mosadi wa me	4
ba lelwapa	5
Ditsala	5
Mongwe o sele? Ke mang?	
Fa mabaka a gore ke eng ba ne ba go patleletsa……	

4. Mo bathing ba ba latelang, ke mang yoo go patleleditseng go tsenlela tshekatsheko e

5. O ne o ikutlwa o patlelesega go le kae go tsenelela patlsisiso e ka gore ngwana wag ago o a lwala? (TLHOPHA E LE NNGWE)

i) Ke ne ke patlelesega thata 1
ii) ke ne ke patlelesega 2
iii) Ke ne ke patlelesega go le go nnye 3
iv) Ga ke a patlelesega gotlhelele 4

6.A ke wena yoo tsereng tshwetso ya go letelela ngwana ya gago go tsenelela patlisiso e?

i) Ee 1
ii) Nnyaa 2

7. A go nale mongwe yoo go thusitseng go tsaya tshwetso ya go letelela ngwana wa gago go tsenelela patlisiso

i) Ee 1
ii) Nnyaa 2

8. Ke mang yoo go thusitseng go tsenya ngwana wa gago mo tshekatshekong e?

Ngaka	1	
Baoki	2	
Badiri ba kokelo	3	
Monna/Mosadi wa me	4	
Ba lelwapa	5	
Ditsala	6	
Mongwe fela? Ke mang		
TLHALOSA GORE KA GO REN		

9. A o ne o ka gana go letelela ngwana wag ago go tsenelela tshekatsheko e fa o ne o batla?

i) Ee 1
ii) Nnyaa 2

10. Fa mabaka a dikarabo tse di fa godimo

_____

11. Go ne go ya go nna motlhofo go le kae mo wena go gana go tsenya ngwana wa gago mo tshekatshekong? (TLHOPHA KARABO E LE NNGWE)

Motlhofo thata 1

Motlhofo 2

Go thata 3

Go thata thata 4

12. O supile jang gore o dumela go tsenelela tshekatseko e? Ke sefe sat se di latelang se o se dirileng? (TLHOPHA KARABO E LE NNGWE)

i) Ke kwadile leina la me mo fomomg 1

ii) Ke beile monwana mo fomong 2

13. A o ne o ka batla go tsenelela patlisiso e ka go bolelela ngaka fela o sa kwale leina la gago kana o sa beye monwana mo fomong?

i) Ee 1

ii) Nnyaa 2

14. Dipotso tsa rona di feletse - a go na le sengwe se o batlang go se re bolelela?

_____

Re lebogela thata go bo o arabile dipotso tsa rona Nako ya go fetsa: __ __:__ __ AM/PM.

APPENDIX 10: PARENT INTERVIEW GUIDE

Title: A Model for Obtaining Parental Informed Consent for HIV Clinical Trials Research with Pediatric Patients

Questionnaire #:____

Date: __ __/__ __/__ _

Start time: __ __:__ __ AM/PM

Thank you for agreeing to do this interview. Your participation in this study is voluntary and you have the liberty not to answer any of the questions; however I hope you will participate in this study, as the information gathered will allow me to find out if there is something during the process that requires adjustment and needs to be suggested to the authorities. Also, if there is need for improvement in any of the steps. All of your responses will be confidential and will not in any way be used to identify you!

Please remember that if you do not want to answer any specific questions, you can let me know and I will go on to the next question. You can stop the survey at any time. If you decide to stop, it will not affect your child's joining the study in any way.

Also, please let me know if you would like me to repeat any questions or if you don't understand a question.

You have just agreed to have your child join the study.

SECTION A

DEMOGRAPHIC DATA

We'd like to know how about you, your child and your family

1	Gender	Male				Female	
2	What is your age in years?						
3	Where do you live?	Town/city		Village		Ward	
4a	What is your highest level of education?	Tertiary	High school	Junior school	Primary	Non-formal education	None
4b	Do you know how to read and write	Yes				No	
4c	In which language can you read fluent and write well?	English		Setswana		Other (specify)	
5	Are you the mother (father, parents/guardians) of this child?	Yes				No	
6	How old is your child?						
7	If you are the guardian to this child, what is your relationship to this child?	Grandmother	Grandfather	Auntie	Uncle	Other	
8	Has your child ever been in other research studies?	Yes				No	
8a	How many research studies has your child ever been involved in?						
8b	Have any of your other children been in any research studies?	Yes				No	
9	How many times have you brought your child to see doctors in the last year?						
10	How many people live in your house?						
11	Who is the head of the house?						
12	What is your marital status?	Married	Single	Divorced	Other		
13	What type of job do you do?						
14	What is the job of the child's father (mother)?						

15	Do you and your family own a house?				
16	The house where you live is it for your --?	Land Lord	My relative	My employer	My spouse
17	What type of house do you live in?	High cost	Medium cost	Low cost	Other
18	Does the house where you live have the following utilities?	Electricity	Running Water	Both electricity and running water	

SECTION B

Information disclosure

We would like to know how important it was to you to get information about certain topics when you were deciding whether to join the study.

1. Who gave you information about this study before you made a decision to enroll your child?

(i) O Doctor (ii) O Nurse (iii) O Social worker (iv) O Friends (v) O Other (specify)

---

2. In which language were you spoken to during the consent process?

(i) Setswana (ii) English (iii)

2a. Were you asked to read and sign the consent form or someone read it to you?

(i) I read and signed the consent form 1(ii) the researcher read it to me 2 (iii) A family member read it to me 3 (iii) I read some sections and was helped to read others 3

3. How much time after were given to respond after being told about the study

(i) Had to decide the same day 1 (ii) A few days 2 (iii) Weeks 3 (iv) Was told to take as much time as I wished. 4

4. When you were discussing about the study, **did** the person who talked to you tell you about ……?

1	The purpose of the study?	1	2	98
2	The risks and side effects	1	2	98
3	The number of clinic visits you and your child will have to make?	1	2	98
4	The number of times your child will receive the treatment?	1	2	98
5	Any compensation/payment you will receive for participation?	1	2	98
6	The possibility of quitting the study freely?	1	2	98
7	The way doctors will decide which treatment to give your child?	1	2	98

YES =1 NO =2

5. As you discussed about the study with doctor/nurse

1	Did he/she communicate clearly in a language you could understand?	**1**	**2**	**98**
2	Did he/she make the reasons why your child needed to join the study?	**1**	**2**	**98**
3	Did he/she explain clearly the treatment your child would receive?	**1**	**2**	**98**
4	Did he/she provide too much information?	**1**	**2**	**98**
5	Did he/she provide too little information?	1	2	98
6	Do you think all the information provided was important for you in deciding whether your child should join the study?	1	2	98

7	Did he/she use too many difficult medical terms?	1	2	98
8	Did he/she explain the difficult terms used?	1	2	98
9	Did he/she provide you information about your child's disease?	1	2	98
10	Did he/she test how well you had understood the information given?	1	2	98
11	Were you given an opportunity to ask questions?	1	2	98
12	Did you ask any questions?	1	2	98

6. When you were deciding whether to join the study, how important was it to you to get information about [TOPIC]? Was it very important (1), moderately important (2), slightly important (3) or not important at all (4)?

1	The purpose of the study?	**1**	**2**	**3**	**4**
2	The risks and side effects?	**1**	**2**	**3**	**4**
3	The number of clinic visits you and your child will have to make?	**1**	**2**	**3**	**4**
4	The number of times your child will receive treatment?	**1**	**2**	**3**	**4**
5	Any compensation you will receive?	1	2	3	4
6	The possibility of quitting the study?	1	2	3	4
7	The way doctors will decide which treatment to give your child?	1	2	3	4

Very Important=1 moderately Important =2 slightly important =3 not at all important =4

7. How well informed do you think you are right now about [TOPIC]? Would you say very well informed (1) moderately informed (2), slightly informed (3) or not at all informed (4)?

1	The purpose of the study?	**1**	**2**	**3**	**4**
2	The risks and side effects?	**1**	**2**	**3**	**4**
3	The number of clinic visits you and your child will have to make?	**1**	**2**	**3**	**4**
4	The number of times your child will receive treatment?	**1**	**2**	**3**	**4**
5	Any compensation you will receive?	**1**	**2**	**3**	**4**
6	The possibility of quitting the study?	**1**	**2**	**3**	**4**
7	The way doctors will decide which treatment to give your child?	**1**	**2**	**3**	**4**

Very informed =1 moderately informed = 2 slightly informed = 3 Not at all informed =4

8. As you discussed the information about the study with the research team member who was consenting, did you feel he/she was …..?

1	Being sincere	1	2	98
2	Using a dictatorial or coercive language	1	2	98
3	Transparent and honest	1	2	98
4	Sensitive and sympathetic to your feelings	1	2	98
5	Competent	1	2	98

9. Generally were you satisfied with the information that was provided?

SECTION B: We would like to know how well you have understood the information you have received about the study. Please tell us whether you agree, disagree or you are not sure about the statements the statements that will be read to you. Please respondent to each statement as best as you can by saying Yes, No or Don't know

No	Statement	Yes	No	Don't know
1	The main reason HIV clinical trials are done is to improve the treatment for future HIV patients	**1**	**2**	**3**
2	The primary reason for my child joining this study is to be involved in research.	**1**	**2**	**3**
3	The primary reason for my child joining this study is to receive treatment	**1**	**2**	**3**
4	The primary reason for my child joining this study is to find out which drugs are cheapest	**1**	**2**	**3**
5	The primary reason for my child joining this study is to find out which drugs work best in order to help future children	**1**	**2**	**3**
6	One of researcher's major purposes is to compare the effects (good or bad) of two or more different ways of treating children with HIV in order to see which is better.	**1**	**2**	**3**
7	One of researcher's major purposes is to test the safety of a new HIV drug or treatment.	**1**	**2**	**3**
8	One of researcher's major purposes is to find out the highest dose of a new drug that can be given without causing severe side effects.	**1**	**2**	**3**
9	In this HIV clinical trial, each group of children will receive a higher dose of treatment than the other groups until some patients start having serious side effects.	**1**	**2**	**3**
10	My child's treatment is an investigational treatment	**1**	**2**	**3**
11	The effect of the drug used in my child's study is unknown	**1**	**2**	**3**
12	It is not clear whether this study will benefit my child	**1**	**2**	**3**
13	There is no better choice to treat my child's illness than using the treatment in this study.	**1**	**2**	**3**
14	I can choose my child's treatment option	**1**	**2**	**3**
15	I know how long my child will participation in the study is likely to last	**1**	**2**	**3**
16	If I had not wanted my child to participate in this clinical trial, I could have refused for my child to do so.	**1**	**2**	**3**
17	I could have had my child participate in this clinical trial without signing or putting a thumb on the consent form	**1**	**2**	**3**
18	I can withdraw my child from the study at any time	**1**	**2**	**3**
19	If I withdraw my child from the study he/she can still be treated at the clinic for his/her illness?	**1**	**2**	**3**

20	All the children in my child's study will get treatment?	**1**	**2**	**3**
21	Some children could be assigned to a group in which the drug given is not active	**1**	**2**	**3**
22	All the children in my child's study will get the same treatment?	**1**	**2**	**3**
23	The study doctor will decide which treatment each child gets based on chance,	**1**	**2**	**3**
24	The study doctor will decide which treatment each child gets based what he/she thinks is best for each child	**1**	**2**	**3**
25	The study doctor will decide which treatment each child gets based what each parent wants	**1**	**2**	**3**
26	You are allowed to quit the study any time.	**1**	**2**	**3**
27	Will you have to bring your child to the clinic many times after joining the study?	**1**	**2**	**3**
28	The treatment my child is getting has got life-threatening side-effects	**1**	**2**	**3**
29	The treatment my child is getting has got no side-effects	**1**	**2**	**3**
30	The treatment my child is getting has got moderate side-effects	**1**	**2**	**3**
31	The treatment my child is getting has got severe side-effects	**1**	**2**	**3**
32	Because my child is participating in this HIV clinical trial, it is possible that the study sponsor, other health workers or other people that are not directly involved in my care could review my child's medical records.	**1**	**2**	**3**
33	The consent form used in this HIV clinical trial describes who will pay for my child's treatment if he/she is injured or becomes ill as a result of participating in this study.	**1**	**2**	**3**
34	The consent form used in this HIV clinical trial lists the names of people I should contact if I have any questions or concerns about my child's clinical trial.	**1**	**2**	**3**

SECTION C: We'd like to know how you made the decision to join the study

1. What is the most important reason you decided to have your child join this study?

_____

2. Were there any other reasons why you had your child join?

i) Yes (GO TO 3) 1

ii) No 2

iii) DON'T KNOW (GO TO 28) 98

3. What were some of those reasons?

4. If the study team was not going to give you P 30.00 each time you brought your child would you still have joined the study?

v) Yes 1

vi) No 2

vii) DON'T KNOW 98

5. How much pressure, if any, did you feel from other people to join the he study? Did you feel…? (CHOOSE ONE)

v) A lot of pressure 1

vi) A moderate amount of pressure 2

vii) A little pressure 3

viii) Or no pressure at all? 4

6. From the following list of people, please pick all the people from whom you felt any pressure to join the study.

1	Doctor	**1**
2	Nurses	**2**
3	The health center	**3**
4	My spouse?	**4**
5	My Family	5
6	Close friends	5
7	Anyone else? *Who was that person?* PLEASE	
8	Give reasons for your answer above…… …	

7. How much pressure, if any, did you feel to join the study because your child is sick? Did you feel…? (CHOOSE ONE)

v) A lot of pressure 1

vi) A moderate amount of pressure 2

vii) A little pressure 3

viii) Or no pressure? 4

8. Did you personally make the decision to have your child join the study?

iii) Yes 1

iv) No 2

9. Did any other person help you make the decision to have your child join the study?

iii) Yes 1

iv) No 2

10. Who helped you decide to have your child join?

1	The doctors	1	
2	The nurses	2	
3	The health center staff	3	
4	My spouse	4	
5	My family	5	
6	Close friends	6	
7	Anyone else? *Who was that person?*		
8	PLEASE EXPLAIN WHY,		

11. Who made the decision to have your child join the study? Was it….

(CHOOSE ONE)

1	The doctors	1	
2	The nurses	2	
3	The health center staff	3	
4	My spouse	4	
5	My family	5	
6	Close friends	6	

7	Anyone else? *Who was that person?*
8	PLEASE EXPLAIN WHY

12. Could you have refused to have your child join the study if you had wanted to refuse?

iii) Yes 1

iv) No 2

13. Give reasons for your answer above?

14. How easy would it have been for you to refuse to have your child join the study?

Would you say…? (CHOOSE ONE)

Very easy 1

Moderately easy 2

Moderately difficult 3

Or very difficult? 4

14. You agreed to join the study either by signing your name or by putting your thumbprint on a form. Which one of the following did you do? (CHOOSE ONE)

iii) Signed my name on a form 1

iv) Put my thumbprint on a form 2

22. Would you have preferred to join the study by telling the doctor, without having to sign your name (put your thumbprint) on the form?

iii) Yes 1

iv) No 2

Those are all of our questions—is there anything else you'd like to tell us?

Thank you very much for answering our questions! End time: __ __:__ __ AM/PM

APPENDIX 11: BOTSWANA RESEARCH ETHICS COMMITTEE CLEARANCE LETTER

Telephone: (267) 363200
FAX (267) 353100
TELEGRAMS: RABONGAKA
TELEX: 2818 CARE BD

MINISTRY OF HEALTH
PRIVATE BAG 0038
GABORONE

REPUBLIC OF BOTSWANA

REF NO: PPME-13/18/1 Vol VII (100) 16 September 2011

Health Research and Development Division

MINISTRY OF HEALTH
DEPT OF POLICY PLANNING, MONITORING AND EVALUATION
16 SEP 2011
P/BAG 0038
GABORONE
REPUBLIC OF BOTSWANA

Notification of IRB Review: Amendment

Mrs Mary Kasule
Private Bag 0074
Gaborone

Dear Mrs Kasule

AMENDMENT: A MODEL FOR OBTAINING PARENTAL INFORMED CONSENT FOR HIV CLINICAL TRIALS RESEARCH WITH PEDIATRIC PATIENTS

Reference is made to the above mentioned protocol amendment application submitted to the Heath Research and Development Committee (HRDC) in the Ministry of Health for review and approval. HRU have reviewed and approved the following amendment on the 16 September 2011.

To pay the potential participants P30.00 to reimburse for their time and transport.

Please note that the amendment will expire together with the initial permit.

Amendments
During the approval period, if you propose any change to the protocol such as its funding source, recruiting materials, or consent documents, you must seek HRDC approval before implementing it.
Please summarize the proposed change and the rationale for it in the amendment form available from the Health Research Division Office (HRDD), Office No. 9A 11 or Ministry of Health website: www.moh.gov.bw or can be requested via e- mail from Mr. Kgomotso Motlhanka, e-mail address: kgmmotlhanka@gov.bw . In addition submit three copies of an updated version of your original protocol application showing all proposed changes in bold or "track changes".

Reporting
Other events which must be reported promptly in writing to the HRDC include:
• Suspension or termination of the protocol by you or the grantor

APPENDIX 12: UNIVERSITY OF WESTERN CAPE RESEARCH ETHICS COMMITTEEN CLEARANCE LETTER

OFFICE OF THE DEAN
DEPARTMENT OF RESEARCH DEVELOPMENT

Private Bag X17, Bellville 7535
South Africa
Telegraph: UNIBEL
Telephone: +27 21 959-2948/2949
fax: +27 21 959-3170
Website: www.uwc.ac.za

26 April 2011

To Whom It May Concern

I hereby certify that the Senate Research Committee of the University of the Western Cape has approved the methodology and ethics of the following research project by: Mrs. M Kasule (School of Public Health)

Research Project:	A model for obtaining informed consent for HIV Clinical Trials Research with Pediatric Patients
Registration no:	11/1/36

Mr. Patrick Syster
Manager: Research Development
University of the Western Cape

UNIVERSITY of the WESTERN CAPE
A place of quality, a place to grow, from hope to action through knowledge

APPENDIX 13: TRANSCRIPTION OF FOCUS GROUP DISCUSSIONS

1. TRANSCRIPT OF A FOCUS GROUP DISCUSSION HELD AT SITE A WITH THE TRIAL STAFF PARTICIPANTS

Date	**15 June, 2011**
Start Time	**15.30hrs**
End Time	**17.00hrs**
Number of participants	**8**
Males	**3**
Females	**5**
Education	**Tertiary and post graduate levels in Nursing**
Mean age	**35.5**
Discussion Language	**English**
Facilitators	**Dr. P. Ndebele**
	Mr. E. Kalengo

F= Facilitator; P= Participant (NB: Participants codes not written for confidentiality purposes, therefore P was used to refer to all the participants).

F: Are we done with the signing of the consent forms? Please sign the individual consent forms and the group consent form
It's the requirement from the Botswana Ethics Committee and the University of Western Cape Ethics Committee. Confidentiality was assured as names will not appear in the write up. During the discussion we will be referring to you by the numbers provided namely; P1, P8, P5, P4, P9, P3, and P2 but these will not appear in the study report.

F: Welcome to you all and we want to thank you for taking time off to participate in this discussion. We hope that through this research project you might benefit directly or some other people might benefit indirectly. I will start by saying that this is a discussion so you should feel free to chip in wherever you feel you want to come in with some contribution. Our role is to facilitate and we hope that we will respect each other's opinion. We would like to get some information on the kind of work you do as related to obtaining of IC. So we will go round and introduce ourselves.

F: Just to follow up on those who said they are involved in recruiting can you explain more about the process. What exactly are you doing? On participants responds; I thought I heard you saying that you are involved in recruiting!

F: Phone rings----------Can you put your phones on silence! *Laughter from the group!*

P: Most of the recruitment we do is from the clinics and the hospital so we work hand in hand with the hospital and the councillors in the community. So if they identify anyone meeting the criteria we ask them to refer them to us and when they come to our site we tell them about the study. If they are willing to participate then we talk to them in detail about the study.

F: You want to add something?

P: Yes, we meet with those who might be eligible for a particular study and talk to them about the study if they show interest we refer them to our site.

F: I just want to find out how many of you have been involved in HIV Clinical trials?
Silence in the room----------

P: One participant answered on behalf of the others. All of us currently we have two studies involving children.

F: You are working with the parents and the children, what are the ages of the children you work with and working with the parents what do you think is the value of knowing about their culture within the country and the community?
Silence……

P: What do you mean? When dealing with the client and the baby. I think it is very important because what they believe in or their cultural background would in a very big way influence the decision that they make. For example if you are asking an HIV positive mother not to breast feed but to formula feed, you want to find out the challenges she will face at home and in the society. When you understand that then both of you are able to know how to work way around it unlike when you do not know. She will be breast feeding at home and formula feed when at the clinic.

F: You saying the knowledge will assist the success of the study and also assist you as a researcher?

P: Yes it assists the participants to make an informed decision.

P: The parents feel involved and accommodated.

P: It helps to understand how many people have an influence on the decision the parent makes, you might be talking directly to the baby's mother but her decision might be influenced by the grandmother. It helps the retention of participants and helps the participant to give

information to other people that are involved in the care of the child.

F: Any other comments? Looking at the parents you deal with what is the level of education of these parents in general?

P: Junior secondary most of them

F: Do you think there is any reason for this level of education?

P: This is likely to happen in a rural setting because of the location being in a rural area. Most people that are highly educated are working in the city.

P: Most of the parents here stay at home they are not working, and this is the group that is most sexually active.

F: The studies that you are participating in what Phase are they? Expressions of surprise from the participants. Uh!! Surprised Phase?

F: Yah! Phase! Phase I, II, III or IV?
Silence……

P: Most of them are phase III.

F: Has any of you participated in a Phase I study? The audience is quiet and facial expression shows they are not sure of the Phases.

F: Looking at how risky the studies are, how would you classify the studies you are working on in terms of risk?

F: Is it minimal risk or high risk it is your own opinion?

P: Both studies I am working on are of minimal risk because we are using drugs which are already there we know the side effects, other countries have been using them. But the vaccine drugs are being given to HIV positive children!!!

F: So you say there is minimal risk because these products are being used elsewhere? Because you know about these products that is how you classify the categories.

F: Asks another participant, do you have a different opinion?

F: How do you look at these studies in terms of risk? Do you think that they are risky or minimal risk?

P: Minimal risk

P: I do not think am very clear with the question!

F: If we were to ask you to bring your child into these studies would you be ok with it?

P: I do not have a problem because I know all about the drugs that are being used, they have been proven safe.

P: I see you laugh and I would like you to explain as to what you mean because when you say, these are interventional studies, the interventions are they of any risk, so far we have talked about drugs but there are other interventions like blood draws, we do understand the risks that come with blood collections. We look at the number of times blood will be collected, the sensitivity around collecting blood from pediatric patients. The other risk is the one associated with HIV because those who see the parents coming to the site will say Oh! So she is in this study it means she is HIV positive or her child is HIV positive. All these are some of the risks.

F: So having heard this description from her you still classify the studies as minimal risk? I am asking your colleague.
Laughter from the group!!!....

P: Adamant... I am still saying that! *Laughing*……

F: Any other contribution on this one? What is our understanding of informed consent? Silence!!!! until the facilitar says 'I will start off with you since you are sitting close to me! *Laughter from the group*…

P: Unfortunately this is the wrong person sitting next to you!! *Laughter again from the group*! I am hardly new here not even a month! But anyway from the professional point of view to me an informed consent means you do understand every process every intervention, every information that you are supposed to be given, you have to understand and you have it in the tip of your mind. So you can make a decision whether to get into it or to get out.

F: So you are emphasizing on total understanding of everything related to that study.
P: Yes and you may be a source of information for other clients.

P: I would say it a process by which you are to know the objectives, the risks and benefits, of entering a study.

F: Do you want to add something?

P: Added that the client must be told of the choices available.

P: Adds…..the emphasis of saying that signing an informed consent does not mean you cannot change your mind. That's why each time they come for a study visit I ask them are you still interested in being in the study? Do you still remember why you in the study just to make sure that they did not bind themselves, they are still volunteers. Even when they come back and change their mind we counsel them and refer as appropriate

F: Now thinking about your own experience in dealing with these clients what do you think is their understanding of the informed consent process? Emphasizes, their own understanding?

P: For me I would say their understanding is related to their understanding of research because in my personal view I believe there is still limited understanding of the difference. There is a thin line between the care they get from the public facilities and the care they can get here such that on referral one can '*I am coming from the clinic because I was told to come'* We ask them do you

understand why you are here and they respond to say *'No I have just come'*. Until you get them to understand that this a research institution not like the other clinics where you just come in to get the baby checked.

F: Ok from what you are saying when they come from the clinic to the research site they think they are coming for routine care. So you have to first make them understand that this is a different situation. From your experiences do you think you are succeeding in doing that?

P: Informed consent is a process which you have to explain again and again to find out whether they understood. I think we have got to that level but we continue reminding them as it is a process.

F: On average for most of the parents referred how long does it usually take to agree to enrol in the study? First day they come?

P: Most of them do agree on first contact may be because of they have already heard about the study in the village , from health care workers, so by the time they come they already have some idea of what is going to happen. Although a few need a longer time to go home and think about but most of them will be ok.

P: Most of the times those who ask for more time it is not that they did not understand , they have to go back and consult somebody or to think more what you have just said to them. We have other clients who have participated in other studies who come as self-referrals because they see our posters some even call to request to come and know more about the study.

P: Some just drop in and say I was in a study which ended and now I am pregnant is there any other study I can enrol in?

F: Why do you think they come as self-referral?

P: Why they want to come? Loud laughter!! 'We do the best' *laughter from the group.*

P. If the previous relationship was beneficial to the child I think that's why they come.

F: Is it because some of the services are not available at the clinics or the hospital?

P: Services like tests take longer like 3 months compared to two weeks at the research site. Also the congestion at the public clinics.

F: So parents are attracted by the benefits like the special treatment they get. Facilitator notices a participant who has been very quiet and probes them to say something. 'Let's hear your views'

P: I do agree but may be one comment. When these clients come, we do not only focus on the study, we use a holistic approach, if they have other illnesses we attend to them.

F; Yes!

P: Yes I was going to say, in one or two encounters in my experiences 'clients never say 'NO' on your face or say I will think about it, they just never come back to you. When you follow up then they either say 'I don't think I am interested or my parents said no'. The can't say no face to face.

F: Why do you think this is the case?

P: I knew this will come!! Loud laughter from the whole group! I don't know but from a professional point of view it is difficult for a patient to say no to a health worker, somebody they believe is always giving them the health care.

F: Do you think it is something cultural?

Everybody nodes!! A participant goes on to say that there might be some other cultural issues like some people say 'my parents said my child should not participate' So the decision is being made by someone else.

F: Yes!

P: According to Batswana culture you do not make a sole decision you have to consult people back home so that is why they can't say no on your face.

F: You have your research site offering high care quality and offer everything special. Do you think the decision they make is voluntary or because of the benefits they receive?

P: Usually we do encourage them to make voluntary decisions even though there are some benefits they can get in the study.

F: What you mean is that you emphasize that they have to make their voluntary decision? But what do you think is the effect of these offers on the side which are better than what the public facilities offer?

P: To guard against undue influence we have an assessment of understanding conducted by an independent person before the final signing. If the person does not get half of them correct we go back and talk about the study until we get satisfactory answers.

F: In your assessment, have you ever told a client that you do not understand we can't enrol you into the study?

P: We re-assess, we give them the form to take home and ask them to ask another person to read for them. Usually we test the understanding again. If this fails we can bring in a witness to listen to what we are saying. If the witness understands what we are saying and the patient wants to enrol in the study the witness will sign and the patient also signs.

F: What if the witness says they understand but still you assess the potential participant and they still fail.

P: The group laughs and many say they have not experienced such a situation. Sometimes patients do not understand because of the anxiety of being in a health

care set up. So they may need to talk to someone they are more comfortable with.

P: We all play a role in the documentation of the informed consent form.

F: For you what role are you playing?

F: Do prepare the form or it is prepared by the sponsor/Principal Investigator?

P: The form is brought to us prepared and we are asked to make comments.

F: How long are the consent forms?

P: Between 13-14 pages

F: What do you think about that length?

P: Yah! It's long. That's the problem

F: Do you think a huge chunk can be chopped out of it?

P: It's lengthy but it is worth it!

P: We are not saying we are happy but what we are saying if there could be model that ensures that all the information is included but not that lengthy!

P: In my opinion I think the pages are Ok although the package looks bulky but if someone is at home with all the time to read they can understand. The form is well detailed unlike when you summarize, the person conducting the consent process would understand but the one helping the patient to read at home might not understand. So may be encouraging the participants to read a few pages at a go until they understand. I think it is important that they get all the information.

P: When designing a consent form you need to think of a broader picture as to who is going to read the consent form different readers require different information, researcher, participant, spouse, public etc. So if all the information is available in the 14 pages. I have attended a workshop which you conducted and you asked that same question 'How long should a consent form be?' and we never reached an agreement up to today. Take into consideration all the reader's needs.

F: So what is your comment now?

P: I am still saying we need to summarize!

F: Let's continue.

P: I hope we can find the best way and I am hoping the student will come back and tell us the best way!! Because even if it is long it is how you administer it that matters!! Establish what the patient wants to know and start with that! Take your time

F: Regarding the documentation of the consent from are there specific challenges that you have encountered?

P: Use of language, we do appreciate that Setswana has the written and spoken part, but now you come to say some English words in the Setswana way translation.

F: What are the participants saying about the ICF? (No answer to this one).

F: Are there any recommendations?

P: Put it in the day-to-day language. Although I do not know how it will be considered by HRDC whether they will think it is ethical.

P: But Setswana has different dialects, from different ethnic groups. Some English words do not exist in Setswana. My recommendation is that; bring all the Setswana language specialist and people of different ethnic groups to contribute to the translation.

F: Who is the first contact person the parents talk to?

P: The receptionists refer them to the research nurses.

F: To what extent are the doctors involved in the informed consent process? Quiet? F: asks again what is the role of the doctors?

P: The administration of the consent form is mainly the role of the nurses; the doctors only try to check levels of understanding.

P. When the patient goes to the doctor they will just ask whether the patient understood what they were told by the nurse.

P: The doctors are not much involved in the IC administration but before the patient is enrolled they ask them some questions to check understanding.

F: We touched on full disclosure earlier on. What is your comment of full disclosure? Do you think that it is feasible? Silence! The facilitator asks again 'Do you think it is?

P: At a go it is not possible!

F: So what are you saying?

P: What I think is to emphasize that it is a process, you keep revisiting, providing more information and encourage asking questions and over time they get to know more.

P: I can start by giving all the necessary information but do not ask me which information is necessary 'Loud laughter!!!' I wish there was a word I can use.

P: I think there is core- information to be given first because a client cannot remember everything.

F: When should the participant have full disclosure, is it at the administration of first dose or before?

P: We must realize that informed consent process is an on-going process so that even when we assess we just want to see a comfortable level of understanding because a client cannot take in all the information first time? That is when in assessment we do not go into too much details.

F: We need a comfortable level of understanding then ask questions later?

P: How long will the study take, benefits, risks?

F: Do you think the parents understand the difference between routine care and research?

P: It differs by parent. Like one parent asked that '*When you say you can't help me with my other problems and you are referring me to the local clinic is it fair? I do not want to go here and there*.

F: You have already said that you are assessing understanding. How do you assess this?

P. We use questionnaires mainly after the first contact. Then you can randomize certain questions at each following visit.

F: Positive!

P: Yesterday I had a client told me that '*I wish 2001 when I had my child this study was there; I do not think I could have lost my child'*.

F: Any other negative comments?

F: In summary can you recommend on how the process can be improved? Now you are only thinking only about going home!!....
P. Although the form looks bulky but it is worth it because everything is inclusive'. I am happy but if we are going to conduct a study in the community let's call the community members to help us translate the ICF as per their community.

P: But then the community has people from different places laughter from the group!! So the issue of language remains an unresolved issue but we have to find a meeting point'

P: Lack of communication due to the shortfall of some Setswana words that do not exist in English or vice-versa.

F: Do you have any other comments or questions?

P: How can we cater for the challenged parents, like those that are deaf, blind, mentally sick or retarded?

F: But so far you haven't had such?

Group answers 'No'.

F: I think that is a very important point you are raising. Thank you very much.

F: Thank you for participating in this study.

Time: **17.00hrs**

APPENDIX 14: TRANSCRIPTION OF FOCUS GROUP DISCUSSIONS

TRANSCRIPTION OF A FOCUS GROUP DISCUSSION WITH TRIAL STAFF PARTICIPANTS AT SITE B

SUMMARY OF PARTICIPANTS

Date	**16 June, 2011**
Start Time	**17.30hrs**
End Time	**18.00hrs**
Number of participants	**10**
Males	**3**
Females	**7**
Education:	**Tertiary and post graduate levels in Nursing**
Mean age	**35.5**
Discussion Language	**English**
Facilitators	**Dr. P. Ndebele**
	Mr. E. Kalengo

F= Facilitator; P= Participant (NB: Participants codes not written for confidentiality purposes, therefore P was used to refer to all the participants).

Time End: 17.00hrs

The discussion started off by the facilitors and participants introducing themselves.

F: Thank you very much for coming to participate in this discussion. It is after work and all of you look tired but bear with us, we deeply appreciate your presence. l will be facilitating this discussion and my two colleagues will also be assisting with making notes and observations. So ladies and gentleman, we want to thank you very much for agreeing to participate in this discussion. I am hoping that it is going to be a short discussion and let me emphasise from the beginning that feel free in this discussion. It's not about... ….the right answers but about our own opinions as individuals.

We are going to be using tags labelled P1-P10, due to confidentiality we are not going to refer to you by your names during the and write up. So l would encourage you to put the tags where l can see them clearly so that when we are transcribing it is easy to know who said what! During the discussion we will be referring to you by the numbers provided namely but these will not appear in the study report.

F: I will give you a few minutes to read through the personal informed consent and the group informed consent. The idea of having the personal informed consent is to indicate that you have been provided with information about the study and have understood that information and you voluntarily agree to participate in the study. The group informed consent is for each participant to assure us that what has been discussed in this room will remain in this room and will not be discussed anywhere outside the group either among yourselves or with anyone else.

F: We are interested in research involving children. Can you confirm whether all of you have been involved in research involving children?

P: All participants confirmed by saying yes or nodding.

F: What is the general education of the parents who bring their children to the research sites where you work?

P: Majority of the parents do not have that much of the literacy may be dependent on age, majority could have primary level.
F: Do you think there is a reason for this?

P: These are the people interested/keen in participating in studies. Those with high education are giving excuses like; *'they are busy at work or will get back to you'*

P: Economic status also plays a very important role and we recruit from facilities where people from the lower economic strata access health services, so we do not see people from the high social economic status that much.

P: The other important factor is that we recruit from public facilities and we are guided by statistics. We go to places where there is high burden of disease where recruitment will be quicker.

P: It is very interesting when you talk about levels of education; you find that majority of these people from the low social economic strata are submissive to health personnel. The other reason might be that they

do not understand policies, their rights etc. So they believe that as patient you have to *'listen'* and that's why they can be exploited and cannot say 'No' to enrolment of their children. They believe in the learned and can be influenced easily.

F: How do you go about reaching your sample size? Can you explain more about the recruitment strategy?

P: Laughs!! The whole process? Pause…….

F: Yes! The whole process!

F: We are so much interested in research that involves children. So I just want to have some confirmation of how many of us have been involved in pediatric research. I guess it is all of us?

P: Everybody nods in agreement and some whispered in agreement.

F: Thank you very much for conforming that! Now we are basically looking at the parents of guardians that we deal with. Let's just look at their levels of education. What is the general level of education of the parents and guardians that you dealing with in research involving the little ones? Yes!

P: Hum…….-Yah no! Majority of our parents do not have that much literacy so they are probably I would say, depending on age some have average education but majority of primary caregivers are relatives, grandparents, aunties an you find that may be a child is being taken care of by the relatives since some are orphans. So these are the people who normally face challenges of signing for consent for the pediatric population.

F: You mentioned the issue of the low literacy. At what level would you place them? Primary, junior secondary, secondary or college level?

P: Majority on average they have primary level.

F: And do you think that there is any reason for this? I am trying to look at the situation that you are looking at; do you think that there might be any reason why you end up having those parents/ guardians with low levels of education?

P: You mean.....which /the reasons that can affect the trial?

F: No the reason why you have the majority of those parents and guardians having low levels of education is that these are the ones you see at your site?

F: Hum ….the question is, for example do you get some university graduates?

P: Well……

P: I think that these are the people whom you approach; they are the only people interested in listening. You find that those people of higher education, they will tell you that they are in a hurry going to work or l welcome back to you. They are always giving excuses those people with higher education (expressed *with anger and frustration)* but the ones with middle and lower education, they are always keen to learn and participate in studies. Probably that is why we have the majority of them.

F: Thank you very much!

P: Yes…….I believe that economics plays a very important role because we don't recruit from private facilities we recruit mainly from public facilities and therefore people who are from the lower strata of the economy will be the ones that access and make use of the public facilities and therefore are easily accessible to us we do not see people of higher education status therefore possibly higher strata income.

F: Oh yes, anyone wants to add something?

Interruption by another participant!

P: I think that these are people …… interruption by another participant.

P: I think the other thing is that like we are using the public facilities and usually when we are choosing the sites we are guided by statistics of the burden of disease because of the timelines of the trials. We want to go to the areas where you know that there will be high chances that you will get the participants and get the numbers quicker, so you find these areas are usually where people in low income/strata and hence they have statistics of diseases like TB. But if you go to high income status areas you hardly get any patients.

P: It is very interesting when you talk about levels of education, concerning clinical trials like we said when we are looking at the economic bracket like my colleague has just said majority of those people are the ones that will access to health facilities. So majority of them it is a fact are of the lowest economic bracket and those are the people who can be submissive like to the instructions of the health workers and even when introducing a study it is easier to be successful if you are targeting those groups because they do not understand the policies and probably they do not understand their rights because of the level of education to an extent that they cannot say "NO" (*said with emphasis and louder!*). They believe that as a health professional if you are from the community or is it culture or how they grew up? You have to know that you must listen to instructions. Sometimes you do not have to question. So that is why sometimes they can be exploited easily by the learned just because they do not understand their rights that much, they have rights but they don't know that much, so they cannot say "NO". So they believe in the learned because they know that whatever they say is what is good for them.

F*: Interrupts,* Thanks very much!

P: (*continues and agitated*)....That's why they can be influenced easily!

F: I think already so many issues have come out and from our colleague here, there was the issue of sampling strategy. As you think about reaching your target. How do you go about it as a researcher or a research team? Then there are issues about the low levels of education and low social economic status which also comes into play. I think we will discuss more of this as we proceed with our discussion. But you touched on the issue of recruiting from public facilities. Can you explain more about the recruitment strategy? How do you recruit?

P: Um.... there are quite a number of strategies but the one we commonly use is referral. We go and talk to the health care workers at the facilities and tell them what we are doing and the kind of people we are looking for so that if they come across the criteria of people they let us know.

F: I am also relating to what you are saying that referral can come from someone that they trust and look up to. Let me look at the phases of the clinical trials that you have been involved in. Has anyone participated in a: PHASE I _ (*Some whispers from group*) No? F continues…..PHASE II, Phase III - (A few 'Yes') Phase III- (Again a few 'Yes') *The facial expression from most group members was that they are not very clear of what these phases were!*

P: Requests an explanation of the phases from the facilitator! How do you categorise your phases?

F: Gives a brief explanation of the Phases. Another participant joins in the explanations and seemed sure of the phases.

Briefly I can say, Phase I is first in human where you have the intervention tested on a few health subjects say up to 20……

Another participant joins in to explain and seemed very confident of the phases.

F: continues, Phase two is dose finding. Another participant comes in to follow up on the explanation: This mainly continues to tests for safety and efficacy .Silence in the room!

F: Phase III tests for efficacy and safety with larger groups of volunteers. How effective the drug will be. Phase IV post approval mainly checking for side effects. Right! We have all agreed that we have been involved in clinical trials.

F: We are always talking about informed consent what does it mean to you?

Silence in the room!

P: Uh…what does it mean to us? Laughter!! Ok it means to me as a research nurse as someone that conducts the informed consent process, it means that the person that I will be obtaining consent from should be informed, they should be knowing about the study, they should be knowing the benefits, risks, the number of participants, just a lot about the study so that when they decide to take part in the study, they really know what we are talking about. It is not just to make someone sign but to make sure that that person has understood and after reading the informed consent form to the potential participant or after they have read it , you have to ascertain that indeed they have understood so that is the most important thing.

F: How do you ascertain that they have understood?

P: We usually have an assessment of understanding after discussing the informed consent form. You have a tool to assess if the person has understood and tool, if they are not able to answer your questions, there is still nothing wrong with going back and discussing the informed consent form to giving it to them so that they can go home and digest it and come back the next day and when you think they have understood that s when they can sign.

F: Have you had any cases where you give this form , you spend so much time with them but still you assess and realize that you are not happy with their level of understanding? Have had any such cases?

P: Personally I have never had such a case because our informed consent forms are '*very easy'* to understand, they are put in a language that is simplified. I think someone who would not understand after going over and over would be someone may be with another problem…Everyone bursts into laughter!!!!. Someone from the audience comments, '*learning disability'* laughter continues.

P: It is possible! We have come across a certain client whereby we have even had to refer her to come with a guardian so the guardian can be able to understand and explain to the potential participant.

F: How old was that client?

P: I am sure was above 18 or 20 can't remember very well! We suspected that probably like we have been discussing or she was saying because of low literacy levels. That's why most of the clients do not understand but they are willing to participate. In such cases we ask them to come with a guardian.

F: Looking back at that one, was the client signing because they had understood or because there was a guardian?

P: Ok, it came out later to be known that the client did not know how to read or write but had not disclosed this to us. So the guardian had to intervene.

P: Raises a hand to contribute. I was once involved in two clinical trials in an assessment of understanding or comprehension and in those we had a set of questions that a client had to get correct. If a participant got any of those questions wrong, it would be clear to us that they had not understood. But there was no harm in asking them to come back and we gave the informed consent form to take home. If they came again and got the question right then they could enrol their children. It was stipulated in the protocol that should a potential participant get any of those particular questions wrong, they should not be enrolled in the study and this was explained to the potential participant at the start.

F: And were there some that you sent home to say we are done with you? Laughter from the group!!! What kind of questions were in that comprehension test?

P: Ah! They were purely questions to answer the study objectives. If we asked a question like; will this medicine prevent your child from getting HIV and the client says 'Yes' we would know they did not understand the study.

P: Interruption! May be just to add on to that, if someone was given a second chance you could use another method of explaining to them about the study. For example in one study potential participants listened to an audio taped consent form so that even if someone was illiterate they would have a chance to listen to the information over and over , then come and re-test. However after a certain number of times of failing, the client would not be allowed to retest because it shows lack of understanding.

F: Thank you very much! So those are the high standards of clinical trials! As we are looking at the issue of informed consent, there is also this thing about the designing of the informant consent form! Ah! One of you said that you play a role in the documentation… Silence in the room…. Right, I thought you said so?

P: No not to design but in validating the translation.
F: Ah! Ok. Has anyone played a role in the designing of the consent form? Yes please go ahead!

P: Yes

F: What was your role?

P: Laughs!! Uh! Designing a consent form? (Laughs like is doubtful whether consenters are involved!)

F: Yes what was your contribution?

P:Ok, first there will be a protocol, then you come up with the informed consent form which involves the potential participants, then it has to have a couple of components that the patient needs to know and endorse with his/her signature.

P: The other thing is that you will also know that there will be a screening part form the protocol and the real participation. The potential participant has to agree to the screening to make sure that the potential participant is interested and it is not automatic that they will participate. It is only when they meet the eligibility criteria, then they can go through the consenting process (*it was not clear whether a separate consent form for screening is prepared and approved by the ethics committee*).When preparing a consent form you highlight the key elements that you want the potential participant to understand, like rights, voluntariness.

P: I think one other thing is that the form needs to be simple, translated and back translated, avoid use of jargon as much as possible.

P: Interruption! And you are also supposed to have a 'lexicon' that standardizes the language so that if you have two research nurses one sort of like a dichotomy all the nurses use the same language.

F: Is this available at all the other institutions or you are going to cook one*? Loud laughter from the audience,* when another participant says *'Yes*'.

F: We have already highlighted some of the challenges in coming up with the forms but we also want to get some of the practical experiences in terms of some of the challenges that colleagues have met be it in terms of designing or using the forms.

P: One of the major challenges is the 'trust' parents have in the health workers. Some research investigators when they are consenting they might just summarize the contents without stressing certain details but the parent will be 'rushing' to append their signatures! *Loud laughter from the group…* Participant continues, the level of education, it is a serious problem. The children are very submissive to the parents. When it comes to assent majority of them do not know what they are being enrolled into, do not know the risks because of lack of competence due to age. The [children] should know that there are no monetary benefits. Majority of them get transport money but they have to know that this is not payment! (*Explained with a lot of emphasis*).

F: Do you make it clear what the money (P30.00) is for?

P: It is clearly stated in the consent form!

F: Insists on the question! I am asking is it clear to them?

P: It is clear that this is money is for transport. Every clinical trial consent form has a statement to say that you will not be paid for participating for participating in the study and then there is a clause about payment for participation! We emphasize that this money is for inconvenience caused, travel fair to your home!! [*The researcher assumes that parents understand all the content of the consent form! This does not seem sensitive to parent needs*].

P: Another participant **c**omes in again and looking like there is pertinent issue to clarify!! And another thing concerning transport money, I still feel that it has to be reviewed by the ethics committee because transport charges are continuously going up! But I do not know when it comes to research they forget about this part! *Loud laughter from the group!!!*....Like in South Africa, our neighbours their standard is around R200.00. Compared to P30.00! You can see that Botswana reviews research policies but does not look at things like transport costs *(Expressed with disappointment*). Those with louder voices should make noise! They should not only be interested in their own academic benefits!!

F: Thank you very much for highlighting that one! It can be one of the study recommendations!

P: Ah!... I am still interested in that one! Sometimes we have very sick patients who need to hire a special tax to get to the research center and the P30.00 is just enough for a single a single trip and the tax will not

wait .*Everybody in the group all nodded in agreement to the problem!!*

F: Somebody mentioned that if the nurse has dealt with client for a long time, the client is not even interested in knowing the details of consenting process. The parent just signs the consent form. How many of you share the same view that being familiar with the parent they just want to participate?

P: As a client whether you explain to me in all possible ways that this is not a clinical care but is research, if I have a child who is very sick, I really want the child to be helped and I would have tried everywhere else. If someone comes to me and says that it is possible for me, at the back of my mind it's like my child is getting care and appropriate help.

P: Some clients come and tell you that 'I have been involved in another study, so just let me sign. I know everything' .They think all the study processes are the same.

F: Why do you think someone would adopt such an attitude? One issue coming up is that of trust. The fact that I know you and you have done nice things for me before in the previous study…. *Laughter from the group*….you can't harm my child in this one. Are there any other reasons why someone would adopt such an attitude?

P: It's often like that! If you have previously interacted with your clients and you get to know them very well. Whether you try to do things professionally you already see that they have already made a tick psychologically have the 'halo effect' you know your master is right and you trust!

P: The care that they receive from the research centers. You find that we are more patient with our clients in the sense that when they have a problem we sit down with them , talk to them and we give a lot of time and we also attend to their other clinical problems. "We take so much care of them". When you tell them that their study is ending… '*laughs'*…and you are taking them off the study they get really sad and will tell you that '*if there is another study that I can enrol into please let me know* ' Sometimes they even come to inquire if there is on-going study they can join because they believe so much in the care given. They tend to forget about the research aspect.

F: Do you think that voluntariness still exists despite what you have just said?

P: Yes, it is still there, because even if they come for another study we go through the consent form information like from A-Z. I keep probing and keep them attentive. I tell them am going to test you at the end and if you do not get the answers correct you will not enrol your child in the study.

F: I see you carrying a carrot on one side and a stick on the other side and you are saying before you sign you cannot enjoy all these benefits!!! *Loud laughter from the group!!...*

F: Yes, the one with the hand up.

P: I wanted to just clear a bit of confusion into the whole thing of participants trusting and … you know there is another element to it. An element of, 'I come here there are not so many people although it's far from where I live, I will come here because people who know me they will not see me, so they avoid stigma. I think there still that element!

P: But again when you talk about stigma amongst our clients, you find that those still having the idea of stigma they are still shy to come and participate in research, they want to go to public facilities.

F: This a general question! Would you consider the care at the research center as coercion or undue influence?

P: I can really say once somebody has participated in a study, even when a friend comes to them and says 'some people approached me and they want me to enrol my child in a study'….and is not sure whether he/she will be making a good decision to participate.

Usually after getting advice from the friend, they come back the next day excited to say '*I have made up my mind' my friend has also told that she was in this study and it is very, very, good*'. I know her child was very, very, ill and now the child is fine'. This I can really say is one thing that attracts people to studies or research.

P: Just to add on to that, I know my institution provides the best care and our clients are very happy and are resistant to go to public facilities after the study ends. May be it might be influencing the consenting in a certain way!!

P: Interrupts! What we can say for sure is that we are doing research and are not interested in just recruiting and we are going to do everything possible to continue being attractive, whether this is ethical or unethical is another thing! *Everybody bursts into laughter!!...*

P: I would say what we are giving is standard care but we are able to do it because we do not have as much burden like lots of patients, or long queues. I am sure the doctors and nurses in the public facilities did not have a lot of work they would probably also does the same thing!

F: Oh you are smiling all the time!!... *Laughter! ....*

P: I think maybe they just said all I wanted to say, but I think as a researcher you have to go through intensive training especially human protection or human rights Also since we know this is voluntary we try as much as possible to be nice so nice to our clients and I think it something that attracts them also. And like P5 said, one argument could be that the work load in research is not as much as in the public facilities.

P: Just another thing, research programs have time frames e.g. three years. *Joke:* I want at the end of that time to have my job done and have my contract renewed so, am going to do what is expected of me. *Laughter!* Unlike in the public facilities where employment is permanent and pensionable. In my

setting if a patient takes a complaint to the PI or the ethics committee it tarnishes the name of the institution and I do not have my contract renewed!! Loud laughter from the group!!...

P:Like myself I worked for an organization for 3 years then went back to public service , but I could see that am a different person than before I passed through research. The way the informed consent is conducted for treatment is like a forceful signing.

Sometimes clients are left until they get to point when they cannot say 'NO' and the health personnel do not have that much time to sit with a patient and explain. For example a health worker might just come to the ward and say *'Mum, am taking to theatre to extract this baby so that you do not have complications, do you understand'* Answer: '*Yes*'. Health worker: '*Sign here' loud laughter from the group*!!... In a study I sit with a client and explain and ask questions, I don't just say…'you give the baby teaspoon every day at 8.00 am and 8.00pm! So [mma] give this medicine, if you do not your child will get infected'. I think they [health workers] need to be taught. Again us we are just doing the research we are not going to be involved in the treatment like the roll out of HAART. I am afraid that we are giving the responsibility to people who have not been in a research environment and they do not know the [instructions]! Surprise!!

P: *Cracks a joke*! The recommendation should go to the permanent Secretary! *Group laughs and gives applause!!!*

F: Let's look at these parents and guardians who are coming to your research sites. Who is the first contact to talk to them about the study even those referred from the clinics?

P: You know at our institution wherever there is a research we have to first teach everyone, all employees at the study site even the cleaners, receptionists and security guards! So they know how/where to direct the clients. Participants should only not be known by certain group of people! After the receptionist has given them a 'warm welcome' laughter! Then clients are directed to the study coordinators who explain everything. Then they are taken to the PI and the investigator [consenter] will be there. Somebody whispers from the audience '*Gives them a cup of tea'* laughter!

P: I do not think tea is ethically allowed! It might be seen as a bribe! Group continues laughing!

F: So what roles to the clinicians/doctors play in consenting?

P: Hum… Not much! Whispers from the group 'No'

P: Depending on the complexity of the study, sometimes the consent is conducted by the doctors especially some studies that are very clinical. But on the whole doctors are not that much involved. More whispers from the group saying 'No'.

F: But what would you like to see? What kind of involvement from the doctors, to what extent should they be involved?

P: The problem with our doctors is that majority are not Batswana, and we administer the consent primarily in Setswana. So this is a challenge.

P: At my site the doctor conducts informed consent sessions, collects specimens etc so it depends on the studies and sites!

F: When you are looking at the informed consent process, do you think full understanding is feasible? Do you think you are achieving that with the parents that you are dealing with?

P: Majority of people do not understand despite the care given. It depends on the study. Some studies are very complex.

F: Thank you so much for your participation the student will make sure to give you a report of the findings and recommendations.

End of interview 18.00 hrs

APPENDIX 15: TRANSCRIPTION OF THE INDEPTH INTERVIEWS

IN-DEPTH INTERVIEW: 1

Date	09.05.2011
Interview No	0001
Stat time	14.55hrs
Gender	Male
Age	30-40
Discussion Language	English
Research Assistant	Ms. Faith Mompati-Ketshogile
Education	Diploma in nursing science

The research assistant began the interview by introducing themselves and going through the consent form and have it signed by the respondent.

Q: Have you had any specialized training in ethics of conducting clinical trials research?
R: Participant: We have done Good Clinical Practice. We do it continuously. We do it annually, like mine expires end of October, 2011.
Q: Do you have any specializations in pediatrics?
R: I have some experience for working in the pediatric ward for about 2 years.
Q: Which Phase of clinical trial have you been involved in?
R: Two clinical trials
Q: What was the risk category of the clinical trial you recently conducted?
R: There is no risk or less than minimal because the other one was just a psycho-social study.
Q: On average, what generally is the highest level of education attained by the majority of the parents/guardian who give consent for their children's participation in clinical trials?
R: Most of them are primary.
Q: On average, what is the average age of the parents/guardians whom you have obtained consent from for their children's participation in clinical research?
R: Mid 50s, mainly mothers and grandmothers. Most of them are grandmothers.
Q: On average how many of your participants have previous experience with research on HIV disease?
R: Most of them because they were previously involved in a clinical trial before.
Q: What generally is social economic status of the majority of the parents/guardians who participate in your studies**?**
R: Mainly low income strata
Q: How do you rate the importance of prior of knowledge of a research investigator about Botswana culture, values and beliefs before the start of the study?
Q: Do you think this knowledge plays any role in the success or failure of a consenting process? (Please explain)
R: Maybe when it comes to language, for example when you go to Bokalaka (Northern Botswana) you have to be knowing the language, you might experience language barriers that you have to be prepared for. Yes, it can affect the success of the study because maybe every time you go, you will meet those who don't speak Setswana.
Q: Who prepares the consent form that you use in the clinical trial?
R: Most of them the PI (Principal Investigator) then most of us do the translation. Maybe...I don't know.
Q: On average how many pages is your consent document?
R: Most of them are 1 page. Most of them are compressed into 1 page or 1 page and a half. You don't have to be long because they have to read.
Q: Which research guidelines are you familiar with regarding the protection of research participants and how helpful they are to the consenting process?
R: We are using Botswana Guidelines and Good Clinical Practice. The Botswana Guidelines from the ministry of Health and Botswana laws.
Q: GCP guidelines recommend that both the informed consent discussion and the informed consent form should include the twenty elements. Do your consent forms include all these elements and are you able to go through all these during your sessions?
R: No, there are no gaps. We follow those rules. Yes, you have to stick to all the guidelines.
Q: What challenges do you encounter from the **sponsors** regarding the requirements for preparation of the informed consent document for the clinical trial if applicable?
R: Um....I don't know because the study coordinator handles most of those so it's a smooth process. We just translate. Maybe if it was in English we translate to Setswana, and then we take them to the ministry, I don't know what they are doing there.
Q: What challenges do you encounter from the **ethics committees** that review your consent form if applicable?

R: Not answered
Information disclosure
Q: What recruitment methods do you use to let parents/guardians know about this study?
PR Mostly clinic contact, especially from the clinics or some referrals. We also use the system from the other studies, so we can just call. If there are no contacts and you can't follow you just go to the next patient.
Q: Who talks to the parents/guardians/children about the clinical trial when they came to the hospital/clinic?
R: Research nurses.
Q: In what language are the discussions of the information about the study held?
R: Primarily Setswana, if they prefer English, it's available.
Q: In what language are the discussions of the information about the study held?
R: Verbally in Setswana but a patient might prefer English.

Q: From your experience, which of the following elements of the consent form do find difficult to communicate to participants and why?

R: Hey, I don't think there is any problem with explaining the consent. The only problems comes with asking questions, some of the questions we are asking are culturally sensitive, they were not polite. Like in one study there were some questions where you had to ask about sex and they are culturally inappropriate. Yes, it's difficult to present that question. The other study we were doing, they didn't like to interrupt the treatment, at first they didn't like but after some time they liked it.

Q: How would you rate the amount of information provided to the parents/guardians in the studies you have conducted?

R: Too much!

Q: Considering the risks involved in clinical trials, when disclosing information to participants, which criteria do you use?

R: You have to state everything because this is voluntary.

Q: How would rate the complexity of the technical language used in the consent document and how do enhance understanding of such language?

R: Sometimes there is too much technical language, so you have to go in and try to explain more. Yes, it's necessary especially when you are dealing with drugs. Yah, you have to break it down or ask in a polite way.

Understanding

Q: How do majority of participants initially react to experimentation on their children?

PR They don't like it before you can even introduce the research. They say their children are being used too many times. They are not interested.b. Do the parents understand the difference between research and treatment? They know! If you come down and explain then they will listen.

Q: Do the parents/guardians ask any questions? If yes what are usually their main concerns?

PR Yes, about the outcome of the studies, what are we supposed to do? Are there any risks to my child? What about the safety of the child, duration of study, the number of visits but we reimburse for transport as they come.

Q: What do you think is the most common reason for the parents/guardians not asking questions?

R: We ask again do you understand, and if they say yes, we assume they are ok. You have to ask if they really understand. I think most of them here, they trust the research team. But some of them it's because they will be given money for transport.

Q: According to your observation, what is usually the general emotional state of the parents/guardians during the consenting process?

R: Um....I think most of them are stressed they don't want to be seen doing many things here; they just want to be seen once and be done. There is stigma associated with the clinic because now the child will be seen coming to the clinic.

Q: How do you test the level of understanding of the information provided about the trial?

R: We just have to ask them do they know what you are talking about. It's verbal. For some they could read but they are just lazy, they are lazy to read then when you ask them they say they are fine.

Q: How would you rate the level of attentiveness of the parent/guardian during the consent process?

R: Most of them they are bored, attentiveness is a bit low. There would usually be about 60 patients at the clinic so by the time we talk to the patients they are tired of waiting. We take patients by referral and self-referral.

Q: How much time do you think is appropriate for the informed consent process to enable understanding?

R: To understand……? About 10 minutes because they don't want to be here longer. I have to read in Setswana then explain to them so about 10 to 20 minutes.

Decision Making

Q: Approximately how much time do you think should be given to the parents/guardians to make a decision?

R: (Laughs)...um but if it's a psycho-social survey they can make the decision then but if it's a clinical study then they have to go back home then they come again next time, so if you have the questionnaires they can make the decision right away in 30 minutes. They can consult the husband, let's say we are here for 3 weeks; we give them a time, like if we are finishing before end of April we tell them to come before end of April.

Q: Is it important to you to always consult the two parents or the **relative(s)** of the participants even if the person who has brought the child to the clinic agrees to participate?

R: Most of the time it's the husband but sometimes the child is accompanied by an aunty so they have to consult the mother. Or for some of them the mother is dead so we see the grandmother.

Q: Do all the parents insist on consulting with the spouse or family before making a decision?

R: Yes, it's very important. There are research nurses or teams.

Q: Who do you mainly consult before enrolment of the child into the study?

P: Mostly the husbands.

Q: Does the involvement of a participant's **spouse or relative(s) influence** the **time** necessary to obtain informed consent?

R: Yes, in some of the systems. But we understand they have to take time.

Q: How do they indicate their agreement to the children's participation in clinical research?

R: By signing on the consent form.

Q: How do the parent(s)/guardian(s) react to being asked to sign a consent form?

R: It depends; I think 5 percent of them would just sign the form and move on. Most of them are just ok; they know what they are doing.

Q: How do you facilitate the decision-making process?

R: One thing is, I have to show the parents the benefits of research.

Q: From your interaction can you identify any social, cultural, economic or any other factors that you think might influence the parents/guardians to agree to enrol their children in the study?

P: Um....I don't know, I don't think I know one because normally we check everything unless it's there culture and they don't want to be involved in the study.

Q: Describe any measures you put in place to ensure that participants and the consenting parents/guardians do not feel coerced or pressured to join the study as well as continued consent during the study.

R: I think most of the time it's included in the consent that this voluntary and at any point you can take your child out of the study.

Q: Describe any general challenges you encounter in seeking informed consent from parents/guardians/child?

R: Translation, some of the words in English it's hard to translate into Setswana then you lose the meaning and the Setswana one seems to be longer and patients get tired.

Q: Please give any recommendations that would help in enhancing the informed consent process for child participation in clinical Trials.

R: Um.....I think the only thing is to make sure the consent is straight to the point as possible so you don't take a lot of time reading.

Q: Do you involve competent children in the consent process?

R: You say children? Yes, we can go to children who are 18 and the mother is the one who gives the consent. If the mother is under 21 then the caregiver gives the consent.

Q: Children of what age do you engage in the consent process?

R: Not answer given.

End: 15.25hrs

IN-DEPTH INTERVIEW: 2

Date	11.05.2011
Interview No	0002
Stat time	15.04 hrs
Gender	Female
Age	30-40
Discussion Language	English
Research Assistant	Ms. Faith Mompati-Ketshogile
Education	Diploma in nursing science

The research assistant began the interview by making introductions and going through the consent form and have it signed by the respondent. Respondent characteristics were not included in the write up for anonymity and confidentiality purposes.

Q: Have you had any specialized training in ethics of conducting clinical trials research?
R: Human subjects protection, GCP
Q: Do you have any specializations in pediatrics?
Participant: Over 10 years of work experience in pediatric environment and 1 year of pediatrics research
Q: Which Phase of clinical trial have you been involved in?
R: No answer
Q. What was the risk category of the clinical trial you recently conducted?
R: You mean the pediatrics study? Minimal risk and benefit? Vaccine has minimal risk with HIV positive children, Could be risky because of the vulnerability of the children
Q: On average, what generally is the highest level of education attained by the majority of the parents/guardian who give consent for their children's participation in clinical trials?
R: On average around junior school, we have some who have gone up to tertiary. Very few have no education at all
Q: On average, what is the average age of the parents/guardians whom you have obtained consent from for their children's participation in clinical research?
R: On average from 26-30, 31-35 fewer as we go up, grandparents
Q14.On average how many of your participants have previous experience with research on HIV disease?
R: No answer
Q: What generally is social economic status of the majority of the parents/guardians who participate in your studies?
R: Very low, Waho!! Majority medium. We find some above average but very few, university but also not extremely high
Q: How do you rate the importance of prior of knowledge of a research investigator about Botswana culture, values and beliefs before the start of the study?
R: A few who use traditional medication but do not want to stop .It is a common practice but very few admit using it.
Q: Do you think this knowledge plays any role in the success or failure of a consenting process. (Pease explain)
R: The belief might affect someone do decline
Q: Who prepares the consent form that you use in the clinical trial?
R: Only involved in translations otherwise it's pre-prepared. At times if we were consulted we could change some things.
Q: On average how many pages is your consent document?
R: The least 5 pages most bulky 19 pages
Q20.Which research guidelines are you familiar with regarding the protection of research participants and how helpful they are to the consenting process? GCP guidelines recommend that both the informed consent discussion and the informed consent form should include the twenty elements. Do your consent forms include all these elements and are you able to go through all these during your sessions?
R: Belmont report, Nuremberg Code but in practice we do not normally apply them Laughter!!I never go back. Botswana Laws are a barrier because in our community there lots of young mothers 18 and able to understand with no other relative that consent for them but would benefit from the study. Some get very emotional and upset if they are declined.
Q21. GCP guidelines recommend that both the informed consent discussion and the informed consent form should include the twenty elements. Do your consent forms include all these elements and are you able to go through all these during your sessions?
R: No answer
Q: What challenges do you encounter from the **ethics committees** that review your consent form if applicable?
R: I do not have much information coordinators are responsible.
R: Challenges: Translation Uh! Ya!... English words which do not exist in Setswana but we find a way. But sometimes lose meaning. I read, encourage questions stop along the way, give a copy to take home and come back with questions. But reading in Setswana is very difficult but with experience am getting used. With the Setswana consent form familiarize so it is a conversation. Participants often get impatient when it is too long lose concentration. Recommend a shorter version some things are made to long or too detailed for the patient. Legally you are expected to give all the information
Q: What challenges do you encounter from the **sponsors** regarding the requirements for preparation of the informed consent document for the clinical trial if applicable?
R: No answer

Information disclosure

Q: What recruitment methods do you use to let parents/guardians know about this study?
R: Put flyers at the clinics, use recruiters give a brief overview and we discourage them to be coercive. We explain details when the patients come to the clinic
Q: Who talks to the parents/guardians/children about the clinical trial when they came to the hospital/clinic?
R: Usually the study nurses.
Q: In what language are the discussions of the information about the study held?
R: Setswana but some prefer English. Laughter!! Most educated Batswana prefer to use English.
Q: How is the information about Clinical trials communicated to participants?
R: Communicate verbally and give them to read at home
Q: From your experience, which of the following elements of the consent form do find difficult to communicate to participants and why?
R: I do not find any section difficult because I lay the points as they are may be studies that are too scientific Pharmacokinetics, pharmacodynamics. Scientific terms in a consent form brief somebody in the simple way, Gastroenteritis =say diarrhoea

Q: How would you rate the amount of information provided to the parents/guardians in the studies you have conducted?
R: Some have too much information others average.
Q: Considering the risks involved in clinical trials, when disclosing information to participants, which criteria do you use?
R: Explain, read, and give the form to take home, ask questions.
Q. How would rate the complexity of the technical language used in the consent document and how do enhance understanding of such language?
R: Quality scientific studies are a challenge some studies can be too complex
Q: Considering the risks involved in clinical trials, when disclosing information to participants, which criteria do you use?
R: Give all the information

Understanding

Q: How do majority of participants initially react to experimentation on their children?
R: Majority are Ok (laughter!!!) meaning happy to be participating others are anxious
Q. Do the parents understand the difference between research and treatment?
R: Initially not but as they are explained they understand
Q: Do the parents/guardians ask any questions?
R: Yes the literate ones usually do but the less educated do not
Q: If yes what are usually their main concerns?
R: Safety of the child, benefits
Q: If no questions are asked do you find out why?
R: They say they have understood everything. A few say (laughter!!!) they did not understand. Those that ask questions it is out of understanding.
Q: What do you think is the most common reason for the parents/guardians not asking questions?
R: When they hear about procedures their children will go through, they go into a bit of panic and even pay more attention.
Q: According to your observation, what is usually the general emotional state of the parents/guardians during the consenting process?
R: Usually not emotionally stable, worried about baby or naturally am not clever but ask you to go over again
Q: How do you test the level of understanding of the information provided about the trial?
R: We have an assessment tool after discussion we test and if not getting the right answers we go back. Ask why they can't grasp, lack of concentration etc
Q: How would you rate the level of attentiveness of the parent/guardian during the consent process?
R: Beginning they concentrate. Along the way ask or talk about the baby to distract, play with the baby, concentration will pick.
Q: How much time do you think is appropriate for the informed consent process to enable understanding?
R: At least 45min I would recommend that those who prepare the consent forms should aim at something not more than 45 min long.

Decision Making

Q: Approximately how much time do you think should be given to the parents/guardians to make a decision?
R: Usually I give an appointment for potential participant to come back. Depending on the potential participant, some say straight away Iam "Sure I want to join" They do not think of the payment because the money paid is too little to coerce them (P30.00).if hesitant, I let them go home and return.
Q: Is it important to you to always consult the two parents or the **relative(s)** of the participants' even if the person who has brought the child to the clinic agrees to participate?
R: No answer
Q: Do all the parents insist on consulting with the spouse or family before making a decision?
R: I only involve them when there is a problem. Those who wish to consult husbands are usually the young mothers.
Q: Who do you mainly consult before enrolment of the child into the study?
R: Grandparents and friends at times
Q: Does the involvement of a participant's **spouse or relative(s) influence** the **time** necessary to obtain informed consent?
R: Yes it does and is necessary
Q: How do the parent(s)/guardian(s) react to being asked to sign a consent form?
R: If they have made a decision they have no problem with signing
Q: How do you facilitate the decision-making process?
R: Explain what the study is about Emphasize freedom to make a decision. Allow as much time as required. Explain asked question to participant satisfaction. Allow and encourage them to consult
Q: From your interaction can you identify any social, cultural, economic or any other factors that you think might influence the parents/guardians to agree to enrol their children in the study?
R: Oh! Those who do not believe in western medicine do not, even come to the clinic because their beliefs do not allow
Q: Describe any measures you put in place to ensure that participants and the consenting parents/guardians do not feel coerced or pressured to join the study as well as continued consent during the study.
R: We assure them that its voluntary and you can withdraw any time .There is a possibility of some things to coerce like care being better than public facilities hem but not obvious thing
Q: Please give any recommendations that would help in enhancing the informed consent process for child participation in clinical Trials.
R: Reduce time spent at the clinic. Educate communities on importance of C/T (new knowledge, medicines to save lives). Put in an education component especially on benefits. Encouraging mothers to recruit, we do not do it but their friends tell them about the study and they come.

Thank you for participating in this study. **End time: 15.30**

IN-DEPTH INTERVIEW: 3

Date	18.05.2011
Interview No	0003
Start time	14.35
Gender	Male
Age	30-40
Discussion Language	English
Research Assistant	Ms. Faith Mompati-Ketshogile
Education	Diploma

The research assistant began the interview by making introductions and going through the consent form and have it signed by the respondent. Respondent characteristics were not included in the write up for anonymity and confidentiality purposes.

Q: Have you had any specialized training in ethics of conducting clinical trials research?
R: GCP, Bioethics, Ethics seminars and workshops,
Q: Do you have any specializations in pediatrics?
R: I worked in the pediatric environment for many years before joining research
Q10. Which Phase of clinical trial have you been involved in?
R: Phase II & III (Drug intervention). Respondent is not confident about the answers.
Q: What was the risk category of the clinical trial you recently conducted?
R: Less than minimal risk
Q: On average, what generally is the highest level of education attained by the majority of the parents/guardian who give consent for their children's participation in clinical trials?
R: Primary and secondary
Q: On average, what is the average age of the parents/guardians whom you have obtained consent from for their children's participation in clinical research?
R: 26 years and above but those over 45 would not be the biological parents majority grandparents/caregivers
Q: On average how many of your participants have previous experience with research on HIV disease?
R: did not answer the question
Q: What generally is social economic status of the majority of the parents/guardians who participate in your studies? Generally low
R: Low income majority
Q: How do you rate the importance of prior of knowledge of a research investigator about Botswana culture, values and beliefs before the start of the study?
R: Very important (Very passionate about this point).To get basic information about a patient; get all the details to understand the client. Consider the rights and welfare
Q: Do you think this knowledge plays any role in the success or failure of a consenting process?
(Please explain)
R: Can affect the success of the process
Q: Who prepares the consent form that you use in the clinical trial?
R: Study coordinator and doctors who is involved in the study
Q: On average how many pages is your consent document?
R: Depends on the study because all details must be included incorporate all information necessary for understanding, not coercive example collection of blood, what they will experience expected discomfort
Q: Which research guidelines are you familiar with regarding the protection of research participants and how helpful they are to the consenting process? GCP guidelines recommend that both the informed consent discussion and the informed consent form should include the twenty elements. Do your consent forms include all these elements and are you able to go through all these during your sessions?
R: Declaration of Helsinki, ICH-GCP, Botswana Clinical Trials Guidelines -Ministry of Health
Q: GCP guidelines recommend that both the informed consent discussion and the informed consent form should include the twenty elements. Do your consent forms include all these elements and are you able to go through all these during your sessions?
What challenges do you encounter from the ethics committees that review your consent form if applicable?
R: Delays especially national ethics committee.
Q: What challenges do you encounter from the sponsors regarding the requirements for preparation of the informed consent document for the clinical trial if applicable?
Not answered
Information disclosure
Q: What recruitment methods do you use to let parents/guardians know about this study?
R: Establish inclusion criteria and phone patients who are eligible .No advertisements at the clinics, do not get referrals, national program
Q: Who talks to the parents/guardians/children about the clinical trial when they came to the hospital/clinic?
R: Study coordinator, PI and doctors-research team
Q: In what language are the discussions of the information about the study held?
R: Mainly Setswana but can be done in English as well
Q: How is the information about Clinical trials communicated to participants (language?)
R: Must be communicated in a language that is appropriate but both verbal English and Setswana choices are made available.
Q: From your experience, which of the following elements of the consent form do find difficult to communicate to participants and why?
R: Technical terms
Q: How would you rate the amount of information provided to the parents/guardians in the studies you have conducted?
R: Too much but it is necessary and part of the ethical principles
Q: Considering the risks involved in clinical trials, when disclosing information to participants, which criteria do you use?
R: Disclose all the information as an ethics principle
Q: How would rate the complexity of the technical language used in the consent document and how do enhance understanding of such language?
R: Too complex
Q: Considering the risks involved in clinical trials, when disclosing information to participants, which criteria do you use?
R: Disclose all the information as an ethics principle
Understanding
Q: How do majority of participants initially react to experimentation on their children?

R: More anxious than when they come in some seem satisfied.
Q: Do the parents understand the difference between research and treatment?
R: Participant: Yes parents understand the difference between research and treatment
Q: Do the parents/guardians ask any questions?
R: Yes
Q. If yes what are usually their main concerns?
R: Safety of child,
Q: If no questions are asked do you find out why?
R: Not answered
Q: What do you think is the most common reason for the parents/guardians not asking questions?
R: Fear to be involved in research, lack of understanding concern about future risks
Q: According to your observation, what is usually the general emotional state of the parents/guardians during the consenting process?
R: Excitement but this should not be taken for granted. Some parents are calm because they are familiar with research
Q: How do you test the level of understanding of the information provided about the trial?
R: verbally but there is no written test to assess understanding
Q: How would you rate the level of attentiveness of the parent/guardian during the consent process?
R: High
Q: How much time do you think is appropriate for the informed consent process to enable understanding?
R: Give as much time as they client needs, do not push them!
Decision Making
Q: Approximately how much time do you think should be given to the parents/guardians to make a decision?
R: Main concern should be protection of participants so give them time to think about your request and to consult
Q: Is it important to you to always consult the two parents or the relative(s) of the participants even if the person who has brought the child to the clinic agrees to participate?
R: Very important because it can help to retain them on the study
Q: Do all the parents insist on consulting with the spouse or family before making a decision?
R: Yes
Q: Who do you mainly consult before enrolment of the child into the study?
R: Spouse, grandmother, grandfather, uncles, auntie or whoever relative is relevant
Q: Does the involvement of a participant's spouse or relative(s) influence the time necessary to obtain informed consent?
R: Yes
Q: How do the parent(s)/guardian(s) react to being asked to sign a consent form?
R: By putting a signature on the consent form
Q: How do you facilitate the decision-making process?
R: Guide them through the information given and give the consent form to carry home and read or be read to
Q: From your interaction can you identify any social, cultural, economic or any other factors that you think might influence the parents/guardians to agree to enrol their children in the study?
R: Economic -some cannot afford transport to get to the clinic so they are attracted by the re-imbursement given.

That's the end of the interview. Thank you so much for your time.

IN-DEPTH INTERVIEW: 4

Date	24.05.2011
Interview No	0004
Start time	15.18 hrs
Gender	Female
Age	30-40
Discussion Language	English
Research Assistant	Ms. Faith Mompati-Ketshogile

The research assistant began the interview by making introductions and going through the consent form and have it signed by the respondent. Respondent characteristics were not included in the write up for anonymity and confidentiality purposes.

Q: Have you had any specialized training in ethics of conducting clinical trials research?
R: Yes, although it was not a specialization.
Q: Do you have any specializations in pediatrics?
R: Yes I did pediatric courses at school. I also have 4 years of experience in conducting studies involving parents and children
Q. Which Phase of clinical trial have you been involved in?
R: Mostly Phase III and IV
Q: What was the risk category of the clinical trial you recently conducted?
Participant: Mostly minimal but one study that involved drug intervention was greater than minimal risk.
Q: On average, what generally is the highest level of education attained by the majority of the parents/guardian who give consent for their children's participation in clinical trials?
R: Mostly Primary and Junior school we have a few tertiary or those who dropped out of school early. I prefer those without too much education because they will follow what they are told
Q: On average, what is the average age of the parents/guardians whom you have obtained consent from for their children's participation in clinical research?
R: Most parents are 21 years and above because of the age of consent but there are also a lot of grandparents to consent for minors
Q: On average how many of your participants have previous experience with research on HIV disease?
Q: What generally is social economic status of the majority of the parents/guardians who participate in your studies? Generally low
R: Very few especially those who have been in studies as pregnant women and they enrol their children in studies.
Q: How do you rate the importance of prior of knowledge of a research investigator about Botswana culture, values and beliefs before the start of the study?
R: Promotes understanding ways of respecting participants for example, those who say must go back and consult-it is usually an indirect way of refusal but some come with their minds made up. Knowledge of the local language is also important for understanding.
Q: Do you think this knowledge plays any role in the success or failure of a consenting process?
R: I think you cannot take out the culture; we go through the Kgotla before. On one study I was asked whether I have talked to the Kgosi before. I have had an experience where they admit that they have taken traditional medicines. Inhalations but we respect their culture we can stop them. It is a problem to ask the mother and father to join because a lot of women are single mothers even those who have are not so much involve come to drop them. Once they say they want to consult it is an indirect way of refusing although a few agree need for education to involve partners.
R: The forms are prepared by the research team, use the format from the sponsor but contextualize to the culture of Botswana setting especially for Multi-center studies. The Principal Investigators consult with the research team and study coordinators and senior nurses help.
Q: On average how many pages is your consent document?
R: Usually long but nurses are able to summarize the information from lengthy forms to about six pages, a page sometimes. Although the forms are long nurses with experience know how to pick important issues
Q: Which research guidelines are you familiar with regarding the protection of research participants and how helpful they are to the consenting process? GCP guidelines recommend that both the informed consent discussion and the informed consent form should include the twenty elements. Do your consent forms include all these elements and are you able to go through all these during your sessions?
R: We all do Good Clinical Trial Practice training so am familiar with GCP guidelines and refer to these documents. All of us are trained in GCP because it is a requirement by the institution that everyone is trained
Q: GCP guidelines recommend that both the informed consent discussion and the informed consent form should include the twenty elements. Do your consent forms include all these elements and are you able to go through all these during your sessions?
What challenges do you encounter from the **ethics committees** that review your consent form if applicable?

R: Uh! I would not say I have encountered much problems. At the Ethics committee I prefer submitting my application to a particular person other than the registry to avoid losses. There are also delays, we asked to do lots of corrections not to pay the participants much but only for compensating transport which is not much compared to what participants in other countries pay.
Q: What challenges do you encounter from the **sponsors** regarding the requirements for preparation of the informed consent document for the clinical trial if applicable?
R: We are not involved with sponsors
Information disclosure
Q: What recruitment methods do you use to let parents/guardians know about this study?
R: We hardly use the radio, but we use mainly posters put at the clinics. We also use the patient meetings, wards antenatal clinics in the rural areas. A few patients come from private clinics
Q: Who talks to the parents/guardians/children about the clinical trial when they came to the hospital/clinic?
R: Recruiters and nurses. The recruiters go with the nurses for better interaction. We also get self-referrals who have heard about the study from the community. Some parents call to inquire about the study after they have heard about the benefits.
Q: In what language are the discussions of the information about the study held?

R: Mainly the local official language Setswana, but a few prefer English.
Q: From your experience, which of the following elements of the consent form do find difficult to communicate to participants and why?
R: The procedures and risks can be a challenge to explain because of the scientific terms. Also concepts like randomization.
Q: How would you rate the amount of information provided to the parents/guardians in the studies you have conducted?
R: The information is usually a lot because of the length of the consent forms and the short time one to go through the form.
Q: Do you consider all the information relevant for the participant to make an autonomous decision?
R: Yes but for the level of the participant some of the information might not be relevant especially the medical explanations and details of treatment and laboratory tests.
Q: How would rate the complexity of the technical language used in the consent document and how do enhance understanding of such language?
Understanding
Q: How do majority of participants initially react to experimentation on their children?
R: You find that initially some are very anxious because of the nature of illness of their children but as we explain some of the things they become calm and with time some even become happy and do not look as hopeless as the time they came.
Q: Do the parents understand the difference between research and treatment?
R: Sh! .. we try to explain but it is difficult to tell for many of them. To me it seems like they think they have come for their child's treatment. But we emphasize this a lot during the consenting process.
Q: Do the parents/guardians ask any questions?
R: Not that much especially those with low education. I feel they still have that mentality that the health professional is always right. But some do especially about the safety of their child.
Q: If yes what are usually their main concerns?
R: They mainly want to know how experimenting on the child might affect the child physically, whether the child will get better, mainly child safety issues.
Q: If no questions are asked do you find out why?
R: Really I have never found out why, but I think it might be a cultural thing where they do not want to look like they are questioning. I t might also be fear of the unknown. Like they would rather not know what lies ahead.
Q: What do you think is the most common reason for the parents/guardians not asking questions?
R: I think it is the culture. The power issue!... considering that the doctor or nurse is a respected member of the community and the assumption that they know what is best for the child.
Q: How do you test the level of understanding of the information provided about the trial?
R: Verbally by using a test of understanding quiz. Sometimes even asking just general questions not really related to the study just to change the topic a little during the consenting process.
Q: How would you rate the level of attentiveness of the parent/guardian during the consent process?
R: Ah! It's is difficult to judge because some just stare at you as you talk or read to them which might look like they are paying attention. Some would be very tired after a long day you can really see they are more worried about how they will get home
Q: How much time do you think is appropriate for the informed consent process to enable understanding?
R: It depends on how understanding is being judged. If the parent does not seem to understand we can even ask them to come another time after having someone read and explain to them.
Decision Making
Q: Is it important to you to always consult the two parents or the **relative(s)** of the participants even if the person who has brought the child to the clinic agrees to participate?
R: It would be good for the two parents to be consulted but we meet a lot of young single mothers whose spouses are not so much involved in the care of the child. It is always good to get the blessing and to have the support of the relatives because they all take care of the child and they show concern. Even the culture encourages this. Also in case anything goes wrong, the blame is not only shifted to the institution.
Q: Do all the parents insist on consulting with the spouse or family before making a decision?
R: Yes a lot of them do even after they have agreed at the clinic they will go back and talk to their families. Sometimes you find that they will not come for the next appointment and when you phone them they say the relatives did not approve. However those whose spouses are not aware of the status of the parent and child are hesitant to consult the spouse.
Q: Who do you mainly consult before enrolment of the child into the study?
R: Mostly the grandmothers to the child or anyone the parent can suggest.
Q: Does the involvement of a participant's **spouse or relative(s) influence** the **time** necessary to obtain informed consent?
R: Ya!.. it really makes a difference because it is like a secret that is coming out and the parent is relieved that someone knows about the situation and will give support. It also improves the level of involvement in the research and adherence to the instructions.
Q. How do the parent(s)/guardian(s) react to being asked to sign a consent form?
R: Again as I said, they do not seem to mind especially before they get a good understanding of the difference between research and treatment. Signing means they will get help. Another thing is the culture of not questioning.
Q: How do you facilitate the decision-making process?
R: Emphasizing that the participation is voluntary and telling the truth about the uncertainties of the study so the parent understands the benefits and risks. Allowing as much time as required for someone to decide not to rush them.
Q: Describe any measures you put in place to ensure that participant and the consenting parents/guardians do not feel coerced or pressured to join the study as well as continued consent during the study.
R: I assure the parents from the beginning that enrolling the child is voluntary. I also do not mention that there will be a compensation for travel at the beginning.
Q: Please give any recommendations that would help in enhancing the informed consent process for child participation in clinical Trials.
R: There is need to shorten the forms and simplify them. More education to the public about the importance of research and clear some of the misconceptions.

Thank you that is the end of our interview. **End time: 15.54 hrs**

IN-DEPTH INTERVIEW: 5

Date	22.03.2011
Interview No	0005
Start time	15.08 hrs
Gender	Female
Age	20-30
Discussion Language	English
Research Assistant	Ms. Faith Mompati-Ketshogile
Education	

The research assistant began the interview by making introductions and going through the consent form and have it signed by the respondent. Respondent characteristics were not included in the write up for anonymity and confidentiality purposes.

Q. Have you had any specialized training in ethics of conducting clinical trials research?
R: I did the GCP, Good clinical practice... and....um I haven't done any communication skills but …….
Q: What on-going training on protection of human subjects are you receiving?
Participant: We do renew every time, it takes a year then we renew.
Q: Tell me about purpose of the clinical trial you are involved in.
R: the studies that we are doing according to my understanding...um...there is this other one, we are dealing with pregnant women and we want to see whether, how many times or how much of the drug can prevent or reduce the virus from the mother to the baby. Its drug intervention. The other one is dealing with babies. That one we are dealing with drugs and we want to see how they help the positive babies, we want babies who are less than 3 months.

Q: Explain your role in clinical trial have you been involved in?
R: um...my role is to go out to clinics and identify people who are eligible for studies then I recruit them to the study. I just tell them everything about the study, if they agree that's when they will come to the site, if they don't agree then that's fine, they don't participate.

Q: Briefly carry me through the consenting process.
R: ....um....I think for people who are consenting for our studies, for us I tell them about the study, I tell them the negative or disadvantages and the advantages. From there, that's when we sign. The consenting and signing is done here, so the agreeing and explaining is done here in our facilities. For them to come here we say everything and show them everything about our study then they agree to join the study, that's when they come. If the don't agree, they don't come here. We don't do any paper work at the clinic; we just explain the whole process of the study and tell them everything about the study and when they come here, that is when they do the writing.

Q: Which phase of clinical trial have you been involved in?
R: drug related studies

Q: What was the risk category of the clinical trial you recently conducted?
R: Low, maybe let me say about the babies. We are doing the same thing they do at the government. They come here and we start with doing the PCR, and do HIV test. With pregnant women, I don't think there is a little risk because we draw blood so we prick them and we do many tests but I haven't seen any other danger.
Q: Are clinicians involved in the consenting process?
R: Yah, the nurses...here, the nurses are the ones who are involved. Normally, as far as I know, for the patients she meets the nurses do most of the consent and tells her what, then the doctor only comes to consult.
Yah, since I came here 3 years ago, it seems like its working well because with the consenting part, they are repeating what we told the patient at the clinic so it's easy to understand.
Q: On average, what generally is the highest level of education attained by the majority of the parents/guardian who give consent for their children's participation in clinical trials?
Participant: ...um.... junior secondary.
Q: On average, what is the average age of the parents/guardians whom you have obtained consent from for their children's participation in clinical research?
Participant: around 30, let's say 30 to 35.
Q: On average how many of your participants have previous experience with research on HIV disease?
R: (sighs) not a lot. Not a lot.
Q: What generally is social economic status of the majority of the parents/guardians who participate in your studies?
R: (Laughs)...one thing that I have noticed is that most of these patients are of low to medium. High or whatever, it's so rare to find them because they are able to go to a private doctor.
Q: Who prepares the consent form that you use in the clinical trial?
R:...um.. consent document.....the last time I heard about consent some of the coordinators...um, they were translating. To tell the truth they are the ones who prepare the consent. Then we have the site or they call the head nurse who is the overseer of everything at the site. They also have the input. Also the doctors, they have input.
Q:GCP requires that consent form be in a language the participant best understands. Does translating only into Setswana have an impact on understanding the study?
R: The consent is in English then we translate. To me, this is not a problem. Some time ago, many people even those who can't read, they felt like Setswana somehow it's difficult. There are some other words that a difficult to understand. So to me, it important to master even for some who feel they understand English better.
When recruiting, I use Setswana.
You mean in Botswana? Yes....what language, what do you mean by language? Yah, that other side of Botswana I think it will be a problem.
Q:. On average how many pages is your consent document?
Participant: (sighs).....um....Sometimes they can take at least 30 pages. You mean the consent. It's like a book, so they have to read everywhere so that the participant can understand, so they can be able to make that decision, so they read everywhere. So sometimes it's long. Sometimes it can take 30 minutes. They also ask questions.
Q: Which methods have you tried for the consenting process?
Participant: Us, we use just use flyers. This is what we have (shows a poster on the wall). Also patient contact

Q: Which guidelines do you use to guide the consenting process?
R:. I go to these places because we look for these pregnant women. We, I have identified the days when the doctor comes to give ARVs, so I target those days.
Q: GCP guidelines recommend that both the informed consent discussion and the informed consent form should include the twenty elements. Do your consent forms include all these elements and are you able to go through all these during your sessions?
R: Yes, we follow them
Q. What challenges do you encounter from the **ethics committees** that review your consent form if applicable?

Information disclosure
Q: What recruitment methods do you use to let parents/guardians know about this study?
R: Us, we use just use flyers or this is what we have (shows a poster on the wall). Also patient contact
Q: Who talks to the parents/guardians/children about the clinical trial when they came to the hospital/clinic?
R: At the clinic, it's the recruiter.
Q: In what language are the discussions of the information about the study held?
R: Setswana
Q: How is the information about the clinical trial communicated?
R: By talking to the patient.
Q: From your experience, which of the following elements of the consent form do find difficult to communicate to participants and why?
R: Um....for now I haven't found any difficult part because normally, for those living with HIV, the babies who are born by HIV mothers according to the Ministry of Health and Government of Botswana, all babies are going to be tested whether HIV positive or not.....so we test babies, after knowing those results, we take it from there because we are more focused on positive babies.
Q: How would you rate the amount of information provided to the parents/guardians in the studies you have conducted?
R: um.....to me, sometimes it feels like it's too much and sometimes I feel like we are just confusing her. We are telling the mother, that time when you came for registration, the baby is going to be tested.....then we start telling them, we are from Harvard, this and that..... We are the ones who weigh them because there is so much shortage at the clinics, we are the ones who do bloods because there is so much shortage and so many things. We do everything, wherever, we help pull out the files in order to identify them. We help the doctors.....by helping the doctor we can identify the patients. You do everything that is going to get the patients, sitting is not going to help.
Q: Concerning risks when disclosing to participants, would you prefer to.....
R: Um...we have forms. Normally if someone has waited for a long time, I just make an appointment then we meet another time. So we have booking forms. Each one of us has these forms
Q: How would rate the complexity of the technical language used in the consent document and how do enhance understanding of such language?
Participant: No, I think most of the time its fine.

Understanding
Q: How do majority of participants initially react to experimentation on their children? Do the parents understand the difference between research and treatment?
R: Um...one thing that I have noticed, there was so much shortage so sometimes if I come and say there is this study, babies being tested what, what, what, to them it's always like when should I come, it's not a struggle because they also believe babies have to be tested. There are so many people, somehow the main focus is to attend to all of those especially with ARVs because it's like ARVs is the main focus.
Q: Do the parents/guardians ask any questions?
R: They, for now I haven't had any questions because to them we are going to help them by testing the babies and after the results that's when we will talk about the study.
Q: If yes what are usually their main concerns?
Participant: None
Q: If no questions are asked do you find out why?
R For now, they just want to test their babies. So we don't force them.
Q: What do you think is the most common reason for the parents/guardians not asking questions?
R: Or for some after we test the baby we explain everything about the study, then they say no, we don't want to participate in the study, they just wanted the baby to be tested. We don't push them. It's not like they don't understand.
Q: According to your observation, what is usually the general emotional state of the parents/guardians during the consenting process?
R: Not answered
Q: How do you test the level of understanding of the information provided about the trial?
R: Because, normally it's not us who do the administration of the consent, we do it but that one, we normally push it to the midwife or nurse. We don't want to make it like we coerce or bribe them to participate. So normally we just ask them....
Q: How would you rate the level of attentiveness of the parent/guardian during the consent process?
R: um.....the illiterate ones look bored so we keep on asking them do you understand or do you understand when you were told about PMTCT, do you understand why you were given those medications, so we can check if they understand.
Q: How much time do you think is appropriate for the informed consent process to enable understanding?
R: Most of the time because people don't understand, they have to come again. Then we have to keep asking why were you given those drugs, when is the baby due, and what did they say about the baby. Those are the questions we ask them.

Decision Making
Q: Approximately how much time do you think should be given to the parents/guardians to make a decision?
R: For me, for me....I think 2 days to a week looking at some of them who have HIV positive babies for them to calm down for a while, for them to go for counselling to offer them that because for some of them we do offer that.
Q: Is it important to you to always consult the two parents or the **relative(s)** of the participants even if the person who has brought the child to the clinic agrees to participate?
R: the partners, their mothers because some will say, I have to go talk to my mother then I'll come back. Then I'll call them mid-week to check them.
Q: Who do you mainly consult before enrolment of the child into the study?
R: The mother.
Q: Does the involvement of a participant's **spouse or relative(s) influence** the **time** necessary to obtain informed consent?
R: It delays the consent process but there's nothing you can do because for me, if someone says I have to consult that one I don't doubt it, I just let them. Another one, she said she had to talk to her mother and father because it was a step child but I had to push her a bit because of the time she was to take the medication so she could take the medications on time. We did the bloods, everything, even when they don't quality for our study.

Q: How do the parents/guardians indicate their agreement for their child to participate?
R: They sign the consent form.
Q: How do the parent(s)/guardian(s) react to being asked to sign a consent form?
R: They are happy because most of the time parents want good health for my child, to them we can help them so even if the child is in the study its fine.
Q: How do you facilitate the decision-making process?
R: um...it's mainly the study nurse. For us, what I can say about recruitment is yes, I feel the way I understand the work, for people to come here it's because of us. As I said, I did counselling and stuff, even in social work, sort of counselling and communication, most of us we did counselling courses I feel we are the root of everything because we recruit and sometimes after some time they disappear then we wander what happened. So in research recruitment has the big part.
Q: From your interaction can you identify any social, cultural, economic or any other factors that you think might influence the parents/guardians to agree to enrol their children in the study?
R: To me, I feel like with working in the with clinic people who are I don't know who are always critical and to them when they see people who are doing research, they see people who are not interested in health but are interested in making money out of them. I think it's going down, because when we go to the clinic today they can start calling me, so that can help. And then the other thing, most of our patients, I don't know if they are poor or what because telling a patient you have to come to the clinic for this and that, you have to call a driver to go collect that person and bring the person to the clinic, it's difficult. Like in Gaborone, most of the people are renting, so we get their contacts then they change and they lose their cell phones and that is a challenge. Or you try to call the partner and the phone is off.
Q: Describe any measures you put in place to ensure that participants and the consenting parents/guardians do not feel coerced or pressured to join the study as well as continued consent during the study.
R: To tell the truth, I know that as recruiters we are the first people to meet so our aim is to protect the people. Our aim is if a participant is coming and they have social problems we get professional counselling for them and take them to professional counselling. Not only that, when they come we give them counselling even after they decide they are not participating to help them. Even in our diaries, you will see a name of somebody who needs to go for counselling.
Q: How do you ensure continued consent during the study?
R: When they come for appointments, we keep asking them about the study.
Q: Please give any recommendations that would help in enhancing the informed consent process for child participation in clinical Trials.
R: Yah...I have to say, I don't remember anything or adding anything on what is done in the process.
I know that for us, sometimes there will be like some decisions have been made about participants and you get to hear. So I am like it's us who get these patients why can't we be involved in decision making or consulted for guidance. But sometimes, we are the ones who call people, so when we see them suffering, it will hit back on us.
Q: How do you involve members of the community to recruit participants?
R: One thing that I feel like we, I feel like many people do not understand what we do when the child comes. Nurses or doctors, I feel like especially like this other time when I was asking one of the doctors, I was asking do you think it's important for people to know because when you go to the communities, they don't know anything about research. Even, with people we make sure that they understand what we do.

That's the end of the interview. Thank you so much for participating in this study.

End time: 16.09 hrs

IN-DEPTH INTERVIEW: 6

Date	18.03.2011
Interview No	0006
Start time	15.00hrs
Gender	Female
Age	40-50
Discussion Language	English
Research Assistant	Ms. Faith Mompati-Ketshogile
Education	

The research assistant began the interview by making introductions and going through the consent form and have it signed by the respondent. Respondent characteristics were not included in the write up for anonymity and confidentiality purposes.

Q: Have you had any specialized training in ethics of conducting clinical trials research? What on-going training on protection of human subjects are you receiving?
R: We do our GCP then do what do they call it.....clinical ethics I think.....but its online, most of the time when you start with Harvard you have to undergo that training before you can even start handling the patients every 2 years. We also have to do the training. You have to renew every 2 years and if you don't renew it usually goes with your contract. Sometimes they cannot renew the training then even your contract may not be renewed.
Q: Tell me about purpose of the clinical trial you are involved in.
R: Most of them that I am involved now in are drug interventions.
Q: Explain your role in clinical trial have you been involved in?
R: No, not necessarily an administrator. I do administration especially concerning the study related things. Maybe dealing with IRBs, making submissions to the IRBs but I do help the nurses in recruitment. Usually there are recruitment officers who go to sites and bring in the patient. But you find when the patient comes here, they come not everything was explained. They are just told, "there is a study at Harvard. It looks like you can qualify for that study, are you interested to join in?" So sometimes when they have a lot of patients I help with that because I am interested in working with patients.
Q: , Briefly carry me through the consenting process.
R: Ok usually what happens; these patients will be recruited and when they come, they will be divided according to where they go because we have different studies at Harvard so it depends whether the patient was recruited for a clinical or non-clinical trial. So you find when the patient comes we take them to the waiting room.....and serve them on first come first serve basis. Then you will bring the patient here and the first thing when they come is to introduce yourself to her, then from there you have to make her know where she is. Because people will just be saying, I'm going to the hospital or clinic; she doesn't even know what we do. So you have to explain that you have come to this clinic to enrol your child in a research study for HIV. So after that, is when you ask the patient is she interested to hear more about the study.
Q: What was the risk category of the clinical trial you recently conducted?
R: For the patient or for us?..... Oh for the patient!.....No I wouldn't say they are at risk because, for the studies I have worked with, they have helped a lot of patients because you will find you are dealing with HIV positive patients and with all those interventions that the studies are doing, at the end of the day, they go back to negative..... Because if I look at the studies I have worked on, at the end of the day, you will find that out of 100 kids that were born to HIV positive mothers only 15 were HIV positive and the rest were HIV negative, and even the patients are very happy about this. Regarding risk, I would say the studies had very minimal, yes very minimal risk! Mostly, you may find that out of 100 patients we see, you can only have 2 patients who reacted to the study. Most of them are doing very well.
Q: Are clinicians involved in the consenting process?
R: Nurses, mostly you may find that for doctors, most of them are not Batswana. Most of the doctors are foreigners so; most of the consent process is done by nurses.
Q: Do you think this is a problem?
R: I don't think that is a problem. No, I think its fine because, during the consultation even those doctors who are foreigners, most of them have learnt Setswana and they are able to greet the patients even to ask the patient, do you understand what you are going to do, do you know the study that you are involved in.....in the consultation, the nurse is always there to help.
Q: On average, what generally is the highest level of education attained by the majority of the parents/guardian who give consent for their children's participation in clinical trials?
R: I think it depends where you are working. The education level of the patients varies in the rural areas but when you come into Gaborone, Gaborone is a city, most of the patients they have their university degree, and they have a diploma. Most of them have gone up to form 5 but when you get to rural areas, you find that most patients are form 3 or standard 7. So it depends on site location.
Q: On average, what is the average age of the parents/guardians whom you have obtained consent from for their children's participation in clinical research?
R: Yes, I think there is every age because I think with our studies; we start from 18 years and above but you mostly find people in their 30s.
Q: On average how many of your participants have previous experience with research on HIV disease?
R: Mmmm... Not a lot of them, but I realise that some patients already knew about research from previous studies It's like they had the decision of having another child because they knew the research centre was going to help them. Laughter!!!!
Q: What generally is social economic status of the majority of the parents/guardians who participate in your studies?
R: Participant: I think most of them they are lower and middle status. I have realised that most of them with high income don't come to the clinic; a lot of them prefer to go to the private doctors.
Q: Who prepares the consent form that you use in the clinical trial?
R: What happens usually with our studies when the sponsor, it's like its prepared by the sponsor, so when it comes, as study coordinators we have to customise it to our standards, to Botswana standards, so we have our standard of care....culturally. Then from there, they come in English, so they are supposed to be translated into Setswana. I translate from Setswana to English then back to Setswana... back translation so I am one of the people who have been highly

involved with the translation even for other studies not necessarily for our studies.
Q: GCP requires that consent form be in a language the participant best understands. Does translating only into Setswana have an impact on understanding the study?
R: I think it would only be a problem if the studies were being conducted in those areas but those people with different languages like Kalanga, Sesame...when they are in Gaborone most of the time they come to work so they don't have a problem with it, Setswana some they even prefer English consent. It's up to the choice of the patient what language to use because usually we have both consents. If she wants to use Setswana its Setswana, if she wants English it's not a problem but majority would love to use Setswana because it's easier when you are talking to them because out of 100 only 1 patient will use the English consent.
Q: On average how many pages is your consent document?
R: On average 20 pages, I know the biggest one was about 22 pages but you will find that sometimes it's up to 22 pages because it involves pages of the intervention which at the end of the day you can take and extract from that and put it aside and wait for the patient to consent and after they have consented that you can tell them about it. They can be short but when you translate to Setswana they will go up to 25 pages.
Q: Which methods have you tried for the consenting process?
R: Most of the intervention studies that we have done before we used to have pictures whereby the mother can see which drug they will be giving the baby. I think they are very good, it made the patient to understand better than when you just explain to them. Those pictures were even in colour form. Mostly, I prefer to use the short forms to describe the long terms used for drugs to make it easier for them to understand.
Q: Which guidelines do you use to guide the consenting process?
R: Yah, usually we use the Botswana Drug Guide, the ARV guidelines for Botswana, we also use them to refer for and to make comparisons because we have to at the same time keep to the standard of Botswana guidelines. We use the same Botswana Guidelines because we are not supposed to give the patient something that when she leaves she is not able to get from the Government. Usually, we make sure that our standard of care goes in line with the standard of care they can get anywhere in Botswana.
Q: Good Clinical Practice (GCP) guidelines recommend that both the informed consent discussion and the informed consent form should include the twenty elements. Do your consent forms include all these elements and are you able to go through all these during your sessions?

R: Yes, we follow them.

Information disclosure
Q: What recruitment methods do you use to let parents/guardians know about this study?
R: Usually we have posters, we have flyers. Our recruiters they go to the public clinics every morning and they talk to the eligible patients. Sometimes we even go to areas outside of Gaborone
Q: Who talks to the parents/guardians/children about the clinical trial when they came to the hospital/clinic?
R: During recruitment, they are being recruited by our recruitment officers from the clinics, then they come to our study clinic then that's when they meet the nurse.
Q: In what language are the discussions of the information about the study held?
R: mainly Setswana
Q: How is the information about the clinical trial communicated?
R: By talking to the patient.
Q: From your experience, which of the following elements of the consent form do find difficult to communicate to participants and why?
R: Ah I think.....Mostly, the consent form is something that is very straightforward. The other thing is it depends, you will find with me, I have an experience, I have worked with research for quite some time, so I'm able to address different patients and I think the best thing is to find out how much your patient can understand so you can use it to talk to her. It's like you break it down into a simple language. There are some patients who are slow learners, you have to observe that, there are some patients who are very shy even to ask you questions, when they don't even understand. So, most the time, when I do it, usually I assess my patient about understanding to understand what kind of patient. Usually I make sure I recap. I read a paragraph then I recap with her then give her time to ask questions.
Q: How would you rate the amount of information provided to the parents/guardians in the studies you have conducted?
Participant: Yah, you can say they have too much information. When you think someone is here and you are reading a 20 page document, you can't really expect her to understand all that depending on the patient, it's too much information. Usually our exercise is that usually after the patient has consented you are supposed to give them a copy. I always encourage them to go and read at home, at least page to page, so at least when she continues to come for her visits, she will have some questions that she would like to ask. And every time you want to be sure that the patient has understood the consent process. So every time the patient comes for every visit, you talk to her, remind her about our study, find out if she still remembers the drugs that are going to be used, it's very important.
Q: Concerning risks when disclosing to participants, would you prefer to.....
R: Mostly, I will give the patients all the information but at the end of the day having the experience of having worked with patients, you always tell them the truth because sometimes you may not experience the side effects but I have to tell you this so you know, because it doesn't mean that everything I have told is going to happen to you. Also you have to tell the patient.....some they may have a headache some have never experienced a headache. Some may have dreams which they do not normally have but you have to tell the patient exactly everything so that the patient makes an informed decision, she understands the risks she is going through when she takes part in the study.
Q: How would rate the complexity of the technical language used in the consent document and how do enhance understanding of such language?
R: I wouldn't say that because when you come to drugs, how you can break it down for the patient to understand. Yah, you have to try to speak the language that the patient will understand....you have to really try to make sure the patient understands
.
Understanding
Q: How do you test the level of understanding of the information provided about the trial?
R: Usually with our studies we have a document called level of understanding. It's just a paper I think it has about 10 to 15 questions. Those questions are like a summary to the whole consent form. So at the end of the day, you talk to those patients if she doesn't understand sometimes we postpone the process or the patient might say we give her the consent and she goes and reads it again at home and tomorrow we make an appointment and she comes again then we test, we ask her all those questions again so you can assess the level of how she has understood the whole process. Then usually we make a score. If somebody has

scores 10 out of 15 we feel that she has understood then we can make a recap on those that she was not clear on. Usually the patient.....it depends on the study, if she gets 7 then maybe you have to go over the process again.

Q: How would you rate the level of attentiveness of the parent/guardian during the consent process?

R: When you deal with pregnant mothers, sometimes it's a bit difficult because you find that this patient was in the clinic the whole morning, then our recruiter maybe finds her around 11 then she comes here to the site, so most of the time when it's like that, we book them for the other day and usually we do ask. We are having a consent form which is about 20 pages and we are going to be reading, explaining and asking questions, so do you think you make it because sometimes it take an hour so we make our patient understand that. I have found that dealing with pregnant mothers it's a bit sensitive unlike dealing with patients who are just.

Decision Making

Q: Approximately how much time do you think should be given to the parents/guardians to make a decision?

R: Sometimes I think it depends on the patient, some patients will say, ok, I have understood that, but since I'm supposed to consult my husband, let me go talk to him. But usually we encourage them to bring those partners so we can do explanation to both of them. You will find if you bring them as partners, she knows the other partner, I mean they have been partners for some time so he knows the level of understanding of that wife of hers. So you find that when the other partner is there, when she doesn't get it, then it's better. So usually we encourage them to bring partners.

Q: How do the parent(s)/guardian(s) react to being asked to sign a consent form?

R: Most of the time you will find they are comfortable with signing the consent document because most of the time if we are suspicious, sometimes we even involve a different counsellor. You might try to talk to that patient, and it's like the patient is not comfortable with you and the patient doesn't really, her level of understanding is low so sometimes you may find that another trial staff can do a better job then you refer the parent too that person. Young people would prefer somebody younger. I think it depends....

Q: How do you facilitate the decision-making process?

R: I think once the patient has understood whatever you have explained; it should be out of interest. Even the patient, she also has to if she thinks it will benefit her, I think it's out of benefit because once you have explained everything to her she has to understand if it will benefit her of what. If she knows that it's going to benefit her, it makes it easier to make the decision.

Q: From your interaction can you identify any social, cultural, economic or any other factors that you think might influence the parents/guardians to agree to enrol their children in the study?

R: I think a lot of them. Sometimes you find that the patient stays in town and she is very interested in participating in the study but when she thinks she will be coming from far, jumping on the combi to the station then from the station to the clinic they may feel that it will be too far and she will not be having money for transport. So most of the time she will prefer not to be in the study because she can access help from nearby centers. Maybe then for us, usually we do some compensation for transport money to help them.

Q: Describe any measures you put in place to ensure that participants and the consenting parents/guardians do not feel coerced or pressured to join the study as well as continued consent during the study.

R Exactly, because sometimes....I mean with HIV/AIDS, it's like a lot of people they know that if somebody is health worker and comes to you and says this can you help, a lot of them develop trust. The doctor cannot say this if this can't help me. Most of the time we don't want to talk about the compensation, it usually comes at last and we even come to a point whereby you ask a patient, do you think you will manage to come to the clinic with all the visits because it's like you are going to have 15 visits in this study then she says yes I think I can manage because I will get the money from somewhere because I need these visits. I will see what to do. Usually that's what they do then you can see that she knows that this can help her, how she's going to get to the place, it doesn't matter. So the compensation usually it comes at last because we don't want to use it as coercion. We don't want to tell them you will get P30 in the consent process because sometimes you may find that the patient just consents because she needs to be helped but she has not understood the consent.

Q: How do you ensure continued consent during the study?

R: So every time she comes, we have to make a recap and ask her do you still understand why you are in this study, do you remember the drugs that are going to be used, do you remember the side effects of the drugs. It has to be an ongoing process throughout the study

Q: Please give any recommendations that would help in enhancing the informed consent process for child participation in clinical Trials.

R: The other thing maybe what we can do is the consent shouldn't be too long maybe because if it's too long it makes the patient to be here for too long, I think that is the thing we need to do. I think it needs to be a bit short and it becomes brief and to the point, it's like at the end of the day, the patient doesn't get all because it's a summary but don't worry that's it's a summary, we elaborate everything.

This is the end of our interview. Thank you for participating in this study.

End time: 15.35hrs

IN-DEPTH INTERVIEW: 7

Date	04.04.2011
Interview No	0007
Start time	15.25hrs
Gender	Female
Age	30-40
Discussion Language	English
Research Assistant	Ms. Faith Mompati-Ketshogile

The research assistant began the interview by making introductions and going through the consent form and have it signed by the respondent. Respondent characteristics were not included in the write up for anonymity and confidentiality purposes.

Q: Have you had any specialized training in ethics of conducting clinical trials research?
R: Yes, although it was not a specialization.
Q: Do you have any specializations in pediatrics?
R: Yes I did pediatric courses at school. I also have 4 years of experience in conducting studies involving parents and children
Q. Which Phase of clinical trial have you been involved in?
R: Mostly Phase III and IV
Q: What was the risk category of the clinical trial you recently conducted?
Participant: Mostly minimal but one study that involved drug intervention was greater than minimal risk.
Q: On average, what generally is the highest level of education attained by the majority of the parents/guardian who give consent for their children's participation in clinical trials?
R: Mostly Primary and Junior school we have a few tertiary or those who dropped out of school early. I prefer those without too much education because they will follow what they are told
Q: On average, what is the average age of the parents/guardians whom you have obtained consent from for their children's participation in clinical research?
R: Most parents are 21 years and above because of the age of consent but there are also a lot of grandparents to consent for minors
Q: On average how many of your participants have previous experience with research on HIV disease?
Q: What generally is social economic status of the majority of the parents/guardians who participate in your studies? Generally low
R: Very few especially those who have been in studies as pregnant women and they enrol their children in studies.
Q: How do you rate the importance of prior of knowledge of a research investigator about Botswana culture, values and beliefs before the start of the study?
R: Promotes understanding ways of respecting participants for example, those who say must go back and consult-it is usually an indirect way of refusal but some come with their minds made up. Knowledge of the local language is also important for understanding.
Q: Do you think this knowledge plays any role in the success or failure of a consenting process?

R: I think you cannot take out the culture; we go through the Kgotla before. On one study I was asked whether I have talked to the Kgosi before. I have had an experience where they admit that they have taken traditional medicines. Inhalations but we respect their culture we can stop them. It is a problem to ask the mother and father to join because a lot of women are single mothers even those who have are not so much involve come to drop them. Once they say they want to consult it is an indirect way of refusing although a few agree need for education to involve partners.
R: The forms are prepared by the research team, use the format from the sponsor but contextualize to the culture of Botswana setting especially for Multi-center studies. The Principal Investigators consult with the research team and study coordinators and senior nurses help.
Q: On average how many pages is your consent document?
R: Usually long but nurses are able to summarize the information from lengthy forms to about six pages, a page sometimes. Although the forms are long nurses with experience know how to pick important issues
Q: Which research guidelines are you familiar with regarding the protection of research participants and how helpful they are to the consenting process? GCP guidelines recommend that both the informed consent discussion and the informed consent form should include the twenty elements. Do your consent forms include all these elements and are you able to go through all these during your sessions?
R: We all do Good Clinical Trial Practice training so am familiar with GCP guidelines and refer to these documents. All of us are trained in GCP because it is a requirement by the institution that everyone is trained
Q: GCP guidelines recommend that both the informed consent discussion and the informed consent form should include the twenty elements. Do your consent forms include all these elements and are you able to go through all these during your sessions?
What challenges do you encounter from the **ethics committees** that review your consent form if applicable?

R: Uh! I would not say I have encountered many problems. At the Ethics committee I prefer submitting my application to a particular person other than the registry to avoid losses. There are also delays, we asked to do lots of corrections not to pay the participants much but only for compensating transport which is not much compared to what participants in other countries pay.
Q: What challenges do you encounter from the **sponsors** regarding the requirements for preparation of the informed consent document for the clinical trial if applicable?
R: We are not involved with sponsors
Information disclosure
Q: What recruitment methods do you use to let parents/guardians know about this study?
R: We hardly use the radio, but we use mainly posters put at the clinics. We also use the patient meetings, wards antenatal clinics in the rural areas. A few patients come from private clinics
Q: Who talks to the parents/guardians/children about the clinical trial when they came to the hospital/clinic?
R: Recruiters and nurses. The recruiters go with the nurses for better interaction. We also get self-referrals who have heard about the study from the community. Some parents call to inquire about the study after they have heard about the benefits.

Q: In what language are the discussions of the information about the study held?
R: Mainly the local official language Setswana, but a few prefer English.
Q: From your experience, which of the following elements of the consent form do find difficult to communicate to participants and why?
R: The procedures and risks can be a challenge to explain because of the scientific terms. Also concepts like randomization.
Q: How would you rate the amount of information provided to the parents/guardians in the studies you have conducted?
R: The information is usually a lot because of the length of the consent forms and the short time one to go through the form.
Q: Do you consider all the information relevant for the participant to make an autonomous decision?
R: Yes but for the level of the participant some of the information might not be relevant especially the medical explanations and details of treatment and laboratory tests.
Q: How would rate the complexity of the technical language used in the consent document and how do enhance understanding of such language?
Understanding
Q: How do majority of participants initially react to experimentation on their children?
R: You find that initially some are very anxious because of the nature of illness of their children but as we explain some of the things they become calm and with time some even become happy and do not look as hopeless as the time they came.
Q: Do the parents understand the difference between research and treatment?
R: Sh! .. we try to explain but it is difficult to tell for many of them. To me it seems like they think they have come for their child's treatment. But we emphasize this a lot during the consenting process.
Q: Do the parents/guardians ask any questions?
R: Not that much especially those with low education. I feel they still have that mentality that the health professional is always right. But some do especially about the safety of their child.
Q: If yes what are usually their main concerns?
R: They mainly want to know how experimenting on the child might affect the child physically, whether the child will get better, mainly child safety issues.
Q: If no questions are asked do you find out why?
R: Really I have never found out why, but I think it might be a cultural thing where they do not want to look like they are questioning. I t might also be fear of the unknown. Like they would rather not know what lies ahead.
Q: What do you think is the most common reason for the parents/guardians not asking questions?
R: I think it is the culture. The power issue!... considering that the doctor or nurse is a respected member of the community and the assumption that they know what is best for the child.
Q: How do you test the level of understanding of the information provided about the trial?
R: Verbally by using a test of understanding quiz. Sometimes even asking just general questions not really related to the study just to change the topic a little during the consenting process.
Q: How would you rate the level of attentiveness of the parent/guardian during the consent process?
R: Ah! It's is difficult to judge because some just stare at you as you talk or read to them which might look like they are paying attention. Some would be very tired after a long day you can really see they are more worried about how they will get home
Q: How much time do you think is appropriate for the informed consent process to enable understanding?
R: It depends on how understanding is being judged. If the parent does not seem to understand we can even ask them to come another time after having someone read and explain to them.
Decision Making
Q: Is it important to you to always consult the two parents or the **relative(s)** of the participants even if the person who has brought the child to the clinic agrees to participate?
R: It would be good for the two parents to be consulted but we meet a lot of young single mothers whose spouses are not so much involved in the care of the child. It is always good to get the blessing and to have the support of the relatives because they all take care of the child and they show concern. Even the culture encourages this. Also in case anything goes wrong, the blame is not only shifted to the institution.
Q: Do all the parents insist on consulting with the spouse or family before making a decision?
R: Yes a lot of them do even after they have agreed at the clinic they will go back and talk to their families. Sometimes you find that they will not come for the next appointment and when you phone them they say the relatives did not approve. However those whose spouses are not aware of the status of the parent and child are hesitant to consult the spouse.
Q: Who do you mainly consult before enrolment of the child into the study?
R: Mostly the grandmothers to the child or anyone the parent can suggest.
Q: Does the involvement of a participant's **spouse or relative(s) influence** the **time** necessary to obtain informed consent?
R: Ya!.. it really makes a difference because it is like a secret that is coming out and the parent is relieved that someone knows about the situation and will give support. It also improves the level of involvement in the research and adherence to the instructions.
Q. How do the parent(s)/guardian(s) react to being asked to sign a consent form?
R: Again as I said, they do not seem to mind especially before they get a good understanding of the difference between research and treatment. Signing means they will get help. Another thing is the culture of not questioning.
Q: How do you facilitate the decision-making process?
R: Emphasizing that the participation is voluntary and telling the truth about the uncertainties of the study so the parent understands the benefits and risks. Allowing as much time as required for someone to decide not to rush them.
Q: From your interaction can you identify any social, cultural, economic or any other factors that you think might influence the parents/guardians to agree to enrol their children in the study?
R: The most important influence is the culture and mentality of trust about health workers that they are always right. Poverty might also play a part for some parents knowing that they can only get help from research. Also the good care and compassion shown to the parents.
Q: Describe any measures you put in place to ensure that participant and the consenting parents/guardians do not feel coerced or pressured to join the study as well as continued consent during the study.
R: I assure the parents from the beginning that enrolling the child is voluntary. I also do not mention that there will be a compensation for travel at the beginning.
Q:Please give any recommendations that would help in enhancing the informed consent process for child participation in clinical Trials.

R: There is need to shorten the forms and simplify them. More education to the public about the importance of research and clear some of the misconceptions.
Thank you that is the end of our interview.

That is the end of our interview. Thank you for participating in this study.

End time: 17.11hrs