UNDERSTANDING THE INFORMED CONSENT PROCESS IN HIV CLINICAL TRIALS IN UGANDA: A CASE STUDY

Ву

AGNES NANFUKA SSALI

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Abstract

The regulatory guidelines on obtaining informed consent require that all protocols be reviewed by an ethics review committee; in addition study information must be presented to volunteers by the research teams in simple and understandable language, to ensure they are able to give informed consent for their participation. Despite the innovative methods that have been developed over the years to improve informed consent, the informed consent process is still a difficult subject and not fully understood particularly in developing countries.

Objective: In this study I sought to understand and evaluate the informed consent process as perceived by the different actors in two HIV clinical trials and how their understandings and interpretation of the process are reflected in standardized informed consent guidelines.

Methodology: The actors included: members of the ethics review committee, senior researchers, the field research teams, the community advisory board members and the research volunteers. Data were collected using semi-structured interview guides and focus group discussion guides and unstructured observation and document review.

Results: A total of sixty three respondents took part in this study. I found that although the informed consent process is emphasised in research ethics guidelines and clinical research protocols which are approved by the ethics research committees before they are implemented, how the process is perceived and interpreted by the actors is very varied. The different actors' beliefs, values, gender, trust, power differentials and decision making all contribute to the negotiations that take place during the informed consent process. The standardised informed consent guidelines are a useful tool to manage the bureaucracy of conducting research in order to protect research volunteers from any form of harm and allow for individual autonomy; it is however the relationships and interactions of the different actors which are built over time during the research process that in practice lead to a meaningful informed consent process as each actor interprets and understands the process within their own context and experience.

Abbreviations

ART	Antiretroviral therapy		
CD4	Cluster of Differentiation		
CIOMS	Council of the International Organisations of Medical Science		
DEV	School of International Development		
GCP	Good Clinical Practice		
HIV	Human immunodeficiency Virus		
AIDS	Acquired immunodeficiency Syndrome		
IAVI	International AIDS Vaccine Initiative		
ICD	Informed consent document		
ICH/GCP	The International Conference on Harmonization of Technical		
	requirements of registration of Pharmaceutical for Human		
	Use /Good Clinical Practice		
IRB	Institutional Review Board		
IRC	Institutional Review Committees		
PIS	Participant Information sheet		
MRC	Medical Research Council		
NDA	National Drug Authority		
REC	Research Ethics Committees		
SEC	Science and Ethics Committee		
SOPs	Standard Operating Procedures		
TASO	The AIDs Support Organisation		
UBOS	Ugandan Bureau of Statistics		
UEA	University of East Anglia		
UNAIDS	United Nations programme on HIV/AIDS		
UNCST	Uganda National Council for Science and Technology		
UNESCO	United Nations Educational Scientific and Cultural		
	Organisation		
UVRI	Uganda Virus Research Institute		
WHO	World Health Organisation		
WMAs' Declaration of Helsinki	World Medical Association		

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DEDICATION

I dedicate this thesis to my beloved husband and friend Fred, and to my children Grace, Gideon, Joshua and Jonathan. God bless you.

Chapter 1 Introduction

Introduction

The term 'informed consent' can be interpreted differently in clinical, legal and ethical settings, and as Berg et al., (2001) state, may be a source of conflict between disciplines. This research aims to contribute to the discussion on informed consent by seeking to understand it from the perspective of the actors involved in HIV (Human immunodeficiency Virus) clinical trials in Uganda, a developing country. I approach my study from an interpretive/constructivist research perspective where I allow my respondents to construct their own experiences and interpretation of the informed consent process (Denzin and Lincoln, 1994; Green and Browne, 2005). Studying what is meaningful in the informed consent process for the different actors involved in HIV clinical trials in Uganda enables me to interpret the process in this context.

1.1 What is the informed consent process?

'Consent' refers to agreement to something. Such an agreement involves at least two people, one of whom wants the other to do something to which he or she must agree. The elements of informed consent include the researcher's provision of information about the purpose, risks, benefits, alternatives and requirements of the study and the recruit's understanding of this information, the recruit's voluntary decision to take part free of coercion, and his or her authorization, which is usually given as a signature on a written document (Beauchamp and Childress, 1994; Emanuel et al., 2000).

Informed consent refers to rules that should guide physicians and other health practitioners about how they interact with their patients or research subjects. If they deviate from these they are likely to face a penalty, particularly if this affects a patient or a subjects' autonomy (Berg et al., 2001). Informed consent, as a principle used in conducting research with human subjects, became prominent after the World War Two because of the atrocities inflicted on research subjects, which included the 'deliberate inoculation of camp inmates and prisoners with typhus bacilli to propagate strains of the bacteria ... exposure to cold water and low air pressure to observe events that would lead to their deaths' (Faden & Beauchamp, 1986; Appelbaum et al., 1987) caused enormous problems. One of the better-known examples of studies conducted without the participants' consent is the Tuskegee syphilis experimentation from 1932 to 1972 in which men with advanced syphilis were denied treatment by researchers who knew of their condition (Emanuel et al., 2008).¹ Because of this and many other studies that did not consider consent of research subjects important, guidelines were enacted to provide a standard law on human experimentation (Annas and Grodin, 1992).

¹ For further examples see Annas and Grodin, 1992; Faden et al., 1986; Brody, 1998.

The first code to be set up to protect research subjects emphasized the need for informed consent, meaning that a volunteer must be given full information about the study concerned and must have the capacity to understand and to agree to participate in it without any coercion and the right to withdraw from it at any time (Doyal and Tobias, 2001). These are the major aspects underpinning informed consent, which applies to all research conducted in all settings.

Informed consent is one of the principles of research ethics that seek to prevent the possible manipulation of research subjects while conducting research. Although systematic research is conducted with the aim of finding new knowledge, filling knowledge gaps or learning how to do things better, bio-ethicists argue that all research must be conducted with respect for the volunteers as a primary objective. In the past research subjects could give their informed consent verbally, and this was the practice for many anthropological and social science studies, but this stance has clearly been changed according to several sets of research ethics regulations. One example of such change is that research studying the impact of HIV and AIDS on rural households in Uganda (Seeley et al., 2008) only required verbal consent in the early 1990s while currently all consent must be in writing to comply with research ethics regulations, unless the ethics committee waives this requirement (UNCST, 2007).

In this thesis, 'informed consent' refers to giving full information about what is involved in conducting an HIV clinical trial and ensuring that the person receiving the information has the capacity to make a decision and voluntarily consents to take part when they are satisfied that they have understood the information (Beauchamp and Childress, 1994; Delany, 2005; Eyler and Jeste, 2006). The 'informed consent process' in this thesis refers to all elements of the process, which include mobilisation for the initial recruitment of volunteers, providing volunteers with information about the study, a review by the ethics committee of the informed consent documents and the signing of documents by a member of the research team with each research volunteer, and includes the various interactions that take place between the key actors over the course of a clinical trial. I view informed consent as more than securing a signature: it requires an investment of the researcher's time (Buccini, 2009). My ontological stance is that 'informed consent' is socially constructed (Mason, 2007). Meanings will be negotiated during the research process by all the actors within particular contexts, and each actor must be viewed within their social and institutional context because they will have different roles and contributions to make to the process as they negotiate around those meanings.

In this thesis I use the term 'volunteers' rather than 'study subjects' for the participants in the clinical trials because they volunteered to be part of the trial. The term 'subject' suggests that the participants are objects with a position subordinate to that of the researcher. This is

important in my approach because the volunteers actively contribute to my understanding of the informed consent process.

My interest in researching this topic emerged as a result of over 10 years of research as a social scientist studying behavioural issues among HIV/AIDS (Acquired immunodeficiency Syndrome) infected and uninfected adults in Uganda. I first became interested when I observed researchers providing volunteers with study information and then assessing their comprehension of the study. This was done prior to enrolling them and I noticed that it was a rigorous process for both the research team and the volunteers, with both usually looking tired at the end of the discussion. A few months into a trial, however, I would hear disappointed remarks from the research team about a volunteer who had not turned up for the scheduled visit or one who had come in pregnant despite avoiding pregnancy being a key message in the information provided to the volunteers.

After a few years of experience in a clinical trial I had the opportunity to sit on the Science and Ethics Committee of the Uganda Virus Research Institute (UVRI) for three years. While on the committee I noticed the tension that sometimes occurred during protocol review meetings about whether a study was worth the procedures it demanded from the volunteers and how the research teams would handle the research risks. I realised that not only were the researchers concerned about how they conducted their studies but also the ethics review committee was concerned about protecting volunteers from any form of social or physical harm.

I started to wonder whether all the actors involved understand informed consent in the same way and what happens in practice as these individuals carry out their roles in the informed consent process. As a social scientist, in the clinical trial I was mainly involved in interviewing volunteers on social behavioural aspects of the trial, but at times I participated in consenting volunteers. It was hard to grasp what the volunteers thought of the experience of signing a consent form and what it meant to them. Some volunteers dropped out of the trials and I wondered what factors in the informed consent process, if any, had led to this. These and other issues about how the research team, volunteers and other actors experienced the informed consent process drove my interest in this topic. This study investigates the actors' perspectives on the process; whether they all share the same understanding of it; and how their understanding and interpretation of informed consent reflects the current standardised guidelines for obtaining informed consent and adds to the existing body of knowledge on understanding it. The first section of this chapter considers the background of informed consent and why it is important in all research involving human subjects. The second section discusses the international guidelines set up to guide the informed consent process in both medical and the clinical research settings and reviews the literature on how these have evolved. The third

section reviews the role of institutional review boards (IRBs) and their contribution to the informed consent process, and why IRBs and research ethics committees (RECs) are necessary. The next section looks at current global trends in HIV and AIDS and the situation in Uganda, where I conducted this study. The fifth section considers critical issues in the informed consent process in clinical trials and is followed by a section describing the two clinical trials on which I conducted my study. In the last section of the chapter I justify the need for this study and present my research questions.

1.2 History of informed consent

The primary goal of informed consent is to protect volunteers' welfare and respect their individual autonomy (Nuffield council of Bioethics, 2002). This involves recognising a person's capacities and perspective on what happens to them during research, including accepting their right to hold certain views, make certain choices and act based on their personal values and beliefs (Faden and Beauchamp, 1986). 'Autonomy' is a challenging concept which can be interpreted differently in different disciplines. Appelbaum et al. (1987: 22) define it as 'personal freedom of action or the right to do as one pleases within certain restrictions'. The principle of autonomy includes respect for others, whether in a medical or a research setting.

Faden and Beauchamp state:

Informed consent is a creature of a broad range of social practices and institutions in the twentieth century. The birth stone of informed consent is about 1957 by both Martin S. Pernick a historian and Jay Katz a psychiatrist. (Faden and Beauchamp, 1986: 55)

Gallin and Ognibene however note that obtaining informed consent and even using written documents to guide the conduct of research have been standard practice for over a hundred years (Gallin and Ognibene, 2007). Selek (2010) dates some form of informed consent in the medical context to about five centuries ago, although at that time it was not a clear intervention as it is today. Selek gives the example of a father who contracted with a surgeon to remove "urinary" stones from his son. He had to agree before a court that he would not sue the doctor if anything went wrong (Selek, 2010).

There are two main theories on the origins of ethics; Kant et al. deontological ethics theory and Mill et al. consequentialist ethics theory (Appelbaum, 1987:19, Wiles et al., 2005). The core issue in deontological theory is the identification and justification of duties that bind an individual, and yet these are seen as independent of the practical concerns that s/he may face. In this theory 'one must always treat another human being as an end and never merely as a means to another end' (Appelbaum, 1987: 19). Deontological theory is concerned with protecting a person's dignity and ability to self-regulate (Delany, 2005). According to this theory

a researcher must never use a research volunteer to meet his (researcher)'s own ends unless the volunteer gains some benefit from participating. Consequentialists, on the other hand, 'hold that the rightness or wrongness of an act is dependent on the consequences of the act' (Appelbaum, 1987: 19). The dominant form of consequentialism is utilitarianism, developed by Bentham and Mill. The utilitarian believes that 'the maximisation of utility is the goal for all human action' (Appelbaum et al., 1987: 20). Right or wrong actions according to the utilitarians are judged depending on what the person feels is fulfilling for them (Delany, 2005).

Underlying both theories is the principle of informed consent, although it is discussed from different perspectives. Appelbaum et al., (1987) note that the underlying purposes of informed consent in research settings are similar to those in a medical treatment setting and that both deontological and consequentialist theory are applicable in a research setting.

From the deontological perspective, informed consent allows participants to make meaningful decisions about their participation; the consequentialist perspective reflects that informed consent helps to reduce inequalities of knowledge and power between the researcher and the research volunteers and in so doing may increase the latter's compliance. It is presumed that increased knowledge would enable research subjects to make decisions that would avoid harm being inflicted on them (Appelbaum et al., 1987). The two theories of ethics as described above are relevant to understanding interaction between the researchers and the research volunteers and how individuals treat others.

Informed consent is fundamental to conducting research, because as a principle in research ethics it emphasises the importance of respecting research subjects as autonomous and protecting their wellbeing (Heath et al., 2007; Tekola et al., 2009; Giordano, 2010). Faden and Beauchamp (1986) report that the practice of research with human subjects is as ancient as medicine itself, but concern about its consequences and about protecting the human subjects is more recent.

It is assumed that a participant can only consent to a study if s/he has sufficient information to be able to make an informed decision about it. This means they know everything necessary to make such a decision, including the aim of the study and the benefits and risks of participating; their decision to participate must be active and free, without coercion and they must know that they are free to withdraw from the research (Gallin and Ognibene, 2007). Informed consent is one of the main requirements that a researcher must fulfil before a potential volunteer is enrolled in research and is crucial in clinical trials (Weiss, 2002; Gikonyo et al., 2008; Van Loon, 2009). Emanuel et al., 2000 note that informed consent is one of the important elements that determine whether research to be conducted is ethical.

In practice, informed consent involves three types of decision-making: it can be policy-oriented, dealing with rules about how to conduct the process of gaining informed consent; it can also be viewed from the philosophical perspective, which calls for individual autonomy; or it can be the shared decision-making linked to institutional practices (Berg et al., 2001). My study investigated how autonomy and decision-making are reflected upon by the actors in a research setting.

In the past, decisions about the clinical treatment to be given to a patient had much to do with the physician/patient relationship and informed consent was generally seen as a single event as long as appropriate information about the treatment plan was shared with the patient. However, today the need to involve participants in research which is not necessarily therapeutic has increased the need to view informed consent as involving more than one interaction between the researcher and the research volunteer or look at more than a one-time event because the process involves a multiplicity of interactions between the key actors involved (Appelbaum et al., 1987; Lidz et al., 1988; Berg et al., 2001; Iphofen, 2009). Research has demonstrated that an on-going dialogue between researchers and research subjects, giving the latter time to reflect and ask questions and to consult family members or others that they trust, can enhance the informed consent process (Lavelle-Jones et al., 1993).

Appelbaum et al. (1987) note that the informed consent process presents several challenges in the research setting, including a conflict between the role of researcher and that of clinician and the question of whether adhering to the informed consent process might inhibit and bias the recruitment of research subjects. Informed consent can also be a challenge for the research subjects, who may find it difficult to differentiate between the experience of treatment in a clinic and the research setting, where they are also treated when they become unwell during a trial. Decision-making and communication issues are part of what makes obtaining informed consent a complex process and its achievement, with research subjects participating voluntarily and autonomously, can be arduous and contested (Appelbaum et al., 1987).

Health professionals and researchers must allow patients and potential research volunteers to make their own decisions about whether they want a treatment option or they want to take part in research.

There are two constraints to autonomy: first, every individual makes decisions, but because they are in relationships with others they may face external pressure or coercion at times; and second, there may be internal constraints with the individual wanting to rely on someone else to make the decision. For example, patients may want their physician, who they see as the expert, to make the final decision for them (Appelbaum et al., 1987). According to Berg et al., (2001), autonomy may mean the autonomous action taken by the subject or patient to allow the professional to involve her/him in the research or initiate a plan.

The emphasis of ethics principles, and particularly of informed consent, is the result of reports of how in the past researchers and medical scientists and practitioners' pursuit of knowledge denied the people they involved in their experiments full knowledge of what was to happen to them, with many of the latter experiencing devastating effects including death and physical damage.

In this thesis I discuss the principle of informed consent drawing on ethical research guidelines including the World Medical Association Declaration of Helsinki (WMA, 1964 and all revisions up to 2008), the Council for International Organizations of Medical Sciences (CIOMS) and the Belmont Report (1979) which identifies three ethical principles that should govern human subject research: respect for persons, beneficence and justice. Beneficence requires the researcher to ensure the wellbeing of the research participant, do no harm and maximise the benefit to him or her (Belmont Report, 1978:6). Justice entails ensuring that the risks and benefits are distributed fairly among the research participants (Belmont Report, 1978:8).

I discuss the ethics research guidelines as I present the Process model of informed consent as discussed by Appelbaum et al., (1987). It is from this background that I study the informed consent process in HIV clinical trials in Uganda.

In this thesis I go beyond referring to informed consent as an event and look at it as a process that can be seen to begin from the point in time when the researchers put the protocol together, plan for its implementation and recruit the volunteers. This is followed by all the interactions occurring throughout the duration of the clinical trial. The next section discusses research regulations and guidelines.

1.3 Regulations and guidelines

The Nuremberg Code of 1947 is regarded as the first major code to contain guidelines on the ethics of medical research for the protection of human subjects in experiments. However, the basic concepts of informed consent were in place before the Second World War and the Nazis' medical experiments in Germany (Volkmann and Winau, 1996).

Central to the Nuremberg Code, which was the first code to target the protection of research subjects, is the concept of subject consent (Berg et al., 2001). The code was mainly enacted to ensure that participants were informed about research and voluntarily consented to participate in it (Rama Rao et al., 2007).

After the Nuremberg Code several declarations containing recommendations for doctors followed over the years to monitor human experiments. The enacting of guidelines in documents such as the Belmont Report and the WMAs' Declaration of Helsinki (since

1964, most recently revised in 2008), followed by the Guidelines for Biomedical Research Involving Human Subjects prepared by the Council of the International Organisations of Medical Science (CIOMS) in collaboration with the World Health Organisation (Bhutta, 2004), the National Bioethics Advisory Committee, the Nuffield Council on Bioethics, and European Union research ethics guidelines have streamlined the guidance on conducting research and specifically how research subjects should be informed about studies in which they are involved (Annas and Grodin, 1992; Berg et al., 2001; Rama Rao et al., 2007).

All of these guidelines refer to the process of obtaining informed consent as a prerequisite to conducting research. They emphasise different aspects of how informed consent should be obtained: for example the Nuffield Council on Bioethics stipulates that the consent of a senior family member or community leader may be required in addition to the that of the individual taking part; the CIOMS prefers participants to give their written consent; the Helsinki guidelines explain how to manage in the case of minors or participants who are not capable of giving consent alone. The aim of all the guidelines is to protect participants from any form of harm (Bhutta, 2004, Rama Rao et al., 2007; CIOMS, 2002; WMA, 2013; WHO, 2000).

Among the issues outlined in these guidelines the three main principles of ethical research – respect for persons, beneficence and justice – serve as the foundation for informed consent and provide guidelines on how any process of gaining informed consent can be handled well. Informed consent is mainly linked to the first principle, which recognises the right of persons to exercise autonomy (Varmus and Satcher, 1997; Rama Rao et al., 2007).

Respect for persons requires that research participants are kept informed about what is happening throughout the study period and are therefore free to modify or even withdraw their participation at any time (Emanuel et al., 2000, cited in Gallin and Ognibene, 2007). Uganda's national guidelines for research on human subjects have largely been adapted from these international guidelines for biomedical research; all the guidelines emphasise the protection of the research subject. Their overall objective is to facilitate the conduct of research while ensuring that the rights and welfare of the participants are not compromised. They protect the rights and welfare of research participants, provide ethical standards and procedures for the conduct of research and ensure that research takes into account social and cultural issues in the participating communities (UNCST 2007).

The Uganda guidelines on research ethics principles are in line with the suggestions in the Belmont Report (1978) and CIOMS (2002). They detail what is expected under each principle; in particular, autonomy is mentioned under the principle of respect for persons; maximising benefit, the reduction of risk and doing no harm are mentioned under beneficence and non-maleficence, and finally justice requires researchers to treat each research participant in

accordance with what is morally right and proper and emphasises the fair and equitable distribution of the burdens and benefits of participation in the research.

Uganda's national research guidelines document fourteen aspects of the informed consent process including explaining that the study involves research; the foreseeable risks; benefits that may be expected from participating in the study; and the disclosure of appropriate alternative procedures. Participants may be made aware of a further eight elements when appropriate, for example the possible risk to pregnant women involved in research in which products are used that have not been tested for the possible effects on the foetus; the cost to the participant; circumstances that may lead to termination of the research; the number of participants to be enrolled in the study, and how specimens will be managed, particularly in genetic studies (UNCST, 2007).

Informed consent must be documented and if a researcher requires the waiving of informed consent and its documentation this can only be granted by the Institutional Review Board (IRB). The guidelines state that assent must be sought from all children aged eight years and over (Uganda Research Ethics Guidelines 2007: 23-26). The Uganda guidelines thus reflect most international guidelines regarding the obtaining of informed consent. The research ethics committee follow the Uganda guidelines when reviewing protocols.

Table 1 summarises these various guidelines.

Guidelines	Declaration of Helsinki	CIOMS*	ICH/GCP-21 CFR 50.20, 21 CFR 50.25(a) and (b)**	UNCST***
Principles	Respect for persons	Respect for persons, beneficence and justice	Respect for persons	Respect for person, beneficence and justice
Whose duty to protect volunteers?	Physician/researcher	Sponsors of research and investigators	IRB, clinical investigators and research sponsors	Researcher
Informed consent seen as a process	Yes	Yes	Yes	Yes
Written consent required?	Must be formally documented in the presence of a witness	General rule to sign a consent form	Sign consent	Sign consent or mark with thumbprint if less literate
An Individual must consent	Yes	Yes	Yes	Yes
Role of IRB	Critical	Important	Critical	Critical
Culturally sensitive to the volunteers' setting?	Especially when sharing information	Yes, even when describing scientific terms such as placebo	Yes	Yes
Witness required?	Yes, if possible witness should be chosen by participant	Yes	Yes, with details of how communication to volunteer was made	Yes
Language	Provide information that is understandable	Convey information in language that suits participant	Understandable and clear to research subject	Clearly understood

*Council of the International organisation of Medical Science

***Uganda National Council for Science and Technology

^{**}The International Conference on Harmonisation of Technical requirements of registration of Pharmaceutical for Human Use /ICH

As Table 1. Shows, all the guidelines emphasise the protection of the research participant and the importance of all researchers acknowledging that the informed consent process may involve asking and answering questions about the research with potential participants. The guidelines emphasise that the informed consent process is more than an event and requires continuous communication between a physician and his patient or the researcher and his study participant, as discussed by Appelbaum et al., (1987) regarding the process model.

All the guidelines highlight the importance of the IRB that reviewed a given protocol regarding having a say in decisions made by the researcher that could affect the research participant. The duty of protecting the research participant lies mainly with the researcher; the CIOMS and ICH/GCP also refer to the study sponsor as having that responsibility. The researcher must ensure that study information is presented in a language understandable to the participant and that a witness must be available in the case of illiterate participants. The Declaration of Helsinki suggests that if possible the researcher should allow the participant to choose a witness. The International Conference on Harmonisation of Technical requirements for Registration of Pharmaceuticals for Human Use ICH guidelines require that the researcher should show how information about the study is communicated to illiterate participants during the initial stages of the informed consent process and suggest video recording this interaction.

In the next section I review the literature and debates on Institutional Review Boards.

1.4 Institutional ethics review boards/research ethics committees

Research ethics committees (RECs) are instituted to facilitate ethical research and all the guidelines refer to them; for example the CIOMS in its second guidelines (CIOMS, 2002) mentions that all proposals to conduct human research must be submitted for scientific and ethical review. The Declaration of Helsinki's guideline 15, under the principles of all medical research also mentions the need for protocol review by an ethics committee (WMA, 2013) RECs are important in the regulation of medical research (Davies, 2008) and one of the important research ethics principles that IRBs must review is informed consent.

IRBs and local ethics committees have been established at biomedical institutions to review proposed research projects and monitor respect for and fulfilment of ethical principles in research projects, including clinical trials (Glasa, 1996). According to Rwabihama (2010), research ethics committees in Africa have only appeared in the past 15 years. Moodley (2007) reports that the current trend in conducting trials puts a lot of pressure and responsibility on RECs to ensure that participants are protected during research.

In Uganda all research involving human subjects is overseen at the institutional level by institutional review committees (IRCs) and at the national level by the Uganda National Council for Science and Technology (UNCST), a semi-autonomous agency established in 1990 to

develop and implement strategies for integrating science and technology into the national development process. The Council advises the government on policy to advance science and technology and oversees and coordinates research and development in Uganda. UNCST liaises with the Research Secretariat at the Office of the President to clear all researchers who undertake research in Uganda, for national security reasons. In addition, clinical trials must be authorised by the Uganda National Drug Authority (NDA), which issues certificates allowing clinical trials of drugs.

IRCs are established by institutions with a mandate to conduct research and must comprise at least five members (UNCST, 2007) from varying backgrounds to ensure adequate review of proposed research activities in their institution. Their function is to conduct initial and continuing reviews and approve research projects with the aim of protecting the rights and welfare of the human subjects involved. IRCs in Uganda must ensure that ethical standards of research are maintained in research practice, that research participants and investigators are protected from harm or exploitation, the rights and welfare of the participants are preserved and society is assured of this, and to ensure that the approved protocol adheres to guidance on the ethical conduct of research (Uganda Guidelines, 2007).

The general aim of the RECs is to ensure that fair and effective protocols allow participants to be fully informed about studies so that they can make a rational decision about whether to participate or not, and to protect them from harm (Gallin and Ognibene, 2007; Parker, 2009). There is much debate on how much a REC should handle during the review of a proposed study protocol: some argue that they should consider the methodology of the protocol (Brabin et al., 2009) and others that the committee should have a legal aspect to it to ensure protection from the courts in case of the violation of moral rights leading to legal complications (Roy-Toole, 2009).

There are various debates about who should be represented on the ethics committees particularly in medical research, what seems clear is that they should include experts on the topics that the committee reviews. In addition there must be some lay members to represent the patient or research participant, and there is also a suggestion that the committee should include an ethicist (Emmerich, 2009).

There has been debate about how the committees review protocols and what the underlying reasons are for the final decisions made by the committee for a given protocol. This has been followed by studies investigating committees' challenges and limitations as they review different protocols (Davies, 2008).

Whereas researchers expect ethics committees to protect research participants and vice versa, Geissler and Pool (2006) suggest that research subjects should be recognised as interlocutors in on-going ethics debates and not seen as objects of ethical responsibility.

My study seeks to capture the voice of the research subjects as one of the important actors in the informed consent process. Kaibara (2010) suggests that the informed consent process can be improved, particularly between patients and medical practitioners, to make it more interactive so that patients and physicians get a consensus about treatment options which can be adopted in a research setting and enables shared decision-making.

A survey conducted among 31 ethics committees in sub-Saharan Africa found that the main challenges for 92 per cent of them are a lack of resources for adequate capacity-building and particularly for training in understanding the scientific design of clinical trials and how to determine risks and benefits to ensure that reviewed protocols meet internationally acceptable and scientific standards (Nyika, 2008).

Although having full regulations to guide research was mentioned by many researchers and people interested in ethics, Bhopal (2008) explains that giving illiterate individuals written information about a research problem may be unethical and undermine their intellect and eventually 'belittle them' (Bhopal: 17), and suggests that it may work out better and be more ethical to telephone or go to their homes. However, ethics committees may not find this acceptable.

The bio-ethicist Humphrey (2008:49) reports:

No matter how consciously bio-ethicists and members of ethics committees might consider any proposals ... ordinary people think about ethical and social issues with 'other cultural reference points' than those considered by ethical theorists/practitioners ... the same ethical issues are located in different contexts by different sets of actors and are ... seen to have different implications and meanings.

Not all practitioners are interested in patients giving their consent. Pothier (2008) a specialist registrar in a department of Otolaryngology criticises the act of getting written consent from patients as in his view informed consent protects the researcher but not the participant. He recommends that ethics committees should consider 'the removal of written consent as a requirement' and instead advocates 'implied consent by patients which he feels is more patient-friendly' (Pothier, 2008: 78).

A study that interviewed REC members and patients in a randomised trial reports a clash between the patients' needs and the rigid requirements of randomised trials (Ames and Thurston, 2008). These challenges and debates, however, do not undermine the importance of regulating research through the RECs (Davies, 2008).

Studies have also been conducted to investigate what cancer patients understand in the informed consent process and to come up with tools that the IRB can use to monitor the process (Meisel and Roth, 1981; Joffe et al., 2001). These are all efforts to reinforce the usefulness of an IRB.

The Uganda Virus Research Institute (UVRI) in Entebbe has its own mandated Science and Ethics Committee (SEC) established in the early 1990s by the then director of the Institute. Its membership evolves according to the requirements and mandate of the institution. This committee functions like IRCs in other research institutions; however, it also reviews the scientific methodology of all protocols in addition to reviewing the ethical issues.

UVRI's SEC is composed of members from all the programmes based on the UVRI campus: the Medical Research Council Uganda Research Unit on AIDS (MRC), the Rakai Health Sciences programme (RHCP), the Center for Disease Control (CDC), the International AIDS Vaccine Initiative (IAVI) and all research studies directly conducted by UVRI itself. The aim of the SEC is to review all the protocols from all the research programmes on the UVRI campus and all collaborative research studies in the country which may not be directly conducted by the UVRI campus programmes. The committee reviews protocols' study methodology to ensure that the science of the study and the ethics, including the informed consent documents, are valid. In reviewing the protocols the committee is guided by standardised operating procedures (SOPs) that reflect national and international IRB guidelines for reviewing protocols (WHO , 2000; UNCST, 2007).

The SEC includes clinicians, statisticians, a public health specialist, laboratory and microbiology scientists, a social behavioural scientist and community representatives. In total eleven regular members sit on the committee. The SEC members are all researchers from Institute programmes apart from the two community representatives, who are part of the community in which research is conducted. The SEC reviews many HIV and AIDS-related protocols because the epidemic remains a public health challenge in Uganda. In the next section I review the literature on the current global HIV and AIDS situation and more specifically in Uganda.

1.5 HIV and AIDS

According to the UNAIDS Global HIV Epidemic Report, sub-Saharan Africa is the most severely affected continent with nearly one in every twenty adults (4.9 per cent) living with HIV. Sub-Saharan Africa accounts for 70.8 per cent of all people living with HIV world-wide, and although

there are reports of progress in the reduction of new infection, sub-Saharan Africa accounted for 70 per cent of newly -infected adults and children in 2012 (UNAIDS 2013).

The first HIV case in Uganda was diagnosed in 1982 (Serwadda et al., 1985); by 1986 about 900 cases had been reported (Slutkin, 2006) and since then HIV prevention has been an important focus of the government through the Ministry of Health's AIDS control programs, with an increased focus on treatment in recent years. HIV is on the rise again in Uganda at a prevalence rate of 6.4% (Uganda National HIV Indicator Survey 2011,). Uganda is currently having a population of 32 million people, with a life expectancy estimated at 50 years. Currently the population aged 15-49 years has an HIV prevalence rate of 7.3 per cent, and this is thought to be higher in women (particularly women aged 15-24, whose HIV prevalence is double that of their male counterparts) at about 8.8 per cent; the rising number of new infections is double the annual number of patients enrolled for antiretroviral treatment (Uganda AIDS Commission, 2012). The health system is still being developed; there are currently a ratio of one doctor to 24,000 patients, and one nurse to 17,000 patients. This is still a very challenging position and although the health system has improved over the years, there is only one referral hospital in the country and 4 regional referral hospitals and health centres right from the parish levels in the community (Kamwesiga, 2011).

The infection figures in Uganda are still worrying and may be due to the failure to create behavioural change driven by knowledge, motivation and the choices that people make (UNAIDS 2012). In Uganda close to 90 per cent of new infections are reported to be a result of adults participating in multiple concurrent sexual relationships, and yet only half of those who need to be on treatment are currently enrolled on treatment programmes in the country (Uganda AIDS Commission, 2010 and 2012).

HIV and AIDS are still a huge national problem in Uganda despite earlier success in prevention (Green et al., 2006; Slutkin, 2006). There have been various government and non-government HIV and AIDS prevention programmes but stigma, fear and discrimination are still largely present in the community (IRIN news, 2013). King et al., (2011) and Wandera et al., (2012) report the challenges experienced even by HIV-positive persons on antiretroviral therapy such as unintended pregnancy, unprotected sex, and partners' non-disclosure of HIV sero-status.

I target HIV and AIDS clinical trials in order to understand the research ethics involved in conducting clinical trials in this setting where a huge population has been affected by the epidemic. I explore the understanding and interpretation of the different actors of the informed consent process in this setting because currently several HIV clinical trials are being conducted on various aspects of HIV, including the trends and epidemiology of the disease in different populations; possible intervention or prevention strategies testing the safety and efficacy of

microbicides and vaccines in uninfected individuals; and studying the effects of HIV treatment drugs among infected adults and children in the country.

With the influx of clinical trials in Uganda is on an increase the issue of research ethics during the trials is important, particularly with regard to how the actors, and in particular the research volunteers, understand and interpret the informed consent process. Essack et al. (2010) study of stakeholders in HIV vaccine trials in South Africa found that informed consent was one of the most frequently-cited concerns about the conduct and implementation of vaccine trials. The authors emphasise the critical importance of understanding how ethical issues are interpreted by stakeholders and the manner in which they are implemented in a given context in developing countries (ibid).

1.6 Clinical Trials

Clinical trials are one of the main designs used by research scientists to find out about disease and explain what is happening in given populations. They are part of clinical research that aims to generate knowledge to improve medical care or public health and serve a common good. They may reveal the benefits and risks of different interventions such as drugs, surgery or radiotherapy. The study products are given to volunteers, who may be patients or healthy, to observe any differences between the groups over time. The trial may be what is termed Phase I, where evaluating safety is the primary purpose, Phase II, evaluating efficacy or Phase III and Phase IV, evaluating the therapeutic use of new medicine in a general patient population (Spilker, 1991). The individual participating in clinical research may or may not benefit from such participation (Gallin and Ognibene, 2007).

Most clinical trials are randomized controlled trials: 'Randomization is the process by which patients in a clinical trial are randomly assigned to receive one of the treatments to be evaluated' (Spilker, 1991:69). Randomization reduces known or unknown bias. Randomized clinical trials are designed to compare two or more treatments as fairly as possible by allocating one of the two treatments to participants on a random basis. To reduce the likelihood of bias both the volunteers and the research team are often blinded to which treatment a participant is assigned to (Tobias and Souhami, 1993; Flather et al., 2001). Randomization procedures in clinical trials are said to be one of the norms for demonstrating the efficacy and safety of investigational products (Spilker, 1991).

There is debate about randomized controlled trials, including about whether it is fair to put volunteers on a placebo. Some researchers argue that the use of placebos is inevitable if scientists are to manage the disease burden in different populations (Varmus and Satcher, 1997). There is also discussion on whether it is fair to conduct trials in developing countries that would not be conducted in developed countries (Nuffield Council on Bioethics, 1999). Other scientists justify increased research in developing countries and note that it makes sense to test

drugs in populations they are designed to benefit on the other hand, people in poorer countries can be vulnerable to exploitation compared to those in wealthier countries (Global Health news, 2010). These are important debates which, however, need to be balanced with the need to find solutions to public health challenges.

Two main ethical questions are posed with regard to clinical research: whether research should be conducted using human subjects; and that if research must be conducted using human subjects, how it should be done (Gallin and Ognibene, 2007). This in my view is where informed consent becomes important as a principle of research ethics. It is therefore important that researchers ensure that the research volunteers contributing to the generation of knowledge for (usually) the public good are protected from any kind of harm, and that the volunteers' dignity and respect is maintained throughout the research process. In research, 'a few individuals are asked to accept some burden or risk as research subjects in order to benefit others and society' (Gallin and Ognibene, 2007: 16), so volunteers need to be well-informed about the research and what it involves for them. This is part of the informed consent process. In most studies a new drug is compared against the best existing treatment, or standard of care. A question that lingers on is whether the standard of care should be based on where the research originates from which are usually the developed countries or whether standard of care should be based on the standards existing in the developing countries where the research is being conducted (Global Health, 2010).

The ethical framework for clinical research reported by Emmanuel et al., (2000) outlines the principle of informed consent and respect for enrolled participants among the main principles of ethical clinical research. The emphasis is on providing all the necessary information, ensuring voluntary participation and the respect and welfare of participants during and at the conclusion of the research (Gallin and Ognibene, 2007). Because informed consent is related to individual autonomy, or what is sometimes referred to as 'respect for persons' (Appelbaum, 1987; Berg, 2001), it is very important when conducting a clinical trial. Most clinical trials are viewed as carrying more than a minimal amount of risk (Gallin and Ognibene, 2007). For example, whereas people may be happy to be involved in research, Sumathipala (2010) found that volunteers in research in Sri Lanka were interested in participating in the testing of new drugs.

Some researchers have noted that for clinical research to be ethical it requires much more than just informed consent because there are other important factors including the social and scientific value of the research, the scientific validity of the study, fair subject selection, a favourable risk-benefit ratio, independent review of the research trial documents and respect for potential and enrolled subjects (Emanuel et al., 2000). In my view all of these important

aspects are linked to the concept of informed consent, which is a desirable principle in clinical trials. As clinical trials continue in Uganda it is necessary to learn from the actors' experiences of the informed consent process to generate empirical knowledge about ethical debate in research and contribute to the tailoring of informed consent to the sociocultural context in which trials take place.

In the next section I give information about the clinical trials in which my qualitative study on informed consent is nested.

1.7 The clinical trials in this qualitative study

The qualitative study reported in this thesis was conducted in two HIV clinical trials conducted by the MRC/UVRI Uganda Research Unit on AIDS, which was started in 1988 following a request by the Ugandan government that the British government collaborate on HIV and AIDS research. There are several reasons for selecting these two clinical trials: the first was that they were ongoing at the time of the inception of and preparation for the qualitative study; the second was that they were both HIV clinical trials being conducted by one research organisation, the MRC at two different study sites, and were accessible to the researcher; and the third, they were both approved by the same ethics research committee of the UVRI and fourth, that there would be a possibility of comparing the perspectives of the actors in both trials on the informed consent process. As one trial recruited healthy HIV-negative volunteers and the other, HIVpositive volunteers this would help to give a balanced view.

Both clinical trials were double-blind and randomised in that neither the researcher nor the volunteers knew which volunteers were assigned to the experimental and which to the control drug. The next section gives a brief summary of the trials; I refer to them as study 1 and study 2.

1.7.1 Study 1: A phase-1 double-blind, placebo-controlled randomized trial in HIV-negative healthy volunteers aged 18-49 and living in a semi-urban community in the study area. The primary purpose for Phase –one trial is to evaluate safety of study products. Study 1 evaluated the safety and immunogenicity of the experimental vaccine drug F4co adjuvanted with $ASO1_B$ or $ASO1_E$ and administered with the experimental vaccine Ad35-GRIN.

The study was funded by IAVI and conducted by the MRC/UVRI Uganda Research Unit on AIDS. The main trial went on for about 16 months and ended in December 2012, with the volunteers making about 18 visits to the study clinic including the screening visit. The study procedures included screening, enrolment and study visits, and involved the volunteers giving a blood sample to be stored for possible blood and genetic testing (Informed consent document (ICD).

The consent form mentioned that not everyone in the study would get the study vaccines, with some getting a placebo (ICD: 2), this was part of the important information discussed with the volunteers in the trial.

1.7.2 Study 2: Safety of discontinuing cotrimoxazole prophylaxis among HIV-infected adults on ART in Uganda. A randomised controlled trial.

Study 2 was a phase IV randomised, double-blind, placebo-controlled non-inferiority trial to evaluate whether long-term primary and secondary prophylaxis with cotrimoxazole can be safely discontinued among Ugandan adults on antiretroviral therapy who have achieved sustained immune restoration (measured as a confirmed increase in CD4 count to 250 or more cells/mm³). The volunteers are HIV-positive patients aged 18 years and above who are stable on ART, and they continue to take their ART while in the trial. The participants have a CD4 count of 250 cells/mm³ and above. The volunteers were randomised to the placebo or control groups at 1:1.

Study 2 is a three-year trial with recruitment over 18 months. Patients are followed for a minimum of 18 and a maximum of 36 months. The study is funded by the MRC (UK) and conducted by the MRC/UVRI Uganda Research Unit on AIDS. The main trial will end in 2014. There are two co-primary outcome measures, one for efficacy and one for safety. The measure of efficacy outcome is the time to the occurrence of the first clinical event after a volunteer has enrolled in a trial (pre-defined as a cotrimoxazole-preventable opportunistic clinical event or death). The safety outcome measure is the time to the occurrence of the first grade 3 or 4 haematological adverse event.

The volunteers' information sheet states: 'Once you have agreed to enter the trial, you will continue taking your usual antiretroviral medicines but will be required to stop taking the Septrin tablets that you have been taking. Instead, you will be allocated to one of two treatment groups:

- Cotrimoxazole treatment group (will take one cotrimoxazole tablet daily)
- Cotrimoxazole placebo group (will take one cotrimoxazole placebo tablet daily)'

(ICD version 5.0, June 2010 pg.2 or 35 in protocol)

See table 2 for summary description of the two trials.

Description	Study 1	Study 2
Trial Phase	Phase I	Phase IV
Type of trial	A double-blind controlled randomised trial	A randomised double-blind placebo controlled non-inferiority trial
Nature of Volunteers	HIV-negative health volunteers, aged 18-49 years	HIV-positive volunteers aged 18+ years, who are stable on ART and continue with ART in the trial, with a CD4 count of 250 cells/mm and above
Primary Purpose of trial	Evaluate the safety and immunogenicity of the experimental vaccine drug F4co adjuvanted with AS01 _B or AS01 _E and administered with the experimental vaccine Ad35- GRIN.	Evaluate whether long-term primary and secondary prophylaxis with cotrimoxazole can be safely discontinued among Ugandan adults on antiretroviral therapy who have achieved sustained immune restoration (measured as a confirmed increase in CD4 count to 250 or more cells/mm ³)
Procedures	Screening, enrolment, collection of blood samples part of which for future genetic tests and urine samples collected from the female volunteers after every three months.	Screening, enrolment, collection of blood samples for various laboratory parameters, urine samples collected from female volunteers collected after every three months
Follow –up period for	16 months	Minimum of 18 months and
volunteers		maximum of 36 months
Funder	IAVI	MRC (UK)
Trial Conducted by	MRC/UVRI Uganda Research Unit on AIDS	MRC/UVRI Uganda Research Unit on AIDS
Trial end date	December 2012	April 2014

Table 2: The description of the two HIV clinical trials where this qualitative study was nested

During this qualitative study I was blinded, as the researchers were in both studies; however, I was aware that all Study 2 volunteers were HIV-positive and that those in Study 1 had been HIV-negative when recruited. All the volunteers that I targeted for my study had been in the trials for at least six months. I enrolled volunteers who were scheduled for clinical visits when my study began. See Table 3 for the informed consent process involved in each of the trials.

|--|

	Study 1	Study 2
Prior group/community information	Community information was given by the community mobilisers as part of community sensitisation and mobilisation in the communities where volunteers where sourced from before volunteers were asked to come to the research clinic	Group information was given by the health educators at the health outreaches where volunteers were sourced from before volunteers were invited to the research clinic
Individual consent information	Individual information was given at the research clinic by the nurses and it usually took an average of 60 minutes. Volunteers who wanted to consult relatives were given the opportunity; from a day to two weeks	Individual information was given by the nurses and health educators at the clinic. The average time spent obtaining informed consent was between 45 minutes to 1 hour. The volunteers who needed to consult were given between 1 and 2 weeks.
Checks on understanding	Understanding of study information was tested using a pre-test of questions with false/true responses and a score given	There were informal questions asked by the clinicians to asses volunteer understanding of the research
Proportion of volunteers who signed	The trial as a whole had 40 volunteers and they all signed on the consent form	The whole trial enrolled 1000 volunteers and 4.3% of them consented with a thumb print mark
Consent Standard Operating Procedures (SOPs)	The SOP for informed consent described the process of administering and obtaining informed consent. Key topics in the SOP were purpose, definition of IC (ICH-GCP), scope, procedure of discussions from screening to causes of termination from the study, assessment of understanding, documentation of IC, handling Illiterate/less literate volunteers and presence of an impartial witness and responsibilities.	There was a brief consent procedure which involved a discussion of treatment and follow up issues of the trial. There was no standard comprehension checklist but there were some questions asked by the clinicians before final consent at enrolment was obtained
Community Advisory Board (CAB) involvement	The CAB is a link between the research team and the community where volunteers are sourced from. There is a CAB which is composed of different representatives in the community beginning from the district Medical health services, the media, religious leaders, other community stakeholders and leaders. The CAB sits to discuss the proposed study and make suggestions on strategies on recruiting volunteers. They are also called in for meetings to discuss updates and are informed about new study developments and they in turn give feedback.	There was no CAB directly involved in this trial, although the source outreach programs like TASO have a CAB
On-going consent processes	There is no post signing follow up "consenting" planned however the community liaison officer keeps in touch with the CAB and also gets questions from volunteers and plans meetings with the study volunteers. At these meetings the research team particularly the principal investigator together with the liaison officer answer volunteer questions.	This was not planned directly as part of "consenting" individual questions would be answered by the research team that the volunteer chose to inform and these are usually the research clinicians.

As part of seeking to understand the informed consent process I was able to access the participant information sheets (PIS) to see what was included in the information given to potential volunteers about the study.

The consent documents for the two studies were structured as presented in Table 4. The subheadings under 'Volunteer information' covered a total of 14 pages and 7 pages for Study 1 and Study 2 respectively in the English versions;

Basic content of information sheets(ICH 21 CFR.50.25)	Study 1	Study 2
Statement that study involves research	Study title	Study title
	Introduction	
Explanation of purpose	What is the purpose of the study?	What is the purpose of the study?
		Why have I been chosen?
	What are the study vaccines?	
	How are the study participants selected?	How can I join the study? Do I have to take part?
	How long will the study last?	
	How is the study set up?	
Description of procedures	What are the study procedures? (screening, enrolment and study visits, storage of blood, genetic testing)	What will happen to me if l take part?
A statement describing the extent, if any to which confidentiality of records identifying the subject will be maintained	Confidentiality	Will my taking part in this study be confidential?
Description of any foreseeable risks	Risks and discomforts	What are the possible disadvantages and risks? What happens when the research study stops?
Description of any benefits to subjects	Benefits	What are the possible benefits of taking part?
For research involving more than a minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs, and if so what they consist of, or where further information may be obtained	Injuries	

 Table 4: Contents of the participant information sheets

A disclosure of appropriate alternative procedures or courses of treatment, if any, that maybe advantageous to the subject	What if you become infected with HIV?	
	Study oversight and supervision	
	Follow-up	
	End of study reimbursement	
An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of research related injury to the subject	Contact numbers (study investigators and Chairman of Uganda Virus Research Institute Science and Ethics committee	Study contacts (doctors, nurses and counsellors) and the contact of chairman of Science and Ethics committee
	Consent form	Consent for enrolment
	Consent for sample storage	Consent form for blood samples
		Who is funding the trial

Both studies used SOPs to obtain informed consent. In general these follow the international and national patterns of regulations and guidelines, but as shown in the table 3, even in this shared context their emphasis differs in terms of what and how much information is given to potential volunteers and how it is presented.

1.8 Rationale for the study

Many research studies, including those investigating participants' comprehension of the information provided to them, have focused on understanding the issue of informed consent from different angles. Valley et al. (2010), studied women who participated in a microbicide study in Mwanza and report that the women were able to recall the key information about the study, although whether their choice to participate in a trial was based on sound understanding of the benefits and risks of the trial or was a result of other factors such as trust, altruism and individual priorities was not clear. Smith et al., (2011) and Behrendt et al., (2011) have also assessed patients' understanding of the informed consent process and note that patients' understanding of informed consent is less developed than anticipated especially concerning elements such as randomisation, content and procedures of randomised controlled trials.

Other research has looked at strategies for sharing information between researchers, professionals and participants in ways that clarify what taking part in a study involves (Flory and Emmanuel, 2004) or researched the best tools for assessing participants' comprehension of study information (Bhutta 2004; Buccini et al., 2009). Other studies have examined the challenges that researchers in clinical trials may face in sharing information, such as differences

in understanding or power between members of the public and researchers (Benatar, 2001; MacQueen et al., 2004; Geissler and Pool, 2006; Humphreys, 2008, Lloyd-Smith, 2005). Mueller (2004), an anthropologist who conducted an ethnographic study on the informed consent process and HIV clinical trials among people with HIV, emphasises the contingencies and uncertainties that volunteers and even researchers experience when conducting clinical trials:

Clinical trials... require that individuals agree, or consent, to expose themselves to uncertain outcomes. They also require that individuals agree to become human 'subjects' (Mueller, 2004: 703).

These aspects of the informed consent process are still not clear and there is on-going debate about how to apply ethical principles in different types of studies and contexts (Molyneux and Geissler, 2008).

Currently most literature shows that researchers have studied modes of communicating information and assessing volunteers' understanding of study information. Various studies explore the challenges perceived by the key actors in trials which include anxiety while reviewing protocols (Glasa, 1996), issues of efficacy and safety (Moodley et al., 2005), involving healthy volunteers and unexpected high rates of pregnancy during trials (Nyika et al., 2009; and Van Loon, 2009).

Reported challenges faced while conducting long-term clinical trials in Uganda include high pregnancy rates among volunteers during trials coupled with high dropout rates, some due to pregnancy, and loss to follow-up (Homsy et al., 2009; McCormack et al., 2010; Ssali et al., 2013). However, the focus of much research is on developing good practice for the research teams using guidelines, and little attention has been paid to how the informed consent process works in practice in the Uganda context. This is the main thrust of the qualitative research presented in this thesis.

Although standard international and national guidelines on obtaining informed consent may be clearly understood by research teams and ethics committee members, these originated in Europe and America, where more people are able to read and write and to question their willingness to participate in studies (Cobbah, 1987), which is not necessarily the case in Uganda and some sub-African countries where literacy levels are still low (Araali, 2011). UNESCO's data bank statistics puts the Uganda literacy rate of adults aged 15+ who can write simple statements and add up some arithmetic at 73 per cent (World Bank, 2011). However the Ugandan Bureau of Statistics (UBOS) demographic survey in 2011 found that only about 39 per cent of adults aged 15–24 in the sampled households had correct and comprehensive knowledge of HIV and AIDS (UBOS report, 2012). The females lagged behind their male counterparts and yet it is the women who usually take part in research. Estimates in 2002 put

the literacy level of adults aged 15+ at 66.8 per cent overall (males 76.8 per cent, females 57.7 per cent).

It must be realized that the standardized procedures for informed consent as formulated by the European and American cultures emphasize individualism and therefore may not be wholly transferable to the African context. The major African feature of moral thought is usually expressed as 'a person is a person through others', or 'I am because we are' (Metz, 2010:50). The African places the individual within his community and sees a person as part of a whole body (Cobbah, 1987, Araali, 2011). This may not fit the underlying expectation of autonomy in the informed consent process.

The recruitment of volunteers for clinical trials is often challenging due to external factors arising from the context such as the individual's community relations and the anticipated benefits and risks of participating in the trial. These factors may influence would-be volunteers and colour their perception of the proposed research, and impact on the informed consent process in practice. Researchers have reported that it is important to balance the international standards of good practice with responding to the situation in a given local context where research is being conducted (Bull, Farsides, & Tekola Ayele, 2012).

Consent is sometimes facilitated by community engagement activities, with both consent and community engagement aimed at helping enhance respect to volunteers and their communities, and the social value of research (Participants, 2013). Participants in a consent and community engagement workshop held in Kilifi in 2011 discussed that consent and community engagement processes are complex and that distinguishing between information provided, comprehension of study information and voluntariness remains a challenge that needs to be understood in relation to many external factors such as social and economic factors in a given context (Participants, 2013).

This research critically analyzes how the informed consent process works in practice by examining experiences, understanding and interpretation of the process by the different key actors in depth in order to better inform the practicalities of the process in HIV clinical trials in Uganda. In exploring the informed consent process I seek to get an understanding of the relational aspects between the actors, how the consent process is designed and implemented by the different actors and the implications this has on research. Here I see the informed consent process as involving on-going communication between the key actors and particularly between the volunteers and the research team (Rama Rao et. al., 2007).

Given the amount of past research on informed consent, as reviewed above, there remains a need to qualify the practical aspects of implementing the process in clinical trials in developing countries such as Uganda, which still has to conduct clinical trials due to the impact of the HIV

epidemic. The meaning and interpretation of the informed consent process for all the actors needs to be understood in context in order to capture the implications of the current rigorous process, which is guided by a set of national and international research ethics guidelines. These guidelines are considered the gold standard, and all researchers must comply with the regulations in their own countries.

It is from this background that I took an interpretive standpoint as a researcher to investigate the informed consent process, interpret how it is constructed by the different stakeholders, and then link my findings to the standardised guidelines. In this qualitative research I critically review the implementation of the informed consent process in the HIV clinical trials conducted in Uganda in order to generate empirical knowledge about the process as understood and interpreted and experienced by the key actors involved in such trials. This will add to the current body of knowledge about how the informed consent process is implemented in practice, and facilitate better application of the principle of informed consent in a sub-Saharan Africa context.

My research questions target various aspects of understanding the informed consent process in the Uganda case study:

- Question 1. How have biomedical research ethics evolved in terms of the research principle of informed consent?
- Question 2. How is the informed consent process in HIV clinical trials defined and interpreted by the different actors?
- Question 3. What factors influence the conduct of the informed consent process in HIV clinical trial research settings?
- Question 4. How is the informed consent process implemented and experienced in the HIV clinical trials in the Uganda case study?
- Question 5. What are the views of the actors in the clinical trials on the signing and thumb-printing consent procedure?
- Question 6. How do the interpretation and understanding of informed consent by the actors in HIV clinical trials in this case study reflect on current standardised international and national guidelines on the informed consent process?
1.9 Organisation of the thesis

The thesis consists of nine chapters. The first has addressed the background and literature on informed consent and covered the context of the case study that forms the core empirical contribution of the research. Chapter 2 addresses the concepts of the study and Chapter 3 presents the research methodology.

The subsequent chapters report and then discuss the case-study findings. Chapter 4 targets the review of biomedical ethics to answer the first research question: 'How have biomedical research ethics evolved in terms of the research principle of informed consent?' This chapter discusses the evolution of biomedical ethics in protocol reviews using both international and national guidelines for the informed consent process.

Chapter 5 explores how the actors attach meaning to and interpret the informed consent process in the clinical trials to answer research questions 2; 'How is the informed consent process in HIV clinical trials defined and interpreted by the different actors?' There are differences in the ways in which the process is interpreted.

Chapter 6 discusses the concepts found in the study and how these are revealed by actors during the conduct of the informed consent process to answer Question 3: 'What factors influence the conduct of the informed consent process in HIV clinical trials in the HIV clinical trial research settings?

Chapter 7 addresses questions 4: 'How is the process of informed consent implemented and experienced by the different actors in the HIV clinical trials?' and 5: 'What are the views of the actors in the clinical trials on the signing and thumb printing consent procedure?'

Chapter 8 addresses how the current process of informed consent is reflected within current standard guidelines and sets out the implications for current practice Question 6: 'How do the interpretation and understanding of informed consent by the actors in HIV clinical trials in this case study reflect on current standardised international and national guidelines on informed consent?'

Chapter 9 draws conclusions and summarises the main findings. It discusses how the case study contributes to the debate of the implementation of the informed consent process in biomedical research, with an emphasis on HIV clinical trials. The conclusion explores why I explore the informed consent process and the importance of understanding the sociocultural context of studies. The concluding chapter also highlights the challenges and lessons that can be learned to further the practicability of implementing a meaningful informed consent process that takes into consideration the needs of all the key actors. The key actors in this thesis include the

volunteers, the research team, the community and regulatory ethics committees in clinical trials in developing countries.

Conclusion

This chapter has reviewed the literature to highlight the need to understand informed consent as it is perceived by the actors in HIV clinical trials in the Ugandan context. Actors' perceptions of the informed consent process may differ, as reported in the literature.

The next chapter discusses the conceptual framework.

Chapter 2. Conceptual framework

Walking up the hill to the research centre in Masaka, one of my study sites, unrecognised as a researcher, I listened to four volunteers going down the hill discussing how much each of them had been refunded for transport costs after attending a scheduled visit to the centre. One woman told the others that she had insisted on being given a certain amount of money. I realized that some volunteers have negotiation skills that they use even in a research setting, but beyond that I understood that this is part of what happens during the informed consent process because volunteers are told how they will be refunded on the information sheet given to them at the beginning of a study. I started to realize that informed consent is more than a single event involving the volunteer and researcher signing a consent form (Appelbaum et al., 1987). As researchers we need to understand the issues that are important to volunteers (Bull et al., 2011) and to learn about what happens after they agree to participate in a trial.

For informed consent to be a process there must be on-going communication and more than one interaction between the researcher and the volunteer (Appelbaum et al., 1987). These interactions happen in a socio cultural context to which the individual actors bring their own beliefs, attitudes and perceptions of the research. This requires the researcher to have an understanding of the concepts that influence the informed consent process.

In clinical research the informed consent process is not entirely straightforward because of the interactions between researchers and volunteers and between volunteers and their relatives and the members of the community in which they live. In this chapter I explore the different factors that affect the consent process: individuals' values and beliefs, gender issues, trust between the actors, the power dynamics during the process, and decision-making. There are several models that have been highlighted for informed consent such as the "transparency model" by Brody which approach is to ensure that adequate information has been disclosed to a patient in a medical encounter. The other model is the "conversation model" developed by Katz which argues that practitioners not only disclose information but also engage in conversation with patients concerning the choices made and practitioners also share what they think. The other model is the 'shared decision-making model" which emphasises the patient's right to receive information as well as the capacity to receive it (Delany, 2005).

I begin by describing the model framework selected to discuss the informed consent process, highlighting the assumptions underlying the process model and the events model of informed

consent. Then I focus on my study concepts, describing each in relation to the informed consent process in the case-study of HIV clinical trials in Uganda.

2.1 The event and process models

My study sought evidence that would assist understanding of the informed consent process in the context of two different HIV clinical trial settings in Uganda. I developed the main framework for the study using two important and relevant models. Appelbaum et al. (1987) event and process models were developed for the clinical practice setting to find out how informed consent could be integrated into the patient-physician relationship (Appelbaum et al., 1987), with the aim of understanding their shared decision-making and the underlying communication issues in the informed consent process.

The importance of and need for informed consent was first pointed out in the clinical medicine setting, and to a great extent the underlying purposes of informed consent in a clinical research setting resemble those in a treatment setting (Appelbaum et al., 1987). Informed consent in a research setting is governed by the standards governing research involving human subjects (Faden and Beauchamp, 1986) and there are professional codes and statutes that shape the consent. I chose to study how the event and process models of informed consent operate in a clinical research setting in Uganda.

Following the history of informed consent in the treatment settings which was created through the case law (Appelbaum: 222), the models link the legal duties of the physician, the prescriptive requirements of codes and statutes and the practice of autonomy by the patient or research volunteer in the informed consent process. They provide a theory-to-practice bridge linking the meaning of autonomy as an ethical ideal and a moral value to the prescribed guidelines and procedures for obtaining informed consent in practice.

2.1.1 The event model of informed consent

The event model of informed consent in a treatment setting sees the process of acquiring informed consent as an event at a single point in time (Appelbaum et al., 1987). The patient informs the physician about his or her medical problem and the physician makes a diagnosis, decides on the treatment path and informs the patient of the risks and possible alternatives involved. What is most important in the interaction between patient and physician in this model is the final decision made by the physician. The patient usually accepts the suggested treatment path because the physician is deemed the 'expert' (Deber, 1994). The consent form is seen as the 'central symbol of the event model' (Appelbaum et al., 1987: 152) that emphasizes that the physician discloses information and the patient consents. It is mainly guided by and conforms to the legal requirements of informed consent, and does not emphasize patient autonomy.

The event model has limitations in terms of the relationship between a patient and the physician because it leaves the overall decision-making authority to the physician (Delany, 2008). The model assumes that one decision is made at one time, and what happens after that one interaction does not matter to the physician; however, it has been reported that it is difficult to know exactly when patients make their medical decisions (Lidz et al. 1983, cited in Appelbaum et al., 1987). The model encourages a one-off information session in which the information imparted by the physician to the patient may not be fully understood or match the patient/research volunteer's values. Kuczewski (1996) views this event model as legalistic, allowing the patient and the physician to deal with their values independently of each other.

Although this single decision-making encounter may appear to be clear and quick, it does not support the patient/research subject's autonomy. Consent-giving as a one-off event may be accorded particular significance by some actors in a research trial because it does not take too much time but does not reflect the different actors' experiences of the research process. In the clinical trial setting of my study, I explore what happens during the interaction between the volunteer and the research team in the single encounter and signing of the consent form.

Having discussed the event model, in the next section I outline the process model that underlies the concepts that I examine in this thesis because it is here that these concepts are experienced in practice.

2.1.2 The process model of informed consent

The process model of informed consent sees medical decision-making as a continuous exchange of information throughout the course of the physician-patient relationship. The model is based on the assumption that decisions made in the physician-patient interaction are continuous in all of the interactions that occur for the duration of the study (Appelbaum et al., 1987; Lidz et al., 1988). In a research setting this means that information about the trial is exchanged between the researcher and the volunteer and both make decisions in their interactions throughout the study. As the HIV clinical trials are part of a research setting, the investigator must follow the trial protocol while conducting the research.

The process model allows for an instructive exchange of information between the physician/researcher and the patient/volunteer in the sense that the former has more than one occasion on which to discuss the treatment or research information. The patient/ research volunteer and physician/researcher both ask each other and respond to questions during the informed consent process. This model assumes that the former is able to make individual decisions during the interaction and that the values of both are open for discussion and not hidden away from the other party because of the short interaction, as occurs in the event model. There is transparency and the roles of the researcher/physician and the volunteer/patient are apparent in their interaction (Kuczewski, 1996; Delany, 2008). The study

volunteers/patients are seen as having an active role in the process model, including giving feedback when required by the physician/researcher (Appelbaum et al., 1987).

The process model highlights both theoretical assumptions, such as patients/research volunteers' active participation in decision-making, and clinical assumptions such that patients perceive that they make their treatment decisions on their own. In the clinical trials that I study, research volunteers are assumed to have understood the trial information before they make the decision to join the research. As discussed, the theoretical and clinical assumptions by the physicians contribute to the practical actions of obtaining informed consent in clinical practice. The process model considers that delineating the roles of the physician and the patient is important because both parties know what to expect from each other, and both parties allow for differences in their values and beliefs to be expressed (Delany, 2008).

The process model is aware that patients and health professionals may hold different values and beliefs associated with models of health and illness. In this model the patient begins to emerge as an autonomous person, unlike what happens in the event model of decision-making in informed consent. Obtaining informed consent in the process model allows for a more meaningful interaction between the physician and the patient or the researcher and research volunteer and for volunteer autonomy in the informed consent process. In the next section I introduce the factors investigated in this study.

2.2 Study concepts

To understand how the event and process models work in a setting in which there is not only a physician/patient or researcher/volunteer relationship but also interactions with other actors, I sought to identify the factors that influence the informed consent process in the clinical research setting. My experience as researcher and ethics committee member, described in Chapter 1 and earlier in this chapter, have shown me that although the informed consent process may be seen by some as a single event, in practice it is a process embedded with events, actions and decision-making (Appelbaum et al., 1987; Berg, 2001; Long, 2001), involving communication and negotiation and working towards a meaningful relationship between the researcher and the volunteer. In this section I explore the factors that are likely to influence the actors' choices and practice in the informed consent process – values, beliefs, power dynamics, gender issues, trust and decision-making – in the case-study HIV clinical trials in the social cultural context of Uganda.

2.2.1 Values

Values are principles or standards of behaviour that guide a person's judgment of what is important in life (Horton & Hunt, 1984). Both of the case-study sites are in central Uganda, and

most of the people living there are of the Baganda tribe, the largest ethnic group in Uganda. They made up the majority of my respondents. Their culture is referred to as the Ganda culture. In a discussion of a people's values it is important to understand the sociocultural context. Culture is about people's way of life, including their customs, beliefs and social organisation. Culture is a collective phenomenon because it is at least partly shared by people who live in the same social environment, and culture is learned from that environment (Geert, 1991). Culture can best be understood by observing behaviour, signs and symbols, social events and the power dynamics in interactions (Geertz, 1993).

The Baganda are mainly united through their traditions. They believe in holding traditional rituals collectively, with marriage, twin births, the naming of children, death and funeral rites particularly important (Roscoe, 1911, 1965:82-97, 2005). Clan and family are very important and individuals usually have very close relationships within the clan. These, among other factors, may affect an individual's values and decision-making (Seeley et al., 2009). The Baganda society is patrilineal: the male is dominant in the home, and this may affect the way decisions are made (Roscoe, 1965:85-97, 2005; Muyinda et al., 1997; Wolff et al., 2000). Societal values may impact on an individual's decision-making, including deciding whether to participate in a clinical trial. For example, according to the Ganda culture every married woman was anxious to become a mother because if this did not happen, she would be despised in the community and this led to the use of charms and drugs to try and obtain a child (Roscoe, 1911). Societal values may also influence the informed consent process, even after an individual has consented to participate in research. The Ganda socio-cultural context requires that there is sharing of information about issues that pertain to a family and its members for example, issues pertaining to marriage and associated ceremonies. In the Ganda community, the law of consanguinity was clearly defined and people would not easily make mistakes on which they might enter into a marriage contract because the clans and sub-clans are so distinct and easy to ascertain to which clan any person whether male or female belonged. This guided part of the decision of who to get married to in the community which practice may challenge the aspect of individual autonomy (Nziza et al., 2011: 14-29; Roscoe, 1911).

'Autonomy' refers to an individual's capacity to make informed decisions free of coercion. The philosophical theory that underpins informed consent defines autonomy as self-governance or self-rule: the capacity to reflect and choose and the freedom to express individual aspirations and preferences (Delany, 2005). It has however been reported that it can be difficult to pin down values because sometimes patients/research volunteers act according to the values of those who are giving them therapy (Odell & Stewart, 1993) and the context in which they live.

Supporting autonomy is at the core of the usual meaning of 'informed consent' so that each of the actors and in particular the volunteers; feel that what is important to them personally is

respected even in a research context (Faden and Beauchamp, 1986; Beauchamp & Childress, 1994). However, this can present a challenge in African societies where 'we' referring to the "community" is more important than 'l' referring to the "individual" (Metz, 2010). Since autonomy and respect are values, we need to be aware of how such values are expressed by different actors and whether they are more or less likely to support informed consent as it is referred to in international guidelines as 'personal freedom of action' (Appelbaum et al., 1987 :22). In the cultural context of this study this may mean that volunteers have to make decisions that balance the social values of the community and their own personal values if they are to participate as independent individuals in the informed consent process in a clinical trial.

In this study I examine the value of autonomy and what it means to the different actors who include the researchers, the ethics committee, the volunteers and the community advisors in the trial setting in this cultural context. A research setting with a large number of actors presents many issues to do with respect for one another and how these are resolved in practice is closely associated with autonomy. One of the nineteenth-century philosophers Kant, while discussing his arguments for autonomy in ethical theory, takes the stance that a person is unique because s/he is self-legislative and therefore respect for the individual is very important: one must always treat another human being as an end and never as a means to another's end (Appelbaum et al., 1987; Berg et al., 2001). Mill, another theorist, emphasises that people should get personal satisfaction or utility from whatever they do as long as they do not affect the rights of another. These two schools of thought emphasise the concept of values during the informed consent process (Appelbaum et al., 1987). In this study I explore the relevance of conceptualising values among actors who have different roles in a clinical trial. Respect for persons may be seen differently in different contexts (Woodsong, 2006).

Bower et al., (2005) report that values are difficult to understand until you hear from the person who holds them, and may vary according to the individual's characteristics and experiences. Kuczewski noted that although the physician is an expert on the medical facts, the patient knows their genuine insight into his/her private values (Kuczewski, 1996). In the informed consent process, are an individual's values to take part in a trial their own or are they influenced by other actors and the cultural context? Participants in a consent and community engagement workshop noted that there is still relatively little information about the issues that may arise when seeking consent and how to best tailor consent processes to specific contexts (Participants, 2013).

It is important to get some understanding of the values that individuals have when conducting or taking part in clinical trials.

2.2.2 Beliefs

Beliefs may be seen as framing the factors that influence individuals' actions. The Ganda culture is influenced by stories and legends passed on from ancestors; if something is seen as taboo it is avoided by all, sometimes even unconsciously (Roscoe, 1965: 87-97, 2005; Nziza et al., 2011: 14-29). The African world view places the individual within his community, there is a sense of collective responsibility, cooperativeness and interdependence (Cobbah, 1987), and this is true in the Ganda culture.

Beliefs are usually held by a group of people in the socio cultural context in which they live. The Baganda believe, for example, that when a child is born the afterbirth must be buried near the doorway of the house to ensure that no one can pick it up and use it to do evil to the baby or even make the woman barren (Nziza et al.,2011: 14-29). The Baganda are known for their politeness, especially in their behaviour and actions; Baganda in rural communities respect medical workers and rarely question what they are told about their health. Some see the researcher as all-knowing and better-educated than themselves and do not question what s/he says. Wiles (2006) reports that one of the challenges for the researchers she studied was that potential research participants disregarded explanations about studies and simply wanted to enrol in them, possibly because they wanted to get answers to their health situations that they believed the researchers could provide (Wiles, 2006).

If a volunteer holds a belief that the trial drug will work for them and do not understand that the trial is testing the drug and that there is a chance that they will be given the placebo a negative study result could cause problems for both the volunteer and the research team if the volunteer's expectation is not met. Knowing the participant's cultural context helps to understand their beliefs because this is where social events and exchanges of information take place.

A study conducted among women of African descent living in the US and with different historical experiences of migration and acculturation found that they still held their traditional African beliefs about pregnancy and the postpartum period, even after many years of being away from home. The beliefs are passed on from generation to generation (Philips, 2005). The fact that people hold on to information that has been passed on from generation to generation, shows the importance of understanding their belief system and culture in order to be able to understand why they do things the way they do (Caplan et al., 2013). Beliefs can also be held about cause-and-effect relationships: for example as a volunteer develops a relationship with a research team member the trust that grows may be the most important reason for taking part in a trial for this volunteer (Jervis, 2006; Molyneux, 2005). Beliefs can be reflected in ideas about how things work, how others act and the consequences of one's own behaviour. It is important to understand people's modes of thought about a given issue and how they express their ideas

about the world (Beattie, 1964). I explore the actors' beliefs, what they thought about, the beliefs they held, how they expressed their thoughts in their exchanges with other actors in the informed consent process and how they interpreted the informed consent process in relation to their beliefs. Discussing their beliefs can help researchers understand why research subjects prefer some options to others.

2.2.3 Trust

Trust is a key factor in the context in which the informed consent process takes place because decision-making can be affected by the kinds of people or support groups that volunteers interact with and trust when making important decisions (Kuczewski, 2002; Molyneux et al., 2004, 2005; Sand et al., 2008). The role of trust cannot be overemphasised, in medical settings where the physician generally makes the final decision; a patient may trust certain physicians more than others. A study of outpatients going in for gynaecological surgery found that although they did not object to medical students being present during the surgery, many did not want them to participate in the surgery itself, depicting a greater sense of trust for those with greater experience, although the patients did not know who the students were (Verslus et al., 2010). This example demonstrates the potential relevance of trust in relationships between actors during a research process.

Many studies have pointed out the importance of trust in dealing with patients and research participants (Molyneux et al., 2005; Hoberman, 2013; Kuthning & Hundt, 2013). A patient's opinion of their physician may influence trust in their interaction (Wise & Rodseth, 2013). Trust is therefore a critical aspect of informed consent in a research setting (Molyneux et al., 2005). My study sought to learn what the actors in the two clinical trials thought about trust and how it influenced the informed consent process.

2.2.4 Gender

Gender is about the socially-produced differences between being feminine and being masculine (Holmes, 2007) and thus is socially constructed (Connell, 2002). Gender identity is affected by many variables such as class, age, power and religion, and as communities become increasingly diversified more factors intersect with gender (Moore 2007; Whitehead et al., 2013). Understanding gender differences in the research setting is important for explaining how interactions are managed within the informed consent process and whether and how it impacts on the actors' decisions and activities during the process.

Gender is constructed through people's relations and interactions with others (Connell, 2002). A study in India found that gender related issues were more likely to affect women volunteer's participation in a trial than the level of education as compared to the men (Gitanjali et al., 2003). Uganda has a patriarchal system and gender differences affect important decisions, including women's decisions about their reproductive health (Wolff et al., 2000; Nziza et al.

2011). In the Buganda culture a lot of emphasis was put on premarital education for women where girls were told they should not deny their husbands' demand for sex (Obbo, 1993). Buganda has a patrilineal system and men are permitted to have multiple wives or sexual partners while women are restricted to one partner (Mason, 1994). It has however, also been reported that bride wealth for marriage is nominal and divorce is common among the Ganda women and therefore there are constant negotiations in communication between partners which may imply some form of communication and negotiations in reproductive issues (Wolf et al., 2002) this may lead to some form of agreement or disagreement during the informed consent process.

In this thesis I study the concept of gender in terms of how the roles and expectations of men and women in their families and community settings affect the informed consent process. Understanding how individuals involved in clinical trials make their decisions in the informed consent process requires understanding of the gender issues that facilitate or hinder them.

2.2.5 Power dynamics

If the reason for an informed consent process is to ensure that people participate voluntarily this implies the possibility of non-voluntary or coerced consent, suggesting that some people exercise power over others. One could argue that the informed consent process is itself about who holds power in a given socio cultural setting.

I take the work of Lukes (1974, 2005) as my starting point. In his essay on power, Lukes (1974; Lorenzi, 2006) proposes three dimensions of power. The first is observable behaviour, which is analysed by observing conflicts between parties with different interests in concrete issues. It operates overtly in that party A may succeed in getting party B to do something against the latter's wishes. This is relevant to studying the informed consent process because a powerful researcher may get volunteers to participate in his or her research without fully taking into account the potential for being harmed, because they fear the consequences of refusing or, especially in low-income settings because they have been promised some money.

Lukes' second dimension of power is exercised where one party has their own feelings and ideas about a given situation or activity but feels compelled to cover these up in the interest of the other party. This second dimension is the ability for one group to set an agenda determining what can be talked about in public and what can be left out, and the permissible ways of talking about the subject in question. In consequence some issues that are important to the individuals involved are never brought up for discussion or consideration (Magnusson & Marecek, 2012). The people who are being induced, influenced or persuaded may avoid making decisions that are in their own interests. A study exploring trust in a large clinical trial setting in Kenya reports that some participants could not refuse what a doctor asked and so participated

in the study despite their misgivings (Molyneux et al., 2005), this in a way reflects some power difference between the participants and the doctors.

Lukes' third dimension of power occurs where there is latent conflict due to contradictions between the interests of the actors exercising power and those over whom they exercise it. The real interests of those being excluded from making important decisions may not be easily observable, and those in power may feel successful in averting a power conflict, but there remains an implicit potential for conflict (Lukes, 1974, 2005). Magnusson and Marecek (2012:24) call this type of power 'ideological power' which shapes peoples' ways of seeing the world, their meanings and their interpretations. Because they accept the way things are, they are not provoked to change the situation.

In this study I explore how these three dimensions of power manifest among the different actors' decision-making during the informed consent process. Clinical settings were historically organized according to the expectation that patients will and should accept their physician's recommendations because medical practice was guided by the 'beneficence' principle in which doctors do no harm (Faden and Beauchamp, 1986). More recently it has become widely accepted that patients must understand and freely agree to their treatment rather than simply accepting what the doctor recommends (Appelbaum et al., 1987). Recognition that the research volunteer has the right not to be damaged or coerced means that volunteers exercise some level of power in the relationship with the researcher when deciding whether to participate in a study. This thesis explores how such power dynamics manifest between the actors in practice.

Volunteers may not exhibit the ability to resolve conflicts or show that they can influence issues in research as the researcher in practice, due to socio cultural differences that prioritise education and economic status, especially in the developing countries (Benatar, 2002). However, they may exercise a combination of overt and covert power and influence in relation to participating in a trial (Molyneux, 2004). This study explores the power dynamics in the interpersonal interactions of the actors, how they relate to one another and how far selfefficacy of the volunteers can be recognised and supported by the researchers (Butler Lowell, cited by Gallin & Ogunibene, 2007:143-153).

2.2.6 Decision-making

Giving informed consent requires making a particular decision about taking part in research. In this section I examine how the different actors make their decisions during the informed consent process.

Decisions can be made independently, communally or in consultation with important others; in some cases decisions made by others influence the individual concerned (Ying-Yi Hong et al.,

2001; Weiss, 2002, Gikonyo, 2008; Seeley et al., 2009; Whitney, 2008). A complex web of decision-making processes operates in the informed consent process. I critically examine what factors affect or lead to the decisions made during the informed consent process in the context of a medical trial. Studies have shown that it is not always easy for physicians to get used to pooled decision-making where they have to consult with others before they make decisions because they have been trained as individual decision-makers (Taylor & Kelner, 1987).

Social or institutional forces that affect whether and how far decision-making is shared or individualised in the informed consent process is important for this study, which took place in a cultural context where individuals' agency may be overridden by their institution's expectations. In Buganda, family members have a close relationship with one another and individual decision-making in the informed consent process may be influenced by important others in the family or the community (Seeley et al., 2009; Roscoe, 1911,1965:82-97). As the research team is part of an institutional setting and the ethics committee performs its reviews as part of that institution it is important to explore how the different actors reach their decisions, what decisions they reach and who influences them during the informed consent process.

In this case-study, the volunteers in study one were healthy and were HIV negative when tested before they enrolled in the study, but many are exposed to HIV since they are in relationships. The volunteers in study two are HIV positive, are already on antiretroviral therapy and are not currently sick. All the actors make decisions in their interactions with others during the informed consent process. I explore what directs and how they reach their decisions in the process, looking particularly at informed consent as a practice of respecting autonomy, although Faden & Beauchamp (1986: 74) report that respect for autonomy 'has never had a sure foothold in medical practice'. Decisions have to be made in the informed consent process but the way they are made in clinical trials is very important, because it may impact on the involvement of the actors in the trial.

In this study I explore how the two models of informed consent – the event model and the process model – work in a clinical research setting with more than two main actors. I explore the actors' values, beliefs, gender, trust, power dynamics and decision-making during the informed consent process in the two HIV clinical trials. These factors may influence how they understand and experience the process. Figure 1 shows a conceptualisation of the study.



Figure 1: The informed consent process, showing the actors and main concepts of this study

In Figure 1, the oval shape encloses the actors to indicate that informed consent happens for a specific study in a given setting. The process may also be influenced by environmental factors including policy guidelines on informed consent, the research funders' expectations, relatives and friends of the volunteers in the community and the setting of the organization in which the research takes place.

The actors interact as shown by the arrows in the figure; the wider, two-way arrow between the researcher and the volunteer shows that most of the interactions in a clinical trial occur between these two actors. The researcher also interacts with the ethics committee, which permits the study to commence and monitors its progress, and with the community advisory board, which represents the community and acts as its gatekeeper, giving feedback to the research team on what goes on in the community during the study. The volunteer lives and belongs to the community and what happens to him/her may impact on other members in the community.

A volunteer with a complaint can report it directly to the ethics committee, which may also elicit information from the volunteers while monitoring a study. The links between the ethics committee, the CAB and the volunteer are not as strong as those between the researcher and the volunteer because their interactions are less frequent. The individual is based in a community and therefore this is a very strong link when discussing the informed consent process. The nature of study whether it involves research volunteers who are not sick such as the ones in the phase 1 study or those who are infected with HIV although not currently sick such as the ones in the phase IV study is important for understanding the informed consent process. Each of these links, whether shown by a thick or a thin arrow, is meaningful in the informed consent process.

All the actors in the informed consent process bring their own values and beliefs to the informed consent process. Gender and power, trust and decision-making issues all influence the process, and this is particularly clear when viewed through the lens of a process model framework.

Conclusion

In this chapter I have discussed the event and process models of informed consent and how I adapted them to the clinical research setting of my case studies. The event model constructs informed consent as a single event involving informing the volunteer about the purpose, risks and benefits of the proposed study that ends with the signing of the consent form. This model may be appropriate for a clinical setting and is preferred by some practitioners who believe in the beneficence model of treatment. When the consent form has been signed and the patient is given a copy the main interaction between these two people ends.

The process model of informed consent, on the other hand, allows for continuous communication between the actors for the whole duration of the study and the interaction sometimes moves from a formal to some level of informal interaction; the information is discussed, the actors mutually ask and answer questions. This is the appropriate model for my study because in a research setting the informed consent process includes more than just the researcher and the research volunteer who sign the consent form. Also involved are the members of the ethics committee and the community advisory board, the research team and some of the volunteers' family and friends.

I studied the interactions between the different actors to understand how the process model works with the informed consent process in a clinical trial and found that values, beliefs, gender, trust, power and decision-making are important factors in the construction and understanding of the informed consent process in a clinical trial setting.

The next chapter presents the methodology used in the study.

Chapter 3: Research methodology and context

Introduction

This chapter describes the research design of my study. In it I set out the context of the two clinical trials that it investigates and the study populations. I describe how I gained access to the setting and the study populations and how I selected the respondents and the data collection methods that I used. I present my approach to the analysis structured by my research question:

How do actors in HIV clinical trials understand and experience the informed consent process, and to what extent is their understanding reflected in the standardized national and international informed consent guidelines?

3.1. The research strategy

This is a qualitative study exploring what happens during the informed consent process, how this process is constructed and interpreted and what is meaningful to each group of actors. These include the research team, the research volunteer, the community advisors and the science and ethics committee (Mason, 1996; Denzin and Lincoln, 2000). Understanding the experiences of the actors can lead to insights into the informed consent process.

This study mainly takes an interpretive methodological approach which is closely linked to constructivism (Denzin, 1994; Green and Browne, 2005). An interpretive approach allows the researcher to find out how all the actors construct their worlds and interpret the findings. In this study I sought to understand how the actors in two clinical HIV trials constructed the informed consent process and what was meaningful to them in their particular social and institutional contexts.

The actors comprised the volunteers, the research teams, the members of the ethics committee and the community advisors. Each belongs to some form of institution: the researchers and ethics committee members belong to their own institutions, which guide their practice; the volunteers, by agreeing to take part in the trial, also belong to a trial cohort and the community from which they come is also a form of institution.

Researching the informed consent process from the different actors' perspectives requires that the researcher interacts directly with them in their contexts. Working from the interpretive/constructivist perspective I realised that the context and what happens in the informed consent process can best be constructed by the actors themselves in accordance with their experience of the process (Silverman, 1997). I therefore took an ethnographic approach, studying and recording the dynamics of the interactions in the informed consent process and

gathering the actors' lived experiences by interviewing them and listening, observing and recording, while being part of the context myself. I had to be present at the clinical trial settings in order to understand what went on and to observe and hear from the various actors what the procedures of informed consent were and how they interpreted them.

Before I started my PhD study I had become interested in the informed consent process while working as part of a research team conducting an HIV clinical trial for several years at one of my research sites. I chose to investigate this process at two different sites of MRC Uganda research unit on AIDS/Uganda Virus Research Institute (MRC/UVRI) which organisation has long experience of clinical trials.

With a focus on allowing the actors to construct and give meaning to the process I took a reflexive approach (Holliday, 2007) which required me to be neutral in the setting, despite the fact that I was not a stranger to the clinical trial research team that I interviewed and interacted with during my study. Although I knew most of the trial research team members, I was now positioned as a researcher researching my fellow researchers. The study team members at one of the clinical trial sites might have seen me as an insider, as I had been an MRC employee myself. But I was also an outsider, in the sense that they had the upper hand in this research situation because they were conducting the clinical trial, which I was not part of, and I had to interview them to understand the trial and their individual experiences of the informed consent process.

The other clinical trial that I chose as a case study was located at a site that was an entirely new environment for me, and I had to create relationships with the research team as a researcher myself in order to gain access to the trial. It took time to build my own understanding and experiences of what was going on in the trial as I interpreted my findings. My intention in taking this approach was to learn what the actors experienced in their research-based social cultural contexts. I call this a culture of research. By 'culture' I mean 'the composite of cohesive behaviour within and social grouping from a neighbourhood to a work group' (Beals et al., 1967:8, cited in Holliday, 2007:12). In this thesis the culture refers to how the group of researchers work in their setting, i.e. their roles and positions in the process.

The study was centrally concerned with the meaning that the actors constructed from the informed consent process. It was my role as a researcher to be reflexive. Delanty (2005:120) notes that 'reflexivity is not merely self-reflection but refers to a self-transformative capacity'. During the study I had to examine my role in the process of conducting the research. Because I had once been part of a similar study I had to balance my former role as an employee and fellow researcher with my current role as a research student interested in understanding the informed consent process. I had to be reflexive in the context of this study. Reflexivity allows the researcher to look at the social world constructed by the actors as also involving her/his

own presence in the context. It is not only about what happens in the outside world but also concerns self-reflection about how, as a researcher, one may influence the actors' constructions in a given context (Steier, 1991; Creswell, 2003; May & Perry 2011).

As a researcher I had interacted with some of the research team members before my study. I realised that some research team members would relate to me as a colleague but I dealt with this by stepping aside as much as possible and asking the research team to explain issues that could be taken for granted in their narratives for example, what happens as they provide study information especially during the follow up of research volunteers. To the volunteers I was like any other research team member but I had to emphasise to the volunteers that I was studying the informed consent process and I had nothing to do with the clinical procedures they were undergoing in the clinical trials.

3.2 Study design

I sought to analyse all aspects of the process of informed consent and the factors that influence it in the long term and not just as a single event in HIV clinical trials. The informed consent process includes various activities including the researcher's initial contact with potential volunteers and providing them with information about the study, and each volunteer and a research team member signing the consent form and what happens during the interactions that go on between the different actors in a research process of a trial. Providing study information and checking volunteer comprehension and willingness before signing a consent form are the aspects that are usually emphasised in this process, (CIOMS, 2002) but in this study I also include research volunteer recruitment and follow-up.

In my process model, informed consent is a continuous process which involves more than simply providing study information, assessing the volunteers' comprehension of this information and the signing of a consent form; it also involves reviews of the study documents which among others are the consent forms, which were mainly carried out by the research team, interaction and discussion between the different actors, and feedback from the different actors in their individual contexts.

The research was situated at two MRC/UVRI sites. Qualitative research with a two-case-study design allowed me to explore what happened in the different HIV clinical trials. The two HIV clinical trials are the cases for this study in the Uganda cultural context. Case studies contribute knowledge about individuals, groups and social and related phenomena. I selected these two case studies because they were both HIV clinical trials being conducted by the same research organisation MRC/UVRI, which meant they could have gone through similar ethical preparations before they were being conducted in two different sites and therefore there was no possible contamination between the volunteers. The targeted volunteers in these cases study

were different because in one trial they were HIV negative volunteers, and in the second trial they were persons living with HIV but who were already on ARVs for at least not less than six months. These case studies would be useful for comparison of the research volunteers' and other actor's experiences of the informed consent process in the Uganda context. Case studies can be exploratory, explanatory or descriptive (Stake, 1995; Yin, 2009).

Using a qualitative methodology enabled me to explore the concepts of my study and examine how event and process models of decision-making in informed consent are experienced in practice (Appelbaum et al., 1987) in the HIV clinical trial setting, and how the implementation of informed consent may be influenced by the understanding of the different actors.

I spent time at the research settings observing the volunteers coming and going for their scheduled visits to the clinics, observing the interactions between the different actors, particularly the trial research team and the research volunteers. As a researcher who was already known to the research team I had to be neutral in my interactions with them. I did not interfere with their work but stayed in their close vicinity, observing their general discussions about the trials. I had meals with the teams so that I could listen to the informal conversations and short chats when they broke for a cup of tea; this led to natural interactions in the research setting.

I avoided the 'researcher culture' (Holliday, 2007: 151) of appearing too professionalized and living in a world far from my respondents by trying to interact with the study team members in whatever was happening at the site, for example by attending research team meetings when invited. However, my interactions with the teams more commonly occurred at the tea and lunch breaks. Attending a follow-up meeting between the research volunteers and the research community liaison officer and a senior investigator at one of the clinical trials gave me an opportunity to listen to the discussion and experience how the two groups of actors interacted.

Many of the volunteers at the study sites were taking part in other trials than my own; I would pass by the waiting rooms or through the corridors and greet the volunteers present as a group and observe what was happening before carrying on with my routine. I used such times to observe what happened in the clinic setting, particularly when a volunteer arrived and to listen to the volunteers' conversations and observe their facial expressions. These expressions differed; whereas some volunteers were relaxed watching the television set in the waiting room, the faces of some showed signs of anxiety about being seen by the research team and others' expressions were not easy to interpret. The observations were made as part of the informed consent process and I had informed my respondents that I will be observing what goes on at the clinic as part of understanding the process. For the volunteers the habit of researchers greeting them and asking about how they are is part of creating rapport with them.

3.3 Study setting

The research setting that I chose was mainly influenced by my having worked on a large HIV and AIDS clinical trial that had sparked my interest in the ethics of informed consent. As a social science researcher I had become interested in understanding the interactions that occur in the informed consent process and what effects they have on the understanding of procedures. I was particularly interested in learning why people volunteer for clinical trials which are testing products which are not already licensed to use in the general population.

The MRC was established in 1988 by the Ugandan and British governments for collaboration on research into HIV infection and AIDS. The various types of research that the unit conducts include clinical trials.

The number of clinical trials in Uganda is increasing due to the devastating effects of diseases including malaria, HIV-related infections and non-communicable diseases. Clinical trials are guided by protocols that outline all the procedures of a given study. The procedures are explained in terms of what should happen to the volunteers' involvement in the trial, which includes but is not limited to the type and number of samples to be collected from them and how frequently these are to be collected, and the number of interviews to be held with them. The research team's daily practices are usually laid out in Standard operating procedures (SOPs).

The many procedures that a volunteer has to go through include giving informed consent. The research protocol usually includes the participant information sheet and consent form as an appendix. The SOP for gaining informed consent usually describes the procedure for the signing of the consent form but rarely includes planned follow-up discussions between the research team and the volunteers. Such meetings are usually initiated by the former but are not obligatory.

The two case-study sites are in central Uganda. At the site of Study 1 most of the population are involved in peasant farming producing a few cash crops like maize and coffee. The site of Study 2 is a semi-urban area near the shores of Lake Victoria where the population is mainly involved in fishing and selling fish, food businesses and running small kiosks, with a few peasant farmers. Both areas have been affected by HIV, with some people currently living with HIV and others losing family members, friends and neighbours.

My first case study, Study 1, was a phase I double-blind placebo-controlled trial to evaluate the safety and immunogenicity of two HIV vaccines with HIV-1 uninfected adult participants. The volunteers in the trial were adults aged 18–40 years.

The second case study, Study 2, investigates a Phase IV randomised trial evaluating the safety of discontinuing treatment with Cotrimoxazole prophylaxis among HIV-infected adults on ART in Uganda. This study is scheduled to take three years, and at the time of my research it was in its second year. The volunteers are adults aged 18–59 living with HIV who are already stabilised on ART and have a CD4 of over 250 cells.

3.4 Gaining access and selection of respondents

Before I left the University of East Anglia (UEA) to carry out field work I sought and was granted permission by the School of International Development (DEV) Ethics Committee to go ahead with the research project. On arriving in Uganda I prepared for a series of activities which included meeting the MRC unit's Science Committee and later sending my study documents to UVRI's Science and Ethics Committee. Obtaining final approval to conduct the study took almost five months. First, I presented my proposed study to the MRC's Science Committee, which is composed of scientists from the different disciplines in the unit including epidemiologists, public health specialists, social scientists, laboratory clinicians, immunologists and statisticians. The committee meets once in a month and one of its roles is to discuss proposed research in the unit. The scientists that may help to clarify the study or about its importance. The researcher must be present at the meeting to present her/his work.

After discussing my proposal with the MRC Science Committee I was given permission to submit my protocol to UVRI's Science and Ethics Committee (SEC), which reviews the science and ethics of all studies undertaken by programmes collaborating with UVRI or directly conducted by the institute. UVRI SEC is mandated by UVRI to approve research protocols and the committee meets once in a month to review research protocols. The question raised in relation to ethics of the study was in relation to the Events and Process models and how they may be used to answer the research question. I responded to this by describing the event and process models and that these models are aimed at understanding the underlying issues of communication in a given context during the informed consent process. The models are a link between the legal and prescriptive requirements and practice of autonomy in the informed consent process. The models provide a theory-practice bridge linking the meaning of autonomy as an ethical ideal and universal moral value to the prescribed guidelines and procedures of obtaining informed consent in practice.

After the protocol was cleared by UVRI SEC I sent the proposal for clearance to UNCST, the national body that oversees all research in the country. All research conducted among human

subjects in Uganda has to be cleared by UNCST, whether it is conducted by a local researcher or an international collaborating researcher or institution. It was a month before I received approval from UNCST. Next the proposal had to be registered with the office of the president of Uganda in charge of research. Each of these steps must be followed to gain permission to conduct research with human research subjects in Uganda.

After I received the final approval from UNCST and was cleared by the president's office I was given a letter introducing me as a researcher to the district resident commissioners (RDCs) so that my research could be included in the district records.

After receiving clearance from the national bodies I contacted the principal trial investigators at both sites and formally requested their permission to nest my qualitative study in their trials. The principle investigators are members of the MRC Science Committee. After meeting the two principal investigators I then started on the plans to start my data collection. The site principal investigators had to communicate about my research plans with the main study sponsors as both clinical trials were being conducted in collaboration with international partners. The process of gaining access to conduct the qualitative study within the clinical trials was rigorous but enabled me to appreciate what it takes to be involved in research. This was the first part of the informed consent process in my study, and took place before I even met the study respondents.

Access to the research team

On being given access to the trials by the sponsors I had to consider how to contact possible respondents for my study. The two study coordinators were my first link to the field research team; they organised meetings with the team where I presented my qualitative study and its objective and outlined the type of respondents that I required. In a sense I was like an MRC employee (an 'insider') but at the same time I was a student conducting research, and this had to be clearly understood by all study team members. As a student researcher I had to be careful how I positioned myself to avoid blurring my role as a researcher in order to gain access and information from my respondents, including my peers in the research teams. All the respondents in this qualitative study were purposively selected according to their role in the two trials. The research team that I interviewed were directly involved in conducting the trial procedures when my study begun. In Study 1 the team included three nurses; two counsellors; one clinician; two senior scientists and a community mobiliser who worked with the counsellor to reach potential volunteers in the communities. The senior scientists were in charge of the overall conduct of the day-to-day trial activities at the site.

In Study 2, I interviewed two counsellors who also doubled as health educators and were at the forefront of reaching out and meeting the volunteers; two nurses, two clinicians and a senior

scientist. Study 2 had no mobiliser because the volunteers are sourced from health outreach clinics by the health educators and nurses.

Access to the trial volunteers

I depended on the research team for access to the volunteers, and in particular on the nurses or counsellors who received the volunteers when they arrived for their scheduled visits. A nurse or counsellor would follow the planned trial procedures for that specific scheduled visit with the volunteer and then mention that there was some research going on and that if they were willing they could participate in it. Those who were positive about it were directed to me, usually led by the nurse or counsellor who would have spoken to the volunteer to the room allocated to me, where they introduced me as *omukyala ono* (this lady) or sometimes *omusawo ono* (this health worker) and told the volunteer that I would be talking to them about some research that I was conducting or asking them about what their experience of the trial. Then I was left with the volunteer.

After that introduction I would explain to the volunteer that I was a researcher, although they seemed to see me as an MRC employee because a research team member had introduced me. I noticed that some volunteers were anxious or suspicious until we had gone through the information sheet. I read the sheet out, regardless of whether the volunteer could read and write, and gave her/him a copy to follow as I read it. I allowed for interruptions with questions, but these were uncommon. The question commonly asked by the few volunteers who did ask was to do with how long the interviews would take and if they required giving any blood samples. They were not interested in giving any extra blood samples beyond what they were giving in their trials. I saw as I read out the document that some went over every word using their finger, following what I was reading. This indicated to me that although some volunteers may have been able to write or sign their names it did not necessarily mean that they could read well, which should be taken into consideration while providing them with information about the research.

After his introduction by the nurse one of the male volunteers told me that I did not need to read the information sheet and requested that I let him sign the consent form immediately, because he was happy to participate. I declined his suggestion and he agreed to listen as I read through the information. I realised that he was one of those who could read quite well. This volunteer's reaction exemplifies some volunteers' trust in the research team during the informed consent process and the research. It was my first interaction with this volunteer but he was ready to sign a consent form before I had even discussed the details of my study. There are two possible explanations: either he chose to trust me because I was introduced by a research team member that he already trusted, or he wanted to spend a short time at the clinic since this had become an additional requirement of his time.

The volunteers were selected purposely from the two trials that I targeted for my study. The cohort of volunteers for my study was of those whose scheduled visits were planned at the time that my study began. The nurses gave the clinic volunteers general information about the research and mentioned that it was a new study. Those who were interested in learning more about it were referred to me for more detailed information. After I read them the study information from the sheet that I gave them I enrolled those who were willing to participate and conducted the first interview with them straight away.

My initial target was to interview a total of 20 volunteers, 10 from each of the trials. I intended to interview them at three different points during their trial (at 0, 3, and 6 months). Once I had a total of 24 volunteers I realised that I was not collecting any new information about the informed consent process. I asked the nurses and counsellors to stop referring volunteers to me for interviews. I recruited the volunteers within the same time periods at each site to enable me to plan the follow-up interviews.

Access to ethics committee members

To the SEC I was both a student researcher and a colleague and my entry into this group of respondents was not complicated, although I had to explain my study in detail before seeking their participation. The SEC was not attached to any of the studies but had approved both trial protocols before they were implemented. The SEC members knew me from the three years I had sat on the committee as a social scientist before embarking on my PhD study. I had a meeting with the chairman of the committee prior to the start of my study after the committee had approved my study. I discussed with the chairman my selection of SEC members for interview and then made individual contact with each of them to schedule the interviews.

I targeted at least five committee members for interview, selecting them purposively according to their expertise. The SEC has eleven members, including a male and a female community representative. I selected the chairman and their deputy, the former being a statistician and the latter a public health specialist; the regulatory officer, who is a social scientist trained in bioethics, a clinician/physician who is an epidemiologist; and the female community representative to help the gender balance, because most of the other respondents are male.

Access to the Community Advisory Board

I was introduced to the Community Advisory Board (CAB) of study by the community liaison officer (a study team member) who works closely with the board. He introduced me briefly to the members, who had been invited to meet me, and left me to describe my research to them

and request their individual consent to participate in my study. Although I was known to one of them I had never directly interacted with any of the board members in my previous research.

The community advisory board (CAB) members for Study 1 were all invited to take part in my study. Fourteen of the fifteen board members invited to attend a focus group discussion for my study turned up. The focus group consisted only of these board members and myself and my research assistant.

The CAB members included a senior medical officer from the district medical office, two nurses representing health units in the trial study area, a media representative, three religious leaders (Anglican, Catholic and Muslim), a counsellor, three political leaders, two of whom were women representatives on their local community councils, two representatives from sister non-government organisations (NGOs) working in the same study area, and a lay community member.

3.5 Research activities in the field

Interacting with the research teams and the volunteers offered opportunities to listen to what was said in one-to-one interactions and in groups and in the clinic corridors and in the waiting rooms. I was able to observe what goes on as the volunteers wait to go in to see the research team and discuss with the actors where I needed any clarification about the informed consent process. Taking part in and recording interactions between and with the actors at different times during the study allowed me to examine the meanings they attached to the informed consent process, how they understood it and how their understandings related to my study concepts.

My data collection strategy was to begin by interviewing the volunteers, as the process of getting the final ethical approval had been lengthy and one of the trials was due to end in about nine months. I had to start recruiting volunteers immediately as I intended to interview them at least three times at intervals of three months. I held the first interview on the day they agreed to participate in the study, followed by a second three months later and the last after another three months. I collected data on each volunteer's experiences of the informed consent process over a period of at least six months. I held focus group discussions with all the trial volunteers a month after I had completed all the follow-up interviews.

My interviews were scheduled for the dates on which the volunteers came to the clinic for their scheduled visits, as shown on their individual volunteer clinic study cards. I had to adhere to this, otherwise it would mean trying to mobilise volunteers for this qualitative study separately and I would miss the opportunity of including the volunteers in the clinic trial that was soon to end. If I gave them different dates for my interviews I would also have to refund their transport costs which were not logistically feasible for me because some of them lived far from the

research centres. I used the same strategy to interview the volunteers for both trials, even though the second trial would continue for another two years. I wanted to enlist volunteers from both trials whose visits were scheduled during the period of my study. The other reason for keeping my interviews in line with the scheduled visits to the clinic was to avoid taking up the volunteers' time, as I had been informed by the research team that the majority were employed or self-employed and planned their clinic visits in advance.

Since my study was nested within the two HIV clinical trials I had to schedule my interviews to follow the already planned trial procedures to avoid disorganising the volunteers, who already knew when they were expected at the clinic. The clinical trial research activities are planned according to the research protocols which state when certain procedures are to be carried out. The research teams use the trial protocol to produce a clinic visit schedule for each of the research volunteers in the trial. Scheduled visits are usually more frequent at the beginning of a study, occurring at least once a month for the first three months after enrolment with follow-up visits scheduled every three months, as was the case in the two case-study trials. These schedules may differ from trial to trial depending on the trial protocol, but all the volunteers in the two trials in my study were being followed up every three months at the time when my qualitative study commenced.

The procedures for the volunteers at the clinic usually involved seeing a study physician, with the women giving samples such as of blood and urine. And the men give blood samples. They also attended counselling sessions at which the trial information was discussed and underlined and they could discuss any concerns they had and attend structured follow-up interviews. In one of the trials (study 2) the volunteers got their study drugs when they attended for their scheduled visit. I interviewed them after they had gone through their clinical procedures scheduled for that visit, and then they would leave the clinic. In a few instances I interviewed volunteers between procedures because there was a long wait, thus reducing the time they had to spend at the clinic. Figure 2 shows a timeline of my study activities.

Activity													
	1	2	3	4	5	6	7	8	9	10	11	12	13
Ethical clearance													
Translation of documents													
Interviews, focus group discussion, on-going analysis													
Analysis													

Figure 2: Timeline of study activities, August 2011-October 2013

Table 5 gives the number of respondents interviewed and the methods of data collection:

Activity	Study Site	Category of respondent	No. of respondents	Gender	Age
In-depth interviews (audio-	1	Senior scientists	2	М	N/A
recorded)		Counsellors	2	M, F	
		Nurses	3	F	
		Clinician	1	M	
		Community mobiliser	1	M	
		Volunteers	13	7 M, 6	18+
				F	
In-depth interviews (audio-	2	Senior scientist	1	М	N/A
recorded)		Counsellors/health	2	M, F	
		educator			
		Nurses	2	F	
		Clinicians	2	F, M	
		Volunteers	11	3M, 8F	18+
- II		<u> </u>	0	4 5 4 5 5	
Focus group discussions	1	Volunteers	9	4 IVI, 5F	
(audio recorded)		САВ	14	/M,8F	
	2	Voluntooro	7	114 6 5	
	2	volunteers	/	11VI, 0 F	
Observations	1	Volunteers and research	5	3F,2 M	
	2	team	5	2M,3F	

Table 5: Data collection methods in this study

In addition to collecting direct information from the different actors, I reviewed several documents to understand the two trials and how they were being conducted. Documents reviewed include; the consent forms, the SOPs, the trial protocols, and recorded reports of meetings held between the research team and the volunteers. I read through the national and international ethics guidelines and the SOPs that the ethics committee uses.

I held meetings with various researchers to gain entry access to the other actors and these meetings included a meeting with the senior principle investigators for each of the trials. I presented my protocol to the MRC/UVRI Science and ethics committee, I held a meeting with each of the trial coordinators, a meeting with the chairman of the UVRI ethics committee, a meeting with a community liaison officer of one of the trials and a meeting with the research teams.

Two of the volunteers who were potential recruits for my study declined the invitation to participate. One was a male in Study 1 and the other, a female in Study 2. They both declined

after I had provided and read through the study information. The female said that she did not have the time and the male that he was not willing to commit himself to new research.

Recruiting the respondents for my study was not a fast process. I had to make appointments to interview the research team and ethics committee members. I tried to schedule the interviews with the research team members at each site as close together as possible as the sites were quite a distance apart. I waited for opportune times when the teams were not overwhelmed by the number of research volunteers that they had to see, and I avoided interrupting trial procedures.

I depended on the trial volunteers agreeing to take part in my study, but it was sometimes difficult to contact them after the first interview because I was dependent on their keeping their appointments for my follow up interviews. It was not always easy to recognise them in a big group after having interviewed them only once. Some of the volunteers wanted to leave immediately after completing the clinical procedures. I therefore had to be very keen in following up their scheduled visits to the research team in order to know which volunteer was going to come and when. I missed some follow-up interviews because the volunteers came in at unscheduled times when they felt unwell and needed to see a physician; usually when such visits are close to the time of a scheduled clinic visit the research team can carry out the procedures intended for the scheduled visit to avoid the need for the volunteer to return a few days later. The research team was very helpful; reminding volunteers at their scheduled visits that I would like to see them. Some volunteers kept my appointments for the follow up interviews without needing to be reminded.

I had originally planned to interview at least ten spouses or close friends of the volunteers about what they think about their partner's involvement in a clinical trial, but I only managed to interview five. The volunteers kept promising to encourage someone from their family/friends network to come for an interview but it did not work out so easily. A few of the volunteers told me that no one could talk about their involvement in my study because they had not told anyone about their participation in the clinical trial. The volunteers were the gatekeepers to their spouses and friends and held the power in this case, so I could not interview the spouses/friends.

3.6 Data collection methods

3.6.1 Interviews and focus group discussions

To gain an understanding of how the informed consent process was experienced and interpreted by the respondents in the two HIV clinical trials I conducted semi-structured and indepth interviews with them all apart from the CAB members whom I wanted to conduct a focus group discussion. The interviews were semi-structured so that I could ask all the different

respondents in my study a similar set of questions. The semi-structured interview allows each actor to discuss their experiences and interpretations of the process in their own words without limiting their responses on the informed consent process. I conducted in-depth interviews with the research team, the ethics committee members and the research volunteers, and held very short interviews with the small sample of spouses and friends.

I held a focus group discussion with the CAB of one of the trials. The other trial did not have a CAB in place because it recruited volunteers from the health outreach programmes of other intervention organisations which may have had their own advisory boards, but I did not talk to these; I remained in the setting of the clinical trial in which my study was nested.

I held focus group discussions with the volunteers that I had interviewed to allow for more general accounts and insights into the informed consent process (Uwe, 2007). I invited all the volunteers, but some were not able to attend. The use of the two data collection methods for the volunteers enabled me to analyse the informed consent process both as described and experienced by them individually and as reported as a group which allowed for flexibility and discussion with other volunteers (Uwe, 2007; Kielmann, Cataldo and Seeley, 2012). I highlighted major topics for discussion with the interview and focus groups (see Appendix 3 for the guides).

3.6.2 Observation

I carried out unstructured observation (Kielmann, Cataldo and Seeley, 2012) at the research clinics, targeting observing the research activities and gaining insights on interactions between volunteers and the research team and among the volunteers themselves at the clinics. In my observation of the volunteers I followed the flow of what happened when they came into the clinic. In general they would meet a nurse on arrival and sign in or report their presence and be recorded in an attendance book, and then the nurse would prepare their files on a first-come-first-served basis. The nurse would ask the volunteer to sit and wait until called to start going through the planned procedures.

There is a waiting room at each of the study sites. At the site of Study 1 the waiting room is a big room in the form of a lounge with plastic chairs and the trial team's office attendant provided tea at a large table nearby, usually with some bread. At the site of Study 2 the waiting room is an open space with benches, with a small tearoom nearby where the volunteers could buy tea, coffee and snacks, and the office attendant provided drinking water. Both waiting rooms have a television set and volunteers watch news, soaps, documentaries or whatever is available at that particular time of the day.

I observed some volunteers talking to each other in the waiting room while waiting their turn and laughing at something fun on the television; others were quiet and reserved. The environment at the site of Study 1 was more relaxed because there was more space in the room where the volunteers waited to go into the next room for the procedures. At the site of Study 2, after being called from the general waiting room the volunteer had to sit in a long corridor waiting to be called to the nurse/counsellor or clinician's room. The corridor had chairs placed along one wall, leaving room for only one person to walk to and from the different clinic rooms at a time (in my estimation the space was probably less than a metre wide). While sitting in line along one side of the corridor there was little conversation apart from that between close neighbours. I observed some tense facial expressions; other volunteers were quiet and looked closed-in as they waited to be called. The only movement happened when someone's name was called out and they had to go to another room or when a member of the research team moved from room to room. The place was usually very busy. I never observed what went on once a volunteer went into a counsellor and clinician's room because of confidentiality between the counsellor/clinician and the research volunteer.

At study site two, my office space was detached from the main clinic building. It was a good place from which to watch the volunteers arrive. At the study site one, I sat far from the entrance to the clinic and did not see what happened as a volunteer came in for their clinic visit. At both sites I continued to observe the interactions between the research teams and the volunteers as I moved around the clinic.

At study site one, I attended a meeting between the volunteers and the research team which was held at the research clinic, the field research team was represented by the community liaison officer and a senior study investigator. The objective of this meeting was to follow up on what was happening in the community in general and discuss any concerns that the volunteers might have. As a participant observer I greeted the volunteers and introduced myself, as was expected of all those present at the meeting, and then listened to the discussion. I did not make any suggestions during the meeting, which had been planned before I started my study, so I was able to observe and listen to the discussion, which helped me to prepare for my study. The volunteers raised questions about the study procedures, and particularly about when the trial would end and what would happen after it ended.

Besides listening to the narratives spoken during the interviews, being part of the research context and being able to observe what happened at the sites and the interactions between the different actors and actor groups helped me to understand the possible reasons behind what happens during the informed consent process in a clinical trial.

3.6.3 Review of documents

Studies are conducted based on what is laid down in the protocols, which document all the procedures to be carried out. In this qualitative study I reviewed some trial documents that

included trial protocols, participant information sheets and the SOPs for informed consent. I also reviewed recordings of follow-up meetings between the research team and the volunteers; the SOPs and national research ethics guidelines on informed consent for the SEC; and international guidelines for conducting research on human subjects, including documents such as the Belmont Report and the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and Council for International Organisations of Medical Sciences (CIOMS) guidelines. Documents exist as social facts- they reveal what happened (Silverman 1997) so it was important for me to review these for my study (see Table 2 for details of the data collection).

3.7 Data analysis

My plan was to review the data as I collected it, picking up the emerging themes, issues and meanings that were coming through the data on the informed consent process. I asked the research team to clarify information or procedures that were not clear to me. I was iterative with the research volunteers in the way that I collected data; as I held more than one interview with each of them I analysed what came out of each interview, which created additional angles for the next interview I held with them to clarify or engage more deeply with issues that were impinging on the informed consent process (Mason, 2002, 2007; Watts, 2014; Denzin & Lincoln, 1994). I looked out for patterns emerging from the experiences of informed consent discussed by the different actors. Thinking through my data as I collected it was useful as I was able to see themes unfolding and to begin to create a coding frame for use later with NVivo, a qualitative data analysis computer program. I started linking the actors' experiences to the concepts I was studying: beliefs and values, power, gender, trust and decision-making. This led to my initial codes, which later contributed to the broad themes that guided my interpretation of the data.

After I had collected data from the respondents, who were all actors in the informed consent process, I picked a sample transcript from each group of actors to identify developing themes. I picked the transcripts of a male and a female volunteer and those of a senior scientist, a clinician from each of the trials, an ethics committee member and the CAB focus group discussion and read through each transcript. While going through the extracts I followed up what my respondents were talking about the informed consent process and this helped me to generate more labels or codes for the themes that were emerging. I used coding in the sense that Coffey and Atkinson (1996: 26) refer to it: 'assigning tags or labels to data', and to help me to reduce the data to understandable chunks. Coding helped me to understand and generate the themes developing in the data. Beyond simply labelling or categorising the data, the codes began to point to some of the topics and themes of my study. I used inductive coding where the data collected led to the codes that I developed for my study (Watts, 2014). I linked the codes to the main discussion topics that I had outlined in the interview and focus group guides.

After analysing my first scripts manually and identifying some of the main topics emerging from the data I imported the transcribed interviews and focus group discussion scripts into NVivo 8, which enabled me to quickly code and analyse the data that I had collected. I worked with NVivo 8 because at the time of data collection and analysis I was conversant with this version. I started checking the data for patterns, similarities, differences and common and uncommon issues reported by the different actors in the informed consent process. After coding or labelling my data sets I started to think through the emerging themes and sub themes and to look for links to my research questions. The major themes that I picked up in the data are reported in the chapters containing the findings of the study.

3.8 Data presentation

The data in this thesis is presented mainly in textual form including some quotes from the respondents. While interviewing the respondents my questions were mainly semi-structured and open-ended to allow them to explore all their experiences and interpretations of the informed consent process. Based on my conceptual framework, I analysed the experiences, meanings and interpretation of the informed consent process by the different actors linking them to the concepts in the study which are: values, beliefs, decision making, trust, power and gender. I analysed what influenced the informed consent process from within the family and the community study setting and the set policy guidelines for conducting HIV clinical trials. The data therefore appears in the form of narratives. The volunteers' experiences are narrated in such a way that they flow from their life histories in relation to HIV. They describe events that happened in the past, current events and their expectations about their future participation in a clinical trial. The other actors' narratives, including those of the research team, emphasise what happened as they followed the study protocols during the research process. The data is deep and enriched by individual experiences of the informed consent process beyond the structure of the trial in which the actors had a role.

The data as presented in this thesis indicates which group the actor is from: a research team member, ethics committee member and so on. The names that I use for the research team, the senior scientists and ethics committee members in the findings are not their own. I use names to allow the reader to experience the discussion in terms of the roles of the different respondents in the clinical trials. I also avoid using the volunteers' names but indicate their gender and age and which trial they participated in as their main identifiers. I have called the trials, Study 1 and Study 2; both are HIV clinical trials but they have different aims and objectives as I discussed in chapter 1. The intention behind referring to Study 1 or Study 2 is to enable the reader to differentiate the responses of the different actors.

3.9 Conclusion

Conducting a qualitative study within a clinical trial is not straightforward. It requires negotiating most of the time and the researcher clearly feels the power dynamics among the actors. Nesting a study within an already existing clinical trial requires that the researcher works closely with the trial research team because the research team has already set its agenda for the trial and the nested study is an additional procedure.

Conducting a study of the informed consent process and having to obtain consent from the potential participants was an interesting experience for me as a researcher because I had given my respondents study information and they knew that I was going to interview them on the topic of informed consent. The experience showed me that the rapport that a researcher creates with the respondents while collecting data is very important.

The value that a respondent may attach to a given study can be felt even in qualitative research such as this. Values and power became clear to me as concepts in this study, as I negotiated for access to the clinical trials and as I interviewed and followed up the research volunteers. The informed consent process can be compromised by the actors; as for example my own experience when a volunteer wanted to sign the consent forms before hearing the details of the study. The informed consent process cannot be taken for granted in clinical trials because it involves far more than just signing a form at the beginning of the research.

The next chapter examines the findings of this study on the ethics of biomedical research, as discussed by the respondents.

Chapter 4: Research ethics and actors' roles in the informed consent process

In this chapter I analyse my findings on the review of proposed research protocols and the place of informed consent in that process in Uganda. My data are drawn from interviews with Science and Ethics Committee (SEC) members and senior scientists who, in their discussion of their experiences and how the review process has developed over the years, provided the background to medical research ethics, the protocol review process and the guidelines used for this in Uganda. The views expressed by the senior scientists and SEC members lay the foundation for the material on the informed consent process in HIV clinical trials in the chapters that follow.

The findings presented in this chapter help me to answer the research question 'How have biomedical research ethics evolved in terms of the research principle of informed consent? 'I discuss how medical research ethics have evolved over time in Uganda and the debates and challenges involved in the protocol review process. I conclude the chapter with scientists' and SEC suggestions for improving the protocol review process.

4.1 Background to ethics review boards and guidelines in Uganda

Medical research has been on-going for many years in Uganda. Because of HIV and AIDS in Uganda and other countries especially the sub-Saharan Africa countries in the I980s, researchers had to be involved more in comprehensive control programs to tackle the epidemic. This led to a need for more vaccine and drug trials particularly in East Africa (Ndinaya-Achola, 1991). At the advent of protocol reviews in the early 1990s there were no guidelines; protocols were processed by the Ministry of Health (MoH), which had constituted an AIDS research committee in 1986 as a direct result of the rise in AIDS-related research in that decade, prompting the creation of formal guidelines for reviewing research protocols. The AIDS research committee became the National AIDS Research Committee as a result of the joint effort of MoH, the Uganda AIDS Commission and the Uganda National Council for Science and technology (UNCST) in the 1990s. The National AIDS Research Committee currently operates as an institutional review committee under UNCST.

The Uganda Virus Research Institute (UVRI) was established in 1936, with funding from the Rockefeller Foundation, to support research on yellow fever, and since then its scientists have been conducting scientific research on communicable and particularly viral diseases. Collaborative research began at the Institute after the discovery of HIV in the late 1980s and
early 1990s, between the Rakai project (later the Rakai Health Sciences Programme) and the MRC Programme on AIDS in Uganda (later the MRC/UVRI Uganda Research Unit on AIDS), the United States Centre for Disease Control and Protection (CDC) and later by the International AIDS Vaccine Initiative (IAVI).

At the start of the 1990s scientists at UVRI realized the need for a protocol review of studies by local researchers or in collaboration with international partners. Led by the UVRI director and heads of collaborating programmes on the UVRI campus, they formed the UVRI Science and Ethics Committee (SEC) to review research protocols. According to some of the SEC members that I interviewed the first SEC was formed in 1990, mainly composed by the heads of the research programmes based on the UVRI campus. The committee comprised seven members including two sourced from the community by the director of the Institute. Over time the committee has grown and it currently has eleven members including researchers from research programmes on the UVRI campus and at Makerere University, these include: statisticians, clinical officers, a nursing officer, a social scientist, a microbiologist, an immunologist, a laboratory technician, a public health scientist and two community representatives from the Entebbe community which is one of the research areas that MRC/UVRI targets, and this is where the Institute is located. UVRI SEC is now one of many institutional research ethics review committees in the country, some of the others being Makerere University, Mulago Hospital and other research organizations such as the Joint Clinical Research Centre (JCRC) in Kampala. These and many other research ethics review boards are coordinated by UNCST, a Uganda government agency operating from the Ministry of Finance's Planning and Economic Development.

UNCST was established in 1990 to facilitate and coordinate the development and implementation of policies and strategies for integrating Science and Technology (S&T) into the national development process. One of the services it offers is research and development (R&D) registration and oversight. Once a protocol has been reviewed and approved by the institutional review board, the researcher concerned must forward the protocol to UNCST, which has a committee that reviews and records all the research protocols in the country. The committee at UNCST works with the President's office to approve the conduct of any given research in the country.

4.2 Evolution of protocol reviews

The SEC members in my study reported that research ethics in Uganda is both new and evolving. Before 1992 research was not reviewed by an institutional review board and it is therefore possible that unethical research may have occurred in the country in the 1980s which was not followed up and the ethics committees were just getting into place. There was also no documentation, as there were no firm regulatory guidelines.

All the SEC members and scientists interviewed mentioned HIV and AIDS as one of the main triggers for the rigorous protocol review process that began in the 1990s. Large numbers of people were getting infected with HIV and there was therefore a growing need to conduct research, but also to protect research volunteers. The review process at UVRI began by considering whether the science contained in the protocols was doable, beneficial to the investigators and likely to be beneficial to those who were being researched upon.

The international regulations and guidelines already in place in Europe and North America were slowly adopted as the SEC continued to review protocols at the Institute. The review of research protocols by the SEC was because research was being conducted through collaborating with researchers and partners from outside Uganda at the time, which included researchers from the US and UK who would not have any knowledge about the social context of the research. Training in ethics was minimal at the inception of the SEC; what was important to the review board members at the advent of the protocol review process was training in their responsibilities. A community committee member who was part of the first SEC recalled that her training had mainly been in ensuring that research was not going to harm the community members who would participate.

Some of the respondents considered ethics a discipline that has been imported into the country. As one committee member said:

We are importing [ethics] with the funds, the protocol and the whole concept of collaboration as a package... The boom in ethics is like the boom in HIV; that is where we saw a lot of collaboration and importation of research coming in Uganda.

This statement by a SEC member shows that the committee has been dependent on the guidance of outside researchers through collaboration. The committee receives funding from collaborating programmes to facilitate the secretariat at the Institute. The research collaborators bring to the table knowledge of how to review research protocols, and this has influenced how ethics reviews have evolved in Uganda. It has the advantage of giving the committee some international guidelines to follow while reviewing protocols; however the quote from the SEC member above may also point to the fact that the review processes do not entirely fit the local context in Uganda; Ugandan committee members have to be careful that the protocols approved during the review process are suited to the sociocultural context because research funds are usually provided by the collaborating partners.

The field of research ethics has continued to grow and more changes are occurring in the review process. According to the scientist respondents the ethical review process has become tighter, with protocols reviewed by both the UVRI's SEC and UNCST. The SEC has also begun conducting monitoring visits to see what is happening on the ground and interacting with

volunteers with the aim of ensuring that they are protected from any form of harm (physical, emotional and social harm) during the research in which they are participating. Scientists mentioned that the current SEC are 'competent members' because the majority of them are researchers and have had training in research ethics as a committee, and noted that there is currently a fast turnaround of the protocols sent to UVRI SEC for review.

Several of the scientists interviewed reported that the International Conference of Harmonisation's (ICH) Good Clinical practice (GCP) guidelines have been helpful as they prepare for research and ethics committee reviews of their protocols. The scientists in both the trials that I studied used these guidelines as their main reference to good clinical practice when conducting clinical trials. Good clinical practice guidelines include the protection of the human rights of subjects involved in trials. The GCP guidelines provide information on how to follow up on the safety and efficacy of newly-developed drug compounds and standards for how clinical trials should be conducted, and define the roles and responsibilities of the sponsors, clinical investigators and study monitors involved. According to the scientists interviewed, the guidelines contain a detailed summary of what a good informed consent procedure should consist of, the information it should contain and how it should be administered.

The SEC members noted that there is more access to information through the Internet and international collaborations that have developed over the years between review committees than there was a decade ago, and that this has enabled greater understanding of ethical issues. UNCST conducts regular audits of on-going research in the country and is introducing training on the ethics of using human subjects in research as a requirement for everyone doing research in Uganda.

The SEC members reported some challenges in the implementation of the review process, which is still evolving. One scientist reported that although the GCP guidelines are quite helpful when conducting trials, they provide little guidance on how to assess volunteers' understanding of the concept of informed consent. The GCP guidelines are a set of regulations developed for clinical trials, some of which do not suit social science or even some epidemiological research, but all researchers are increasingly expected to follow them. A SEC member noted that there is no formal curriculum targeting training for research assistants and research fieldworkers. Training on ethical issues in research is mainly focused on scientists and study coordinators in the hope that they will pass it on to their research teams.

There is still no national policy on ethics for human research subjects in Uganda, although the SEC members hoped that this would soon change. The first version of the ethics review guidelines was developed in 1997, according to a SEC member, and the current version was revised in 2007 by a large task force that included scientists from Makerere University, Mulago Hospital's Medicine, Public Health and Paediatrics departments and members of other research

organizations such as the JCRC. Many gaps are still being identified in the guidelines and the necessary adjustments will soon be integrated by UNCST. My respondents reported that there are funding challenges in the field of ethics, preventing the speedy training of committees and researchers.

In the next section I discuss issues of research collaboration and how the researchers and the SEC incorporate collaborator's issues into the review of the informed consent documents.

4.3 Collaboration and partnerships in ethics

As noted above, most research in Uganda is conducted in collaboration with partners from Europe and North America. The scientists and SEC members noted that most research globally, even in very well-resourced settings such as Europe and North America, usually involves collaboration and partnerships. The SEC members in this study viewed collaboration in research ethics as important, but mentioned that local researchers in Uganda need to discuss the protection of Ugandan research participants with their partners. The scientists emphasized the importance of beginning the review of research protocols with a thorough discussion of the methodology and ethics of a protocol by a science committee in the organization that is to conduct the research. After a protocol has been reviewed at this stage, it would then be forwarded to the UVRI institutional ethics committee. After the UVRI ethics committee has reviewed the proposal, it advises the researcher to send the protocols to Uganda's National Council for Science and Technology for final approval. They suggested that this way of working would help the local researchers to manage collaborations better because they and those with whom they collaborate would appreciate the systematic research ethics review.

The SEC members reported that most research, and particularly HIV and AIDS clinical trials, is externally funded, meaning that ethics committees have to adopt the external standards of the collaborating partners because the protocols are usually prepared by the senior principle investigators of the studies who are collaborators from Europe and North America. It is therefore important to consider the Ugandan cultural context in detail during the review process to ensure that research participants are protected from any form of locally-specific harm.

The ethics committee review process is formal. Each committee member is tasked with reviewing the whole protocol, although a few members with expertise in the given study area take the lead in the discussion. Elements such as the target group, what the study may contribute to current knowledge, the stated possible outcomes of the study and what these mean for the research volunteers in the long term are discussed at length to ensure that the science behind them is feasible. The scientific aspects are usually discussed before turning to the informed consent documents.

4.4 Current debate about informed consent

One of the important aspects of a protocol is the information presented in the informed consent documents. This must be clear to the ethics committee as well as to the research volunteers. There are various global debates about the informed consent process, including how to appropriately manage the bureaucratic and perhaps too inflexible ethics regulations that are applied to research, whether biomedical or ethnographic in nature (Murphy & Dingwall, 2007); and whether the rational model of informed consent is suitable for communities that offer few healthcare alternatives for potential research participants, particularly in terms of treatment and care (Molyneux et al., 2005). There is also debate about how best to ensure a participant's full understanding of the study information and the decisions they need to make (CIOMS, 2002).

While discussing informed consent process questions that are specific to the Ugandan context, SEC members stressed the importance of ensuring that research volunteers have understood the information given to them about the research in which they are thinking of enrolling. The low level of literacy of the majority of research volunteers, particularly in some rural communities, was the main reason attributed to why they never question some of the information discussed early on in a study. Volunteers do not refer back to documents, and the study information is communicated only verbally to the illiterate volunteers by the research team although a written copy of the information sheets is given to them to carry home. One scientist expressed this concern:

It's difficult to know whether, when a volunteer consents, they have actually understood the contents of the informed consent document or what the whole process of the trial entails; [this] may or may not be a problem in the West where people have high levels of literacy.

This is a difficult question from the researcher's point of view, as the best person to answer it is the volunteer.

The second issue for debate that the SEC members mentioned is how to balance research volunteers' need for medical care and their understanding of the demands and requirements of the research in the Ugandan sociocultural context. One SEC member said: 'Poor people are so desperate to get treatment and would rather have a steady supply of drugs whatever the cost; you don't know whether their consent is fully voluntary'. Because of the limited availability of adequate services, particularly in rural communities where most research takes place and where the people are poor, participating in medical research can offer crucial access to better medical care without pay and the opportunity to see a clinician.

The SEC members particularly noted the absence of a policy guideline in research ethics involving human research subjects. The existence of such a policy would facilitate discussion between ethicists, scientists and civil society to ensure that research with human research subjects in Uganda is ethical. The SEC hoped that such a policy would soon be tabled for discussion by the country's legislating body.

One scientist commented during an interview that the only controversy reported concerning studies in Uganda was about the lack of proper documentation of the data-collecting process in an otherwise credible study of Nevirapine (Guay et al., 1999). It turned out to be a breakthrough study, and the lessons learnt from the findings have influenced clinician's practice in Uganda in the handling of HIV-positive pregnant mothers to prevent mother-to-child transmission of HIV. A policy and guidelines on how to manage the ethics during research would prevent such problems occurring in clinical trials.

4.5 Ethical challenges in implementing the informed consent process

One of the particular challenges noted by the SEC members is ensuring that research participants can distinguish research from healthcare, particularly when there is a conflict of interests, and particularly in rural areas where a local health unit which is also used for research is never able to provide a certain service, but is seen to provide it in medical research conducted in the same unit. A SEC member commented:

... because there are no services in [the community health centre] and there are services at the research clinic, people would rather participate in research because they don't have many options for accessing appropriate healthcare.

Similarly in Kenya participants found it difficult to distinguish research from health interventions taking place in their communities (Molyneux, et al., 2005).

A further challenge is the provision of compensation for volunteers participating in research. A committee member asked: 'When you try to compensate someone, is that coercion?' It can be difficult for poor people to differentiate between coercion and ethical compensation.

The SEC members noted that researchers are increasingly seeking volunteers' consent to store their blood samples, even without the researcher being clear about what they will be used for.

The scientists discussed further practical challenges during the informed consent process, including translating the informed consent document into the local language before they send it to SEC for review and accurately capturing all the aspects originally developed in the English document, and not knowing whether the tools they use to assess volunteers' understanding of study information simply test their ability to recall it accurately. Assessing volunteer understanding of key information in the two trials was different. For study 1(trial 1) there were

pre-set questions which required a volunteer to respond by indicating whether a statement read to him by the research team was False or True. In trial 2, it was upon the clinician to ask some questions to ensure that the research volunteer has understood the study trial.

The challenge to adapt to some documents and forms formulated by the collaborating partners is most clearly seen in participant information sheets which can be very long, making it difficult for the volunteers to take in and understand. It becomes hard to differentiate between a volunteer who has understood the information and one who has recalled what they have been told a few minutes before assessing their comprehension because the documents are usually long. A SEC member said:

Once we received a consent form which was about 12 pages long. The research idea could have been explained in only two pages showing [the reasons for the research] and why the volunteer was being asked to participate.

Although these challenges are real to the SEC members, they noted that as most protocols are implemented in collaboration with European and North American partners and there is no tested Ugandan framework they have to adopt the ethical standards set by their partners, whose countries already have a framework in place.

4.6 Suggested improvements to the review process

The scientists participating in this study suggested that for a thorough review of protocols the ethics review should commence internally within the main research team before sending the protocol to the main ethics regulatory bodies.

The SEC members suggested that researchers should make the effort to translate difficult medical terms into simple words that are easy for all volunteers to understand; for instance, instead of using the word 'randomization', explaining exactly what is going to happen: 'two groups are going to participate and they may not be given the same drug'. Lengthy information forms should be avoided and instead participants should be given information sheets with 'simple content to facilitate their comprehension of the study.

They suggested that researchers should ensure that the wide communities from which research volunteers are sourced are made aware of trials planned for a given community and why they are being conducted before the trials begin, to prevent misperceptions of the study information which could in turn impact on the implementation of the research. One SEC member reported a scenario where a study was brought to an end because two participants had died. The trial was stopped by the political authorities but after further investigation into the nature and causes of death, the deaths were found to have had nothing to do with the

research. The ethics committee that had approved the study was asked to explain the conditions of its review to the politicians.

The SEC members noted that although it is not a common practice, there have been occasions when they requested a change to certain protocols and the collaborating partners undermined their suggestions and went ahead with the research after going to another review board for a more favourable ethics review. The SEC members suggested that all collaborating partners and funders should respect the review committee that handles a given protocol and avoid taking directions that are contrary to the suggestions of the IRB and Uganda's standardized national research ethics guidelines.

They proposed that ethicists should come up with a model policy framework to show collaborating partners how to conduct their research and request volunteers' consent in a way that suits the Ugandan context, and that researchers should try to balance the benefits of their work with the potential harm to volunteers. Consent forms should not offer too much detail: statements such as 'If anything happens to you...' are for the protection of the researcher and do not benefit the volunteer. According to one SEC member the volunteer 'needs a simple form that explains...why they are being invited [to participate] and ensures that they understand the research'. It is important to avoid overloading the volunteers with unnecessary information.

4.7 Conclusion

Ethics reviews of medical research in Uganda are evolving and are usually implemented in collaboration with partners from the West. The process of informed consent is embedded in the protocol review process to ensure that research volunteers are protected from harm and are given adequate and understandable information about the study. Ethics review committees working in partnership with others must ensure that imported ethics are not adapted wholesale without considering the context in which the research subjects are recruited.

The informed consent process is central to but not the only aspect to be discussed during the review process. The lack of a national policy framework to manage the review process for all research targeting human subjects leaves room for misconduct in research and for protocols to be implemented without an ethics review.

The SEC members and scientists who participated in this study all emphasized the importance of following the ethical guidelines in medical research; however, the findings have shown that the topic of research ethics is perceived differently by the different actors in the informed consent process. This has led to some researchers whose protocol is challenged by the ethics committee resorting to seeking ethical approval elsewhere. Having discussed ethics in medical research as described by the SEC members and scientists in the Ugandan case studies, the next chapter discusses the meaning and interpretation of the informed consent process by the different actors.

Chapter 5: Meaning and interpretation of the informed consent process

Introduction

This chapter focuses on the meaning and interpretation of the informed consent process in two HIV clinical trials in 2012 in Uganda. It addresses my research question 2.

How is the informed consent process in HIV clinical trials defined and interpreted by the different actors? (What is the process of informed consent? What is the role of the different actors in a clinical trial?).

The findings presented here identify how the actors defined the consent process and offer their comments about their roles and procedures in the informed consent process. I discuss this process in relation to Appelbaum et al. (1987) process model, which emphasizes continuous communication between the physician and patient or the researcher and research volunteer to enhance decision-making by the research volunteer.

This chapter discusses the different actors' definitions and interpretations of the informed consent process and explores how they implement it. The chapter concludes with an examination of the roles of the different actors in the informed consent process.

5.1. Actor's definition of the informed consent process in HIV clinical trials

This section explores how the informed consent process is defined by the different key actors and what they see as critical in the consent process. I examine the roles in the informed consent process as stipulated by the actors, and how each views the process from their own perspective.

Appelbaum et al., (1986 & 1987), the academic researchers who collaborated on empirical and theoretical works on informed consent, see informed consent as involving three main elements: sharing information, comprehension, and the voluntary participation of volunteers. They see it as a process that involves deliberation and discussion, the assessment of understanding, choices of participation by the volunteers and eventually some form of authorization by the volunteer, usually through signing a consent form (Beauchamp & Childress, 1994).

The findings in this thesis are specifically related to the context of Uganda, where the study was conducted. The Uganda National Guidelines for Research involving Humans as Research

Participants guide researchers handling the informed consent process. The guidelines outline the importance of respect for persons and state that 'research participants [must] be given the opportunity to make choices about what should be done to them' (Uganda National Guidelines for Research, 2007: 23). In the same guidelines, consent is defined as '... not just a form or a signature (mark) but a process of information exchange between the researcher and the research participants on the whole research process' (p.23). This is similar to the Belmont report of 1978, which was instituted as a primary ethical framework for protecting human research subjects in the US and is usually referred to in research ethics dealing with human research subjects and how they should be treated. The report asserts three central principles in research with human subjects: respect for persons, beneficence, and justice. The first of these, respect for persons, is central in the informed consent process (Belmont Report 1978).

There is evidence, however, that the way informed consent is defined may vary from individual to individual. A report from a seminar on informed consent held in New York with participants involved in informed consent process issues showed variability in the way they defined informed consent (Wood et al., 2001). In my findings there were variations of what was emphasised by the different actors when defining the informed consent process.

To frame the informed consent process in this study, I started by investigating how it was defined by the different key actors in the two case studies reported in this thesis. When I asked the research team to define the informed consent process some expressed surprise, probably because they are involved in the consent process daily in their work. Most research team members defined it by discussing the activities they carried out as part of the process. The ethics committee members and scientists defined informed consent as a process and did not link it to trial procedures. In many cases what the scientists and ethics committee members (SEC) said was close in wording to the definition of the informed consent process in national and international research ethics regulations and guidelines.

The different actors' perspectives had very different emphases. The SEC member quoted below emphasizes the content and the process of how the informed consent process is administered. His main concern was that participants are given all the relevant trial information:

Informed consent is the content, the process of administering the informed consent form: simple content bringing out everything that needs to be known, especially the risks and benefits for the participants and the protection [from any form of harm during research]; those are the two issues we need to continue standing up for as SECs. (Ken, SEC member)

One scientist emphasized providing documents that volunteers can understand easily, which can be challenging for research teams because some research documents contain many scientific terms:

... prepare the informed consent document, translate it into a language they understand. Sometimes that is difficult in science; some scientific words are difficult to put clearly ... and I feel we must always pilot those informed consent documents before using them. (Robert, scientist, Study 1)

Another scientist's definition, echoing that of the SEC member above, added the volunteer's need to know why they have been invited to take part in the research:

For me, informed consent is a process by which you tell someone what you are doing and you try to tell them what the study is about – the risks and the potential benefits, why you are doing the study, why you are choosing them. (Festo, scientist, Study 2)

The definitions from all of the different perspectives emphasize the importance of the volunteers' welfare and making sure that they were properly informed about the research.

In contrast to the ethics committee and senior scientists, the field team members appeared to give less thought to the informed consent process in terms of a formal definition. Clinicians' definitions of the process related to activities carried out during the trials and introduced the aspect of relations and communication with the volunteers:

The informed consent process is all the activities that are performed during the trial with volunteers ... to ensure that the volunteers' rights are respected and taken into consideration. (Paul, clinician, Study 1)

Another clinician emphasized the formalities of the process:

It is a formal agreement between an investigator and a participant trying to create a working relationship ... where you can collect data from this participant voluntarily, but they still reserve the right to withdraw at any time. (James, clinician, Study 2)

James' definition refers to the agreement between the researcher and the volunteer in a way similar to Appelbaum et al. (1987) discussion of the relationship between the legal theory of informed consent and clinical practice. The legal theory of informed consent draws on the law and mainly targets the agreement required between the patient and the clinician in the clinical setting before treatment can be begun. Consent in clinical research, however, is mainly shaped by professional codes, statutes and regulations, and not necessarily by the law (Appelbaum et al., 1987).

The counsellors and nurses defined informed consent in relation to the trial information that they provided to the volunteers at different times including at their screening, enrolment and follow-up visits:

A process where a researcher is trying to pass on information to a participant so that they can give their informed consent and participate(Timothy, health educator/counsellor, Study 2)

Another counsellor emphasized the legal aspect of signing the consent form:

It is a legal agreement, a mutual agreement between the person obtaining consent and the person who is consenting, so it is a binding agreement between the two parties. (Benon, counsellor, Study 1)

The two counsellors quoted here have differing perspectives on what informed consent involves. While Timothy looks at the process from the point of view of giving information that will lead to consent, Benon emphasizes the legal relationship of the volunteer and the researcher and looks to the end point, which is agreement. The issue of making an agreement reflects on the history of the informed consent concept which emphasised the legal theory of informed consent with the intention of protecting patients from doctors applying treatments without their permission (Appelbaum et al. 1987). As the counsellors were working in different trials I initially imagined that they might have had different training or that the emphasis in the informed consent process was different in the two trials. However, examining the responses of Faith, a nurse, and Geoffrey, a community mobilizer, I found that they too mentioned the provision of information and the signing of the consent form in their definitions of the informed consent process. The way they define the process was linked to their role in it.

Faith defined the process in terms of giving information and signing a consent form:

This is where someone signs after being given proper information and the person has understood what he or she is signing up to (Faith, nurse counsellor, Study 2)

The mobilizer is involved in giving general information about the research and not in getting volunteers to sign the consent form. He defined the process in terms of giving the volunteers information about the trial.

The community advisory committee members defined the informed consent process in the first person, looking at themselves as if they were the volunteers. For example, when discussing how a volunteer should not be coerced an advisory committee member said 'I should not be coerced'. The advisory board members emphasized that volunteers should not be coerced to

join a trial and should be given enough information to ensure that they are free to agree or disagree to take part.

The advisory board members' definitions were reflecting the kind of group they represented on the board. The media representative emphasized the volunteer's understanding the trial information and not being coerced; the medical workers' representative emphasized the volunteer's understanding why the trial is being conducted; and the religious leader looked at the importance of describing the research procedures just as they would to the people they lead, stating:

I have received enough information about what is going to be done, and I can therefore make a decision that is right. (Community Advisory Board, religious leader, FGD)

The definition of informed consent was expressed informally by the field research team as the activities that occur during the process, and the CAB members defined it in terms of how to protect the volunteers and avoid any form of coercion. The senior scientists and SEC members saw the process in formal terms similar to those in national and international informed consent guidelines. The research team placed greater emphasis on the response of the potential volunteer than on defining the process. Appelbaum et al., (1987) note that it is very difficult to get one definition of informed consent as the term is usually defined differently by different disciplines. My findings confirm this: although they all aim at ensuring that volunteers make an informed decision to take part in research, there are differences in emphasis on how the different actors define the process of informed consent.

I conclude that the process is defined in terms of how each category of actors perceives their role in it. For the ethics committee members it is a rite of passage: are the volunteers signing the consent form? Are the research teams following the standard operating procedures? The research team is more interested in getting potential volunteers to sign the consent form agreeing to take part in the trial. To some extent these two categories of actors can be seen to be driven by the institutional processes they represent and what is expected of them. The ethics committee is more distant from the practical circumstances and their emphasis is on the documents containing information to be provided to volunteers, which must be in a simple format to enable the volunteers to understand.

The research volunteers were not able to define the informed consent process directly because they did not see the process as critical in itself; what was critical for them was what they might gain from taking part in the research. Comments about the informed consent process were made when they discussed the importance of being involved in research. Two of the twentythree volunteers who gave a direct response when asked to define the informed consent process referred mainly to what they expected from their participation in the trials in terms of treatment and protection from acquiring HIV:

The meaning is to get the patient to reduce the drugs he is taking daily after they have examined whether it is true that the medicine works. (Male volunteer aged 50, Study 2)

For a volunteer in Study 1 it was about staying free from HIV:

For me the process means I should protect myself well to avoid HIV. (Female volunteer aged 25, Study 1)

Such findings show that the research teams' definitions are linked to their activities. The CAB committee members emphasised that the information given should be clear and easily understood by the volunteers and that the volunteers should join a trial of their own free will. For the SEC members the important thing was ensuring that volunteers are fully informed and the process is conducted following the structure and guidelines that have been laid down.

The individual actors' perceptions of informed consent may have implications for the process. Most of the definitions show that providing trial information to volunteers is important, but much less was said about how the discussions between the volunteer and the researcher take place. It is possible that volunteers may understand information differently from the researcher, as can also happen in a clinical setting when a physician and a patient discuss a treatment.

The results here confirm Appelbaum et al. (1987: 138) statement:

Since the goal of scientific investigation is the production of generalizable knowledge, not primarily the promotion of individual health, there is at least a potential for a divergence of interests between subject and researcher.

When a research team member views the informed consent process as a legal agreement or views it as the volunteer having understood the information given about the trial, as the volunteer's signing of the consent form, or as supporting volunteer autonomy, that team member is likely to handle the process according to that interpretation.

The ethics committee members' interest in the institutional legitimization of the event of informed consent includes their stamping the information sheet and giving permission for the trial to take place, thus sanctioning it. On the other hand the research team see the volunteers as participants whose agency is limited; although they ask questions throughout the trial and demand certain care, procedures are followed according to the protocol, changes to which can only be effected after a review by the SEC.

These findings suggest that the volunteers are not necessarily in a position to adjust any aspect of their role during the informed consent process and are required to follow set trial procedures as laid down in the protocols, although the research field team emphasize the volunteers' welfare when defining the informed consent process.

5.1.1 When does the informed consent process begin and end?

The answers of my respondents mostly reflected that the process begins with a potential volunteer's first contact with the trial when they are given information about it. One research team member, however, reported that the process begins after obtaining consent. Although this was not a common response, it indicates that this particular member may not give the process sufficient attention until the potential volunteer expresses his clear commitment to participate in the research.

One scientist noted that it is difficult to predict when the process ends, observing that the volunteers' consent to the storage of collected samples is part of the consent process and should not be overlooked by researchers when communicating information about the trial to them:

You could say that [informed consent] ends literally when a person finishes taking part in a study [and so] participating in a study lasts as long as the study lasts, but consent to use their data and to use their stored blood is supposed to last as long as it lasts ... If you are going to do something with stored blood you might have to go back and ask for fresh permission ... I don't know whether you can say the person's consent has ended. (Festo, scientist, Study 2).

David, another scientist, reported that there is no end to the informed consent process:

I would think it doesn't end, because even when a trial closes the informed consent continues because there will be a time when you need to feed back; once the results are back you still need to go back and give [the volunteers] those results ... I think the informed consent process goes on even after the trial has ended. (David, scientist, Study1)

Responses on when the informed consent process ends varied according to the research experience of the respondent. The most common response was that it ends with the trial. However the 'end' was not defined by most respondents groups apart from the scientists, who mentioned sample storage and disseminating the trial findings to the volunteers as important in the informed consent process. There are implications here for the way the informed consent

process is handled if the end is not clear to the research team, and this may need to be reflected in the guidelines.

The Uganda National Research Guidelines do not mention when the informed consent process starts and ends, but they do state:

The investigator shall ensure that there is initial monitoring at the start of the study and continued adequacy of the informed consent process and renewal of the informed consent process if there are significant changes in the conditions or procedures in the research project. (Uganda National Guidelines for Research involving Humans as Research participants, 2007, p. 23).

This statement leaves the decisions about the start and end points of the informed consent process to the discretion of the researchers and their field teams.

5.2. What is critical in the informed consent process?

All the research team reported that it is very important that the volunteer understands the study information before consenting to participate in the research. There were some differences however in how each respondent expressed this. A study mobilizer and a clinician called this 'volunteer autonomy' and 'a volunteer deciding on his/her own'.

To the study nurses, the volunteer signing the consent form was critical, perhaps because it is one of the key activities in the part of the informed consent process in which they are involved. As a nurse reported:

I think it is [the volunteer] doing something after understanding about it; the main aspect is to understand and sign the consent. (Beatrice, nurse, Study 2)

The nurse's response suggests that to her, signing the consent form means that the volunteer has understood the information about the trial.

James, a clinician, reported that the critical issue in the process is that the volunteer understands the information and expresses willingness to abide by what the trial requires of him/her:

The volunteer understanding what the study is about and willingness to abide by what the inclusion criteria entails. (James, clinician, Study 2)

For the volunteers, protecting their welfare and that of their family is the critical aspect of the informed consent process:

The important thing in research is to try to learn your health status, and when you are sick you are given treatment and when [members of your family] are sick they can also be treated. (Male volunteer aged 21, Study 1)

The actors' responses about the critical aspects of the informed consent process varied. The volunteers tended to look at the process in terms of their own health and particularly of being able to get treatment whenever they needed it, while the research team focused on assessing volunteers' understanding of the trial and willingness to sign the consent form.

Appelbaum et al. (1987, pp.22–23) define autonomy as:

... personal freedom of action, or the right to do as one pleases, within certain restrictions ... the principle of autonomy in general refers to respect for the autonomy of others.

Although the research team referred to this, the key aspect for them was how far the volunteers exercised their autonomy in the process. Autonomy is not easy to judge in a clinical trial situation but the research team's expectations were that whoever has put a signature or thumbprint on a consent form without coercion has done so willingly. This is questionable in a situation where the volunteer's overriding intent in taking part in research is to learn their HIV health status and receive treatment when sick, as this study has found.

5.3. Volunteers' views of the benefits of participating in a trial

Since the informed consent process is a central ethical principle governing research, to find out why people participate in research I asked the volunteers what benefits they gained from being involved in the trials.

These are two typical examples of their responses:

I realized that it helps you to protect yourself because you are advised to avoid sex without a condom; you get more informed. (Female volunteer aged 25, Study 1)

When these people talked to us about this research project most people listened because they told us they would check our blood and inform us about our health. So if you hear about such an opportunity for a check-up, you feel you should go so you can learn your health status. (Male volunteer aged 50, Study 2)

The volunteers mentioned the specific benefits in terms of their welfare; frequent medical check-ups, information about how to avoid HIV, being encouraged to use condoms and medical treatment when sick. These are positive outcomes for the volunteer, but they are not the researchers' or trial sponsors' direct reasons for carrying out the research. The volunteer's end goal is good health while the researcher needs an answer to the research questions. This highlights the issue of utility and end result; the researcher may be looking at the volunteer as a

means to their research end, while the volunteer may participate in order to realize his/her own specific goal of good health. Such views reflect the values that the different actors bring to the informed consent process during the clinical trials.

5.4. Implementing the informed consent process in the trials

Implementing the process of informed consent is commonly seen as involving three main elements: information-sharing, comprehension and voluntary participation (Beauchamp & Childress, 1994). I asked the actors in this context what was involved in implementing the informed consent process.

The different actors described the process in terms of how it was implemented in the specific trials in which they were involved. The SEC members are also researchers who are sometimes directly involved in the research process, and some are involved in the informed consent process. Those interviewed in this thesis were not directly involved in the research process of either of my case studies. One described implementing the informed consent process as a series of activities that involve more than the individual volunteer taking part in the trial; it also involves some level of community engagement:

The informed consent process, I think, has about three layers [levels]: there is informing the community leaders; there is informing the community; and then there is informing the individual about the study. However, these are linked. (Ken, SEC member)

Ken described the structured path that the researcher needs to take before they get to the volunteer, using the term 'layers'. The researcher's work should be made transparent to the community and its leadership before reaching out for potential volunteers.

Another viewpoint emphasized the discussion of the study information before moving on to the written documents:

We have to reverse [the way informed consent is sought] so that the [consent form] is the last thing that should be given out. I think holding a discussion with potential participants is more useful in our part of the world (Bosco, SEC member)

The health educator described the informed consent process as following a formal structure:

There are structures in the process. As a health educator I initiate the process by making sure the client understands all the procedures regarding the study. If the volunteer understands and agrees to participate, then we move on to the next step where the doctor or any other person assesses the eligibility criteria. (Timothy, health educator, Study 2) Informed consent is a specialized process and each research team member makes their input into it.

The responses emphasize different aspects of the informed consent process and highlight its complexity. Nothing can be taken for granted from gaining access to the community via the leadership structure to sharing information with the community and dialogue with the volunteer. This reflects the importance of engaging the community when implementing the informed consent process for research in the Ugandan setting.

5.5 Roles in the informed consent process

I asked the respondents to describe their and the other actors' roles in the informed consent process to find out how they value their own contribution and those of all the actors in the research. I asked them: Who are the main actors in the informed consent process, and why? A clinician summarized it this way:

The study team includes the principal investigator, the trial coordinators ... and the nurses, the counsellors, so the whole team has to be involved in the informed consent process at one point or another because this information-giving process crosses all the levels of the team.

The SEC assessed the structure of a study and ensures that the volunteers' rights are not infringed by the researchers. The volunteers were reported as having a central role in the informed consent process; however they need to be empowered by knowing that they have the right to a full understanding of the informed consent process in order to be able to participate willingly in the research trials.

The respondents in my study identified two aspects of the informed consent process in response to my question; the importance that each actor attributes to the others' contributions during the process and what the individual actors see as their own contribution to the process.

All the respondents referred to the volunteer as central to the informed consent process:

I think the person at the centre is the volunteer, because ... [one,] this is somebody who is supposed to come in willingly; two, he has rights which he may not be aware of and yet these rights should not be compromised at any time and without him or her no study can take place, even if you have all the money. (Robert, scientist, Study 1)

The volunteers often have a precise awareness of their contribution to the process:

My role is important because if we don't enrol then who will they conduct the research on? Will they do it on animals? So that all shows that the research team has to handle us well. (Female volunteer aged 26, Study 2). Another volunteer explained the importance of her involvement as a way of encouraging other people to join research:

My main responsibility is to avoid getting HIV and to discuss information that I have with other people ... after this experience when I meet people and there is research being done, I encourage them to join. (Female volunteer aged 30, Study 1)

The CAB members reported that the Board has a significant role to play in supporting the selection of participants, because it mobilizes and informs potential volunteers of trials.

The roles of the research team are not independent of each other because a volunteer moves from one procedure to the next. The volunteer interacts with a different research team member in each procedure. Teamwork among the research team was reported to be important in the informed consent process. Whereas some research team members saw all the actors as important, the member who obtains consent from the volunteer and the volunteer who gives consent were seen as most important in the informed consent process.

The volunteers said that their own role was to keep their appointments, and once at the research clinic, to follow what was planned for that visit. A volunteer described a typical followup visit day:

When I arrive I give in my card, they write my name and then I wait for about ten minutes. Then I go to see the doctor; from there I come back and they take my blood, then they reimburse my transport costs, then I get the drugs and I leave. (Female volunteer aged 50, Study 2)

Thus although the role of each group of actors appears to be clear in terms of what they do during the informed consent process, getting a volunteer to consent to take part is not easy in practice because the consent process can be affected by the actors' varying values and beliefs and the level of power that they can exercise during the process. My findings show that some respondents, particularly the research team nurses who attend to the practical elements of the volunteers' signing the consent forms, feel that their role is less visible but still key to the process. Two nurses noted that although they are the ones who give the bulk of the study information to the volunteers and ask them to consent to participate in it, it is the clinicians and not they who co-sign the consent form.

The national and international guidelines emphasize the role of the principal investigator as the person who oversees the study, the project sponsors and the research volunteers. The rest of the research team even though their roles are important in the informed consent process as has been reported by the actors, they are not described in the research guidelines. It is the principle investigator who delegates responsibilities for them in the process.

These findings show that the accountability of the actors during the informed consent process differs, as reported by the actors themselves. Their singling out of the person who obtains consent from the volunteer may reflect less commitment to the research ethics on the part of those who are not directly involved in the 'event'. And because the SEC is usually most interested in the structure of how informed consent is obtained, as evidenced through the signed consent documents, the number of actors involved in the implementation of the informed consent process may not be important. Yet informed consent is more than a one-off event and can be affected by any of the actors during the different interactions that occur during the trial. My findings also suggest that senior trial researchers and sponsors should consider the amount of time required from volunteers for clinical procedures and how volunteer fatigue can be managed.

5.6. Actors' feelings about the time required for the trial procedures

Participating in the trial procedures may present the volunteers with many difficulties. Many in Study 1 reported that they found the length of time spent at the research clinics challenging. This was not the case for most Study 2 volunteers, some of whom compared their involvement in the research to collecting their ARVs from service institutions where they had to wait longer to be seen than they did at the research clinic, which helps to explain the different reactions of the two groups of volunteers. A Study 2 volunteer explained the importance of time spent at the research clinic:

There is such a big difference between institution D [a service institution] and this trial clinic. In D you may wait from morning to 2 pm for your turn to be seen by the counsellor or clinician – at least here they work fast and then you can go back and do your work. (Female volunteer aged 26, Study 2)

Study 2 volunteers reported that they faced delays at the pharmacy when they attended the clinic. Observing the pharmacy, I realized that one research team member usually worked alone providing refills and dealing with prescriptions for all the research volunteers. This was a slow process and a source of some discomfort for some of the volunteers.

For the volunteers in Study 1 the acute problem of time spent at the clinic was repeatedly related to their job commitments; they identified what they gave up mainly in monetary terms to attend the clinic. A quotation from a focus group discussion highlights their concern:

I think there are too few doctors. Although we agreed to be volunteers we have other things we want to go and do. I think the issue of time can actually cause people to drop out, even if they volunteered willingly. My brother here said he can forego 60,000 Uganda shillings about £15 GBP] for a day at the research clinic, but [someone may not

be able to] afford to lose that money, and when he weighs up the money and the research he decides to quit the research. (FGD Study 1)

Despite their complaints about lost time, the research team has to take the volunteers through the procedures as planned on each scheduled clinic visit. This in itself could indirectly affect the way procedures are handled, because the research team has to work very fast in response to the volunteer's demands. There is the sense of a power conflict here, the volunteers demanding to spend less time at the clinic and the research team demanding that they go through all the planned procedures at each visit. If the needs of both are not balanced there is bound to be a power conflict which could lead to research volunteers dropping out.

The volunteers in Study 1 were not often sick, and it was not easy to handle their time because even on arriving for their interviews with me they always began by announcing that they did not have much time. A Study 1 volunteer suggested that the research team should separate the volunteers who require health care from those who are invited for the research scheduled visits in order to minimise time spent at the clinic. When I asked the team about this they reported that the volunteers who came when they were sick were part of the same trial or of other trials taking place at the research clinic. The volunteers did not know this, and it would help if they did, as wanting to drop out due to the long time they have to spend waiting to be seen can affect the informed consent process. A female and male volunteer in Study 1, however, reported that no time was wasted when they went to the clinic; they always planned for it early enough to avoid planning to do other things on the days when they were scheduled to visit the clinic.

Since time was critical to the volunteers in Study 1, I interviewed the research team about their views on the time taken by the research procedures. All the team and the SEC members reported that having enough time is very important when conducting a trial because the volunteers are able to ask questions and have them answered by the research team, which helps them to understand the study they are involved in and the reasons for conducting it. A clinician reported that the lengthiest procedure is screening volunteers for the study:

It is inevitable; to ensure good participation you must ensure that the informed consent process is done very well ... so there is a tendency at screening to allow limitless time because you can only finish with a participant if you know they have understood. It may not matter how much time you take explaining the trial; what matters is ensuring that the volunteer has understood what is required. (Paul, clinician, Study 1)

A scientist emphasized that working in a process rather than an event requires time:

Informed consent should be a process, not an event, so I think we should aim at giving [volunteers] as much time as possible. Sometimes I think it is not wise to give

information and ask them to consent on the same day ... some of them may be too eager to get into the [trial and] want to give you the impression that they have understood everything, just to be able to join the study. (Robert, scientist, Study 1)

The research team and SEC generally reported that spending time on the procedures, especially at the start of a trial, is essential. This view however is challenged by my own finding that procedures such as the collection for blood and urine samples are reported spontaneously by the volunteers and other procedures are less significant to them, so spending much time on explaining procedures that are less significant to the volunteer is not appreciated by them. The volunteers offered some suggestions for reducing the time spent at the clinic. These included dividing the research team into two groups, one to take care of sick volunteers and the other to handle the research volunteers' scheduled appointments. One volunteer reported that he had decided to start coming to the clinic in the afternoon, because this worked out well for him. However, it was not easy for the research team; in an informal conversation a laboratory technician mentioned that some samples have to be transferred to a laboratory which is not at the research site and therefore if a volunteer came in the afternoon, the sample is sent late and yet some of the samples need to be handled in the laboratory within a few hours after collection. It is not convenient for the laboratory team. This shows that volunteers and researchers need to have an in-depth discussion in the early stages of a trial about the time to be spent at the research clinic.

The issue of the time spent at the clinic by the trial volunteers requires consideration by senior scientists and trial sponsors when planning the informed consent process. The procedures have to be conducted along stringent timelines and the research volunteers also have other demands on their time. Reconsidering the time a research volunteer needs to stay at the clinic will help to support their interests and avoid their giving biased information and responses to the research team because they are in a hurry. In the next section I discuss the different actors' roles in the informed consent process, as discussed in their interviews.

5.7 Conclusion

The volunteer who consents to participate and the research team member who obtains this consent are seen by the research team as the most important actors in the informed consent process.

The research team were seen to be concerned with providing information about the trials to the volunteers and assessing their understanding of it. The SEC was interested in the way information is transmitted to volunteers according to set national and international guidelines on informed consent; the CAB was specifically interested in the free participation of the volunteer in a study. However the volunteers were more inclined to seek ways of promoting their health and welfare while participating in a research trial. The roles of the different actors are usually well refined and the implementation of the informed consent process is institutional. However, the impact of individual agency cannot be taken lightly because individuals bring values and beliefs to the trial that may impact on the way the informed consent process is implemented in trials. The issue of the time demanded by the trial was critical for some volunteers who, when they decided to take part in a trial, reported that the time they could spend at the research clinic needed to be minimized so that they could also carry on with their other activities outside the research. Power differentials amongst the research team are controlled by the institution through the clear definition of the roles of the different research team members, who each know who to report to during a trial. However, the time demands of the trial were seen to create conflict between the volunteers and the research team.

In the next chapter I examine my findings on the concepts that I found reflected in the informed consent process.

Chapter 6 Factors influencing the informed consent process in this study

In this chapter I discuss the factors that influence the informed consent process: beliefs, values, trust, power dynamics, decision-making, gender and sociocultural factors. The chapter addresses my research question 4: *What factors influence the informed consent process in a clinical trial research setting?* In the first section I consider the values and beliefs, and in the second section the remaining factors evident in the informed consent process; trust, gender and sociocultural factors, power and decision-making. Decision-making cuts across all the others, which all lead to the decisions that actors make during the informed consent process.

6.1 Values

As discussed in chapter two of this thesis, values are ideas which enable people to judge whether experiences are important or unimportant and so guide their behaviour (Horton & Hunt, 1984). Support for an individual's autonomy is at the core of the usual meaning of 'informed consent' so that each actor, and in particular the volunteer, has a sense that what is important to them personally and their part in the research context are respected (Faden and Beauchamp, 1986; Beauchamp & Childress, 1994). In this section I discuss how values and beliefs are felt and responded to in the informed consent process. The process model that I use in this thesis emphasizes a volunteer autonomy. The process model highlights the importance of communication and collaboration between patients and doctors, and between research volunteers and researchers. My aim was to understand how the respondents' values impact on the informed consent process. I was interested in finding out whether individual values are communicated during the informed consent process.

In this study values may not be voiced directly by the actors and can be understood by analysing their responses. The value that a volunteer attached to their participation might be expressed in their account, for instance, of what they expected the study outcomes to be and the possible repercussions of their failure to complete the trial as planned. Values can be expressed differently by actors undergoing generally similar experiences. Two examples show what volunteers with different expectations of the trial valued in the informed consent process. One made the decision to complete the trial because he wanted to know its final outcome:

We were told that there were going to be sixteen visits but if you wanted to withdraw at any point no one would blame you, but I decided that as I had agreed to start this trial I should complete it. If you complete it you have the right to ask about the findings. (Male volunteer aged 30, Study 1) This volunteer mentions the 'right' to ask for the results if he completes the trial because he values his contribution to the research and awaits the outcome.

A second volunteer saw the trial as an opportunity for autonomy and altruism:

Research where they are testing a drug is voluntary. You just need to tell the person all the information and you show them the good things about being involved in that research, and if he or she cares about himself and his nation, he will choose to agree to participate. (Male volunteer aged 39, Study 1)

According to the second volunteer, when the research team gives the trial information to a volunteer they should leave him/her to make a decision about participating. In both examples, being provided with information about the study is important but the choice to participate lies with the potential volunteer and is driven by his/her personal values what they think about the research and how they value their contribution and the research. The first volunteer values the research outcome and its implications for him as an individual; for the second, what is important is what will happen in the general population. Values also helped to reinforce positive behaviour:

I used to protect myself [from catching HIV] but when I joined this research and they checked the whole of my body and I was fine, I started valuing my life even more than before. (Female volunteer aged 30, Study 1)

The responses that could be related to the concept of value were mainly offered by Study 1 volunteers. They show an interest in preventing HIV and understanding the outcomes of the research they were volunteering in. For Study 2 volunteers, the value was mainly in taking ARVs in order to live longer and experience less opportunistic infection. Some attached value to taking part in the research because they were hoping that the results might lead to their having to take fewer pills.

The research team did not reflect any distinctive aspect of value in the research process. The teams' aim is to ensure that volunteers comprehend the information given to them about the study, and to implement the study until it ends. The underlying "social" value is volunteer autonomy, but research team members did not voice this directly. A SEC member did state explicitly that the informed consent process can be affected by the value system that the actors subscribe to:

I think everybody has a value system which they use to process everything. So I will bring my value system to the table and they will bring theirs and if we agree, it will work out, and if we don't agree it will not work out ... If you believe the end justifies the means then you are probably going to overlook many things, and it also depends what the goal is: my goal may not be the patient's goal. The patient's goal might be treatment while my goal is data. The patients sign up for treatment, while I sign up for them giving me data. (Bosco, SEC member)

Individual values may not be voiced, but they may still influence a person's actions during the informed consent process.

6.2 Beliefs

Beliefs are closely linked to values. According to Beattie (1964), beliefs can be reflected in ideas about how things work, how others act and the consequences of one's own behaviour. It is important to understand people's modes of thought about a given situation and the language they use to express their ideas about the world, because these reveal what they believe (Beattie, 1964). In my study I was not able to identify specific modes of thought but I listened to how the respondents expressed their ideas about the informed consent process. As stated in Chapter 2, beliefs influence action and can be held about cause-and-effect relationships (Jervis, 2006). Much of my data reflects the factors that cause individual actors to take certain actions, which helped me to understand how the respondents voiced their ideas in their own words.

One volunteer noted that a person's attitude to an issue may influence their beliefs. He showed in the way he expressed this:

If you hear about research aiming to find a cure for HIV and you just relax and say it doesn't matter, where will the researchers begin? ... We are volunteers and we are not paid. So there isn't anything that attracts a person to take part in research; it depends on a person's attitude (Male volunteer aged 30, Study 1)

The volunteer introduces the importance of appreciating different people's attitudes and these are influenced by ones inner belief and values. The findings show how it can be difficult to explain another person's belief unless you hear them expressed because beliefs are assumptions and convictions we hold to be true based on past experiences. This is true in the informed consent process: unless a volunteer or other actor expresses it, the researcher can only guess at what they believe.

One scientist reported that more women than men are involved in research, but could only wonder about the cause of this:

If you look at research populations many times you will find that between 60 and 70 per cent are women, so a lot more women are interested in research than men. I don't know whether this reflects the general population; I don't know, maybe it does. (Festo, scientist, Study 2)

The research team reported that beliefs affect how people understand the information they are given about the trial. A clinician noted that the volunteers had a belief about the drugs used in the trial despite the information provided by the study team:

[In] Study 2 there are a few beliefs like 'They told us that in this study we will take fewer tablets'- this is partly correct but it totally misses the point of the study. (James, clinician, Study 2)

The way the volunteer that James quoted synthesized the information he received from the research team was affected by his belief.

Beliefs were cited by the institutional review board members as playing a role in the discussion of protocols. Although the individuals on the board may have different beliefs about a given protocol, they must act in a way that gives credibility to their decisions as a committee guided by the research protocol review procedure. One member of the SEC explained that beliefs about what a protocol is aiming for may differ during the review process, but the SEC members try to find a solution to this:

[The beliefs] do get balanced; you have to have strong reasons for objecting to something in the protocol. And if we disagree we just don't take it back to the investigator and tell him 'You have to do it this way'. We give the investigator a chance to discuss it with someone on the board. (Ken, SEC member)

Beliefs can also affect the recruitment of potential volunteers into research. The partner of one of the volunteers, herself a university graduate, who had known about Study 1 for some time and even participated in some information sessions, said:

Yeah, I was here, even at the sensitization sessions, but I don't agree with [the trial], it's about taking somebody's blood and taking it somewhere to test[they test] everything in somebody's life. (Girlfriend of a Study 1 volunteer)

While this indicates an underlying attitude or belief about sample collection during a trial, the respondent does not mention any other detail of the trial, emphasizing the taking of blood. The different actors' narratives about values and beliefs reveal why some people may choose to volunteer in HIV clinical trials while others choose not to. Volunteers' decisions may not be linked to the level of their education, as seen in the quotation above, but on the individual's perception. The Study 1 volunteers' participation may reflect altruism, as they were healthy young people at the time of recruitment. However, there was an underlying expectation that there would be health check-ups, as reported by many of the volunteers. The impact of HIV in Uganda has influenced some volunteers to participate because they have lost friends and relatives and they want to see an end to the HIV epidemic. Beliefs, values and attitudes are not

discussed directly in the informed consent process but nevertheless these are constructs that seem to affect the actors' decisions in this study context. The ways in which the actors manage the procedures and interactions with one another during the informed consent process reflect their varying beliefs and value systems. Trust also emerged as relevant, and is discussed in the following section.

6.3 The place of trust in the informed consent process

Trust was reported by some researchers as an important factor in the research process, and particularly in the informed consent process as the different actors carry out their roles (Molyneux et al., 2005). I sought to understand the actors' view of the role of trust in the informed consent process in this Ugandan context.

Trust was particularly seen to depend on volunteers' confidence that his/her information was valued and was being held confidentially.

When describing trust, one of the scientists reported that it cuts across all the different actors in the informed consent process. The investigators must trust that the sponsor's study is feasible and will not harm the research subjects. The sponsor in turn has to trust the research team to accomplish the trial as planned in the protocol. Each of the actors has to attain some level of trust in the other actors in order to commit to carrying out their individual role.

Some research team members reported that the trust of volunteers in a clinical trial/study can be assessed from their response to the study activities and procedures: for instance if they turn up for their appointments and are honest with the study team about what happens to them during the trial. It is however difficult to separate trust from other factors in a volunteer's environment that may affect his/her participation in a clinical trial.

The research team reported that some volunteers' trust may be attributed to the difference in the quality of care given at the research centres, which is usually not available elsewhere from public health services. They also reported that if they promise to treat a volunteer when sick and then keep their promise the volunteer will in turn trust that the procedures are all being enacted correctly:

Trust [can always be] improved upon ... it is delivering what you said you would; it is doing what you said you would do. You said you are going to give a transport refund, you give it; you said you are going to treat me when I am sick and you treat me when I am sick. (Festo, scientist Study 2)

From the SEC's perspective, the participant has to trust the research team during the informed consent process. One member said:

We don't see any aspect of a clinician having to put their trust in the patient. This [situation where a researcher is in control and is perceived as such by the research volunteer] is important for the SEC to ensure that the researchers carrying out the trials are competent. (Ken, SEC)

Some respondents considered that trust in the process was influenced by the social status attached to the medical profession in Uganda, this is even more emphasised because of the limited infrastructure and few clinicians in the country (MOH, Survey Report, 2008). A SEC member, who was also a clinician, said that the SEC needs to be aware of how the general population in this study area views the medical workers:

I think in Africa trust is the first thing [most important], especially in clinical trials. Patients and participants tend to trust clinicians. Someone comes to you and says ... 'I accept what you tell me I will not refuse – how do I refuse? My life is in your hands'. They abrogate responsibility and they trust that you are going to do the best for them without harming them ... Once you [lose] their trust they will not participate. (Bosco, SEC member)

The researchers also depended on the volunteers' trust to conduct their work. A clinician reported that being truthful to the volunteer and discussing possible negative side effects that may occur during a trial could enhance the volunteers' trust in the research team. The community mobilizer who met the potential volunteers in the community relied on their trusting him. He noted that the volunteers' trust reflects their performance:

When I have given them information and they turn up [at the clinic] I think 'They have trusted me'. (Geoffrey, community mobilizer)

Many different respondents mentioned that trust is an important factor in the research setting and the informed consent process. Two of the volunteers in study 2 had participated in a trial that preceded the treatment trial. A clinician noted that trust may sometimes be questionable particularly when the volunteers are used to participating in research, they answer according to what they expect the researchers want to know:

You cannot guarantee that [volunteers] are always right, because the challenge would be for participants who have been in previous studies – they would have learnt the questions that they need to answer or the responses they have to give to certain questions, so the ones who are study-experienced will have certain standard answers they will always give you. (James, clinician, Study 2)

The volunteers also reported some doubt about information the researchers gave them; some questioned whether the study was really double-blinded with even the researchers not

knowing what drug the volunteers received. Information received from the researchers to the volunteers was questioned by volunteers in both trials who were not sure they had been told the whole truth, as also reported earlier.

Some volunteers in Study 2 linked trust in the informed consent process to having experienced no side effects or sickness from the research intervention:

R3: For me, because I am not sick I don't feel that I have a problem with the research.

R5: For me, since I joined I have never had any serious sickness, maybe some headaches, and I don't even have a cough. (Volunteers' FGD, Study 2)

Trust was important not only between the volunteers and the researchers but also in the SEC when reviewing protocols. A SEC member reported that before a protocol is approved the board has to go through the researchers' credentials for them to ascertain that the researcher can be trusted to move to the community and conduct research:

As a SEC member you need to have read the investigators' CVs, you need to prove that they are going to do the right thing because they must understand their responsibilities. So you do that by examining their background, their history, what they've been doing, and if somebody is new, who else he or she is going to work with, and once you are sure of that then it is for the investigator to build trust at the community level. (Ken, SEC member)

So, while trust is needed in relationships and how the interactions were interpreted by the actors, it is also conditioned by what the SEC's protocol review recommends for the researchers. The SEC community representative said:

For us, we trust that what [the investigators] give us is correct, but the investigators ... gain our trust after we have approved the protocol. (Cathy, SEC community representative)

I sought to learn from the study teams whether they had encountered any refusals to participate in the trials and whether the reasons for refusal were due to lack of trust. Most refusals were said to be the result of potential volunteers' misunderstanding of study information. It has been reported elsewhere that it is possible for the volunteers to misunderstand the information (Krosin et al., 2004). I discussed a section of the information that states 'We don't know whether your risk of getting HIV is going to increase or remain the same or decrease' with Study 1 volunteers. It had led some potential volunteers to refuse to participate, thinking they would be infected with the virus and mistrusting assurance that this was not the case. Another common reason for refusing to participate was advice from relatives

and friends consulted before joining a trial, who may have had similar reasons for mistrusting the researchers.

It is possible that those who decided not to take part misunderstood information given to them, as reported by the research team, or did understand the implications of participating in a trial and chose not to do so.

The reasons volunteers gave for staying in a trial included being treated when sick, a good reception from the research team, and on-going seminars to discuss rumours with the research team. All of these enhanced trust. Trust was built when the research team fulfilled what was outlined in the study information sheets and the volunteers fulfilled what they had agreed to do in the trial, further building trustful relationships. This created reciprocity within the informed consent process.

Rumours reported by relatives and friends of the volunteers could affect trust; some volunteers reported that they had decided not to tell their relatives about the trial to avoid being discouraged from participating. Others only made their decision to participate after consulting trusted family members such as their parents.

Examples of the rumours cited by the volunteers include the research team injecting them with HIV and that they might change into vampires or die suddenly and mysteriously. Rumours cannot be taken lightly because they can deter a whole community from participation if the researchers ignore them (Geissler and Pool, 2006). Those reported by volunteers may need to be counteracted with specific information; the volunteers in my study said that they were able to continue participating because the research team gave them information that led them to trust the trial.

Trust was also built through communication between the volunteers themselves. They shared what they had gone through during the trial procedures and this encouraged them to continue participating:

When we are waiting at the clinic we keep talking to each other as volunteers, and when you hear what others have gone through and that they have been treated well you're encouraged to trust what is happening. (Male volunteer aged 50, Study 2)

Trust was extensively discussed by most of the respondents from various angles. The research team had to trust the volunteers; the volunteers had to trust the research team. The ethics review board (SEC) had to trust that the researchers would conduct research according to their submitted proposal; the researchers hoped that their protocols would not be rejected by the ethics board during the review process. The informed consent process involved reciprocity between the different actors as they interacted and communicated with each other, receiving,

giving and checking information, all of which built trust in the process. Trust helped to construct relationships that were seen as reliable and facilitated the flow of information between the different actors. A low level of trust would hamper a trial in this context.

One scientist summarized trust as something that develops over time:

I think trust is at the core on both sides, but you know trust is not something you develop in a day; you are probably bringing in a volunteer who is seeing you for the first time, who is probably hearing about this organization for the first time.

He went on to point out that the researcher was supposed to take the lead in assuring the volunteer that he can be trusted as a researcher:

The onus is on us to win their trust and sometimes that takes a bit of time, and it depends so much on how you talk, how you interact with them, how you manage their condition, how you manage them when they come in with an illness, probably how you manage their partners, their children. It's complex. (Robert, scientist, Study 1)

This discussion of trust makes it clear that the informed consent process in a research setting is not a single event; it is a continuous process which involves on-going communication between the different actors. While the findings here were collected in a research setting in HIV clinical trials and not a clinic treatment setting, they affirm the importance of the continuous element of the relationship between a volunteer and a researcher, as Appelbaum et al., (1987) suggest in advancing the process model. In this case, trust is important not only between individual actors but also in a given system. In my study the system may be seen as the research institution, the SEC, the research team and the community of volunteers involved in the informed consent process.

In the next section I discuss the findings on the influence of gender and sociocultural factors in the informed consent process.

6.4 Gender relations and sociocultural factors in the informed consent process

Gender relations in the informed consent process were discussed by my respondents in a rather general way. Only a few volunteers mentioned direct issues with their partners. Some women had made the decision to join the trial without informing their spouse, or if they had informed the spouse they had eventually made their own decision to participate, backed by someone they believed in or respected, even if not their spouse. A female volunteer explained:

[My husband] never wanted me to take part, and whatever I told him he refused[to let] me[volunteer], but my parent [father]felt it was okay; he even came and saw what was happening here, so I gave up involving my husband. (Female volunteer aged 19, Study 1)

In the case-study area men are usually the household heads and make most of the family decisions (Roscoe 1911; Wyrod, 2008), this is generally true in rural and peri-urban areas but some of the female volunteers did make decisions without involving their partners. A study clinician reported an experience which, he said, was not common but occasionally happens, where a man cannot consent without his wife's approval, and in this case the wife was not interested in the research:

There is a man who came; before he could sign the consent form he said that first he had to go and discuss it with his wife, and the wife said 'NO' ... whoever is participating is doing so voluntarily. He wanted to participate and the wife said no. (James, clinician, Study 2)

The issue of gender among the volunteers was discussed when I related a scenario to them about a woman who got pregnant while participating in a trial similar to the one they were in. I asked the volunteers whether they thought the woman in the scenario had understood the information given to her by the research team at the beginning of the trial. The majority of them argued that she had understood the information, but because she needed her spouse's financial support she may have allowed herself to get pregnant. A few thought she had decided to join the trial without having understood the study information. Part of the information conveyed to her was that she was to avoid getting pregnant during the trial, as the researchers did not know the likely effects of the drug on the foetus. This information is included in most consent forms for clinical trials of medications.

In a focus group, the majority of the volunteers and the CAB emphasized the importance of involving one's partner in the session giving information about the research, reporting that this can impact on adherence to a trial. The responses showed that even though some women may have had the courage to make an independent decision about participating in the research, women's independent decisions about reproductive health issues are not always viewed positively by men.

The majority of respondents pointed out that the woman in the vignette got pregnant because she had not informed her sexual partner about her participation in the research. Below are two typical responses from the men. In the first, the man introduces the importance of a woman informing her partner of what is happening, pointing to the man being in charge:

She needs to inform her partner because this is about life; if she suffers any side effects this may annoy her partner. (Male volunteer aged 50, Study 2)

In the second example, the volunteer asserts the need for researchers to make both partners in couple relationships aware of research, again confirming the role of the husband in decisions about having children:

That is where the problem starts, because if her husband was not in the trial it would be difficult for her to avoid getting pregnant. Maybe she should have taken contraceptive drugs, because the man was not aware [that she was taking drugs] and if he wanted a child [the woman had to obey his need]. (Male volunteer aged 35, Study 1)

Avoiding pregnancy in a trial was seen as an important challenge for many potential volunteers in this context. This may be due to the cultural beliefs in this community in which a married woman, especially if she has not had a child, is expected to produce children. A volunteer gave an example of a woman who wanted to participate in a trial but who decided not to join because of the information she had been given about the researchers discouraging volunteers from getting pregnant:

There is a lady I came with and [she and her partner] were waiting for a while to get a child, but when she heard that the trial was going to take two years and in that period her husband would want her to have a baby she decided not to participate in it. She is actually about to give birth. (Male volunteer aged 30, Study 1)

Gender issues can influence decision-making in the informed consent process, but some volunteers knew what they wanted and felt able to make their own decisions about participating in the research, as seen in the quotation above. However, the men's influence, even if it is not voiced openly by the women, can underlie the actions that women take in secret such as seeking family planning services without informing their husband. The secrecy reflects fear of the man's reaction and can be seen as an issue of gender, cultural beliefs and power between the spouses at work in making a decision about joining a trial.

While discussing gender issues during a focus group discussion, the CAB members noted some changes that were happening in the community. They reported that although the individual decisions that women can make, including the decision to join a trial, are still limited, women who have improved their livelihoods by working and earning an income are increasingly gaining a say in the way they make decisions, including about participating in research.

When the same focus group discussed the scenario of the woman who got pregnant during a trial they mentioned the possible causes of pregnancy including inadequate family planning information from the research team, lack of access to family planning methods, and the man wanting a child. A male discussant reported that the man needs to be informed about the research even when he does not need a child. This attitude, even from the CAB members, shows that in this cultural context men consider that they have the right to be given information about a study before their wives get involved in it. This reflects gender inequality among men and women in this community. A discussant mentioned women in research being issued with condoms, and there was a reaction which drew out cultural norms:
R11: if the husband is not involved and doesn't know anything and the wife comes and they give her condoms [all laugh; they [men] do not believe in women introducing the use of condoms with their spouses] the husband will not accept the condoms she brings, so I think if women are to be involved the man needs to be told [the majority signal their agreement] or be well-informed, otherwise it may not work. (CAB FGD)

However, during the same discussion another community member said that he had noticed that although women in the community are generally seen to be silent in decision-making this is changing:

R7: There is a campaign going on about family planning, and many women have gone in without first consulting their husbands ... I have been travelling with some people in [X] organization, but I realized that the majority of people there are women who have defied their husband's involvement. I was in [Z] hospital ... of the 74 female patients, 52 were saying: 'When I left home I held a hoe like I was going to dig [miming], because I knew he would not allow me'. [all laugh]

The women are devising means of accessing contraceptives without their spouse's knowledge. It was reported in the discussion that women in some branches of Islam were not allowed to make personal decisions and still complied with their husbands' decisions. Some board members mentioned couples whose decisions were made after consulting together, so families had different experiences. The extract from the focus group shows that while there have been some changes in household decision-making; it is still affected by sociocultural beliefs and values. For example, in this discussion even the CAB members laughed at the idea of a woman initiating the use of condoms with her husband. Religion can also impact on decision-making in some religious sects, as reported above.

There is still strong belief on the part of some men that some women can be persuaded to do what they may not have intended to do but because they need money they do it. One male volunteer reported that the woman who got pregnant in the scenario might have been in a new relationship:

That woman may have had a new sexual partner who wanted a child, and especially if she wanted to please him and he was a source of income, that by itself could have made her forget what she was doing. (Male volunteer aged 50, Study 2)

Although not openly discussed, the gendered experiences that the volunteers reported and the CAB discussion create a picture of what is happening in the community. Gender and social issues are embedded in the day-to-day decisions of potential and actual volunteers in the informed consent process in research studies. Some of the individuals' responses are indicative of some female volunteers' experiences at home when they make the decision to join research.

A female volunteer said that her husband had told her not to complain to him about her involvement in a trial, thus leaving her responsible for her own difficult decisions. Participating in research is not without challenges, and these results offer an important insight into the need for adequate communication between researchers and potential volunteers and their spouses in order to avoid conflict that may impact on the informed consent process. A forty-year-old female volunteer reported that some women inform their partners about what they intend to do out of fear of the repercussions if anything were to go wrong during the trial.

One of the scientists suggested that gender may not be an important factor in the informed consent process and that education may have more impact on volunteer participation and decision-making. However, my findings and the responses of the other actors in my findings show that gender roles and inequality between men and women can impact on the informed consent process if research teams do not address it early in discussion with potential volunteers.

6.4.1 Cultural issues in the informed consent process

The findings from this study do not point directly to cultural factors impacting the informed consent process, but the responses were similar to those discussed in the gender section. There are some community expectations of individuals, especially those in a marital relationship.

Two senior scientists, one a member of the SEC, noted that culture may affect the informed consent process if activities proposed in the trials do not conform to the cultural setting, explaining:

Because we are Ugandans and live in Uganda we know what will work and what will not. If you come and you want to see pregnant women every two weeks and after they have delivered, we will tell you that it can't work because culturally they are on a different path, so you would be inconveniencing them. We live here and we know our culture, and the ethics must fit the culture. (Bosco, SEC)

Bosco's emphasis is on understanding a research context and learning what happens in different sociocultural situations, including those of pregnant and nursing mothers and their involvement in research.

A scientist discussing cultural issues in the informed consent process reported that respect for medical doctors seems to have become the cultural norm in Uganda; however, he reported that the volunteers in the research study in which he was involved in seemed able to discuss and talk with the clinician in a way that reflected less respect of the health workers' title than what the clinician has known in the past.

My study findings show that it is important to understand cultural issues before studies are initiated in communities, particularly in the African context, where decisions are not made entirely individually (Metz, 2010). The level of an actor's education may influence how much the culture affects the informed consent process, although in this study there is no evidence that it overrides cultural beliefs. When volunteers are aware of their rights they are able to question long-held beliefs in their community, for example that medical doctors' decisions about their patients are always correct, although gender roles are not easily changed. The implication for the informed consent process is that although the culture may not appear to impact directly on research outcomes, it cannot be ignored when dealing with volunteers in communities that still consider that important decisions should be made in consultation with others in the community (Seeley et al., 2009; Metz, 2010).

6.5 Power dynamics in the informed consent process

To understand the power dynamics in the informed consent process I discussed with respondents their comments on power relations in their interactions with one another and with others outside the research study setting. The concept of power and how it works in a research setting is not obvious, particularly where everyone has a role. Lukes argues that while people in institutions such as political organizations may use their power overtly, some behaviour is covert yet still contributes to outcomes (Lukes, 1974, 2005). In this study I engaged in some unstructured observation of processes in a clinical research setting. Because the setting was not unfamiliar to me, I complemented my observations with questions from my interview guide about the power differentials among the different actors in the informed consent process. This helped me to understand how they perceived the power dynamics in this process. Below is a brief description of my observations at the research clinics.

A typical day at the clinic

At a research clinic: the volunteers are reporting their arrival to reception or sitting in the waiting area waiting to be called to go through the trial procedures. Some relax as they watch the television, and others talk to fellow volunteers, although most sit silently.

Each of the researchers is in his or her room talking to, examining or taking samples from a volunteer, or waiting for the next volunteer to come in. Sometimes research team members consult one another or discuss what is happening. Everyone is busy particularly in the mornings. It is not until, around 3.30-4.00pm that there is a sense of relaxation in the research team because usually by then most volunteers have left. This is true at both sites; most work with volunteers is done in the morning, and paper work, sorting queries and filing documents is done in the afternoon.

In my observation I realized that these procedures followed the study protocol. The power differentials were clear in the protocol; the site principal investigator was accountable for the conduct of the study and in charge of the rest of the team, delegating roles and responsibilities to research team members at the start of the study – for example the nurses usually conducted the initial discussions and questionnaire interviews with volunteers and reported to the study physicians. Both trials had a study coordinator to whom all team members; nurses, counsellors, and study physicians reported. Power here was realized mainly through the reporting structure of the research team, with the site investigator holding more power in terms of the final decision on a given situation in the study.

While discussing power in the informed consent process I asked the volunteers what brought them to the clinic for their scheduled visit. I asked what compelled them; most reported that it was their responsibility to turn up as they had agreed to participate in the study. Their responses reveal self-motivation, although some reported that the study team encouraged them to come. Volunteers expected that their participation would lead to positive research results and so some were keen to attend follow-up visits at the clinic. From the volunteers' accounts I realized that their decision to go to the clinic had been autonomous without any outside pressure. The volunteer's quote below explains that the doctors' emphasis on their attendance early in the trial led her to decide to turn up that day, but also reflects a certain level of power attached to the study physician:

Actually today I was not going to come, but I remembered the doctor had made the point that we should keep our appointment dates. (Female volunteer aged 31, Study 1)

Volunteers also encouraged each other to continue to attend the scheduled clinic visits because they were interested in the end result of the study:

On my way to the centre I met my [fellow volunteers] and we encouraged each other to keep coming and to provide the correct information so that we can know what happens at the end of the trial. (Male volunteer aged 36, Study 1)

When I analysed the data gathered from the research team I could see the role that power dynamics played as the research team interacted with the other actors in their roles in the informed consent process. The SEC has the upper hand in reviewing protocols and monitoring studies. A nurse said:

If you have violated the protocol you have to report to [the SEC]

The principal investigator has the power to assign activities to each member of the research team. Respect for colleagues in the research team is stipulated in the research institution's code of work ethics, and the other members accord the principal investigator the most respect.

There is a difference between reporting within a clinical setting and what happens in a research setting, as discussed by a clinician who explained that while nurses' respect for doctors is important in the day-to-day running of a clinic, work in a research setting is usually evaluated in terms of the study output. The nurses' respect for the clinician remains important, as per their training hierarchy, and the work nurses can do is conditioned by their level of training, but they are free to ask questions and give their opinions in a research setting:

Structural differences are almost abolished in the informed consent process, because all the staff are free to walk into the site principal investigators' office at any time to report the challenges they face with volunteers. There is 100 per cent freedom and no fear between the different levels. (Paul, clinician, Study 1)

In the research team the principal investigator is in charge of the trial overall and the findings reflect the level of power that he/she commands over others in the process:

The principal investigator has to ensure that this informed consent process is conducted correctly; he is the general overseer of the process on behalf of the study sponsor. (Paul, clinician, Study 1))

Some power dynamics within the process may be tacit. This study found that the different actors' roles were managed by the different actors according to the institutional rules in that group of actors. For example, while discussing protocols SEC members must declare individual conflicts of interest in a given protocol, and the deliberations on that protocol are made in their absence.

Monitoring approved studies by the SEC started in 2011, and a committee member reported that this was a time which could lead to anxiety for the research teams because the SEC could ask them anything about the informed consent process. SEC members reported that they were careful not to appear to be policing the researchers and their teams during their monitoring visits. When the SEC goes into a clinic to monitor studies, the principal investigator is usually present to manage the visit. I found that the monitoring of studies, even by an internal body, is not taken as a simple procedure by the senior scientists, the research team or even the SEC members conducting the monitoring. Power dynamics are evident during the exercise; the SEC members may ask to speak to randomly-selected volunteers about the informed consent process. The volunteers are less involved in monitoring visits unless they are asked to talk about their experiences.

Although the SEC is independent of the other actors, as a board its members too are influenced by power dynamics in the informed consent process. They are accountable for approved protocols, but whereas they have the right to monitor studies, one SEC member reported that after such monitoring visitors at the sites, the research scientists demand that they be given reports after the monitoring visit. The SEC also has to give feedback to the researchers, just as the research team is answerable to the SEC if procedures are not conducted according to the guidelines.

There does not seem to be any directly observable behaviour indicating any group of actors forcing another to do what it requires, but the system of work involves power dynamics that were mentioned by respondents.

The actors, including the volunteers, have some level of independence from each other despite the power differentials in the research study. Although the research team ask the volunteers to adhere to the requirements of the trial they have the choice to withdraw if they want to.

My study found that the research team had to be careful in dealing with volunteers even though the two groups of actors were interdependent in the research process, as reported by a scientist:

When you are providing clinical care, people come to you because they are unwell and need you to treat them ... In a way they are dependent on you, [and] when you are in research you are dependent on the participant. You want them to be in your trial; you want them to remain interested and you don't want them to withdraw, so in a way you have to be nice, be patient – but this is professionalism really. (Festo, scientist, study 2)

The other fact of which the research team must be aware is that volunteers may not question clinicians' suggestions:

Medical workers have power. Very often once a doctor says 'Do this', patients will do it, whether in a research setting or not. So you have to be aware of this, even in research. You try not to abuse it. I guess that's where the SECs come in: to try and curb that power. (Festo, scientist, Study 2)

Some narratives demonstrated that a small percentage of volunteers know their rights and demand to talk to the principal investigator if they have an issue they want to discuss privately during their visit to the clinic. They have enough power to get their own way. A counsellor who had had an experience with some volunteers who demanded to talk to the site principal investigator reported:

There are some volunteers who are well-informed; they come and say 'We want to talk to the [principal investigator]', and they go and chat with him. I'd say about five per cent, depending on the literacy rate. They may say they just want to say hello, but in the process the chat continues and they can ask many questions. (Susan, counsellor, Study 1) A senior scientist cited an experience of some volunteers making demands about the amount of time they had to spend at the clinic:

We have some volunteers who are students who come and tell you, 'I have an exam at two and you have to see me very quickly'. We have a businessman who calls and says 'I'm coming at eight, but at nine I have to go'. So when we're delayed and haven't finished by nine he ... says 'Doctor, I said by nine' and he's getting phone calls as we talk. (David, scientist, Study 1)

All the discussions about power in the informed consent process in a clinical trial point to show the interdependence between the different actors to accomplish their roles. While each actor was independent in some aspects, in general in the informed consent process power cannot be seen in the same way as political power, where A impacts on B and causes B to do what s/he would not have done otherwise (Lukes, 2005). The power here could be seen as shared, with actors managing on-going dynamics through communication with each other and each enabling the others to play their roles. The volunteers' reasons for joining a trial, examined later in this thesis, were mainly linked to their expectation of the benefits, but on studying the process in more detail this does not always reflect that the volunteer is a less influential actor in the informed consent process.

6.6 Interactions between the research team and the volunteers

The interactions between members of the research team and volunteers were reported to be friendly, and over time they tended to become informal with volunteers talking about their personal circumstances with the research team members and revealing information that was not necessarily related to the research.

The interactions between research team members were formal. They had to adhere to professional work ethics in their dealings with each other, knowing who to report to and when. The unifying factor in their relationship was the trial and how it was conducted. Team meetings to discuss the study and the challenges they encountered were reported by the research study team at both trial sites as a regular activity. Personal differences in their beliefs and values regarding any aspect of the research were usually toned down by the formal institutional working environment and by adhering to the requirements of the protocol. Power differences in their interactions were neutralized because of the need to attend to their work. A team member noted:

Even if you had your beef [disagreement] with someone yesterday, somehow the working relationship is there, somehow I have to come back to you and we work together. (Aida, clinician, Study 2)

The volunteers reported that their interactions with the research team were satisfactory, noting the importance of knowing their role as volunteers and expecting the research team to fulfil what is emphasized during the information sessions about the procedures of a trial:

The important thing is knowing what you're going to do. If you know that, when you arrive you know where to go, how your file moves from office to office; it is also important to keep your appointment. (Male volunteer aged 50, Study 2)

Another volunteer, reporting on their relationship with the research team, mentioned the transport refund:

The relationship isn't bad, because when we came they told us they would reimburse our transport costs and give us a bonus. They have kept their word. (Female volunteer aged 25, Study 1)

This volunteer was concerned that the study team members kept their promise, and in my interpretation, was not concerned with the details of the procedures involved in the informed consent process.

The male volunteers appeared to act independently of other family members in their decisionmaking but the female volunteers usually had to inform their spouses. While some volunteers informed some of their relatives about their participation in the research, they were not obliged to give details about it. Not revealing details to relatives was more common among the Study 2 volunteers.

6.7 Conclusion

The factors that have emerged as relevant to the informed consent process include beliefs and values, gender roles, sociocultural beliefs, trust, power dynamics and decision-making. Gender, as demonstrated in this chapter, is important in volunteers' relationships with their sexual partners. The different positions of women and men in decision-making in this highly patriarchal community cannot be overlooked, particularly if volunteers are not to drop out in the course of a research trial.

Individuals' beliefs and values can impact on informed consent positively or negatively depending on rumours about the trials in the community and the volunteers' common need to keep within community norms even when participating in a research trial. It is therefore important to understand that local cultural beliefs impact on how volunteers deal with issues arising during clinical research and in the informed consent process.

Power issues ran throughout the informed consent process and were managed during the interactions of the different actors. For the research team interactions were guided by what

was expected according to the trial protocol. The volunteers kept their commitment to come for the research but they also had the ability to decide whether to attend or withdraw from the study. The SEC power was mainly referred to by the research team during the time of protocol review and monitoring of studies. Interactions during the informed consent process were generally formal between the research team and the volunteers, although over time the relationship became more informal, with volunteers confiding in team members and revealing personal issues not necessarily related to the trial.

Trust was built and built upon during the duration of the trial. However, this cannot be taken for granted if the information that the research team provides to the volunteers is not clear.

Having discussed factors influencing this study, in the next chapter I discuss the experiences of the different actors in the informed consent process and how they implemented it in practice.

Chapter 7 Experiences of the actors in the informed consent process

This chapter discusses the findings on the actors' experiences and implementation of the informed consent process in the two case-study clinical trials. It focuses on research questions 4: How is the process of informed consent experienced and implemented by the different actors in the HIV clinical trials? And 5: What are the views of the actors in the clinical trials on the signing and thumb printing consent procedure?

The chapter begins by examining the research volunteers' experiences with HIV and why they joined the clinical trials. The next section in this chapter discusses how volunteers make decisions during the informed consent process and how they interpret the process of signing the screening and enrolment consent forms. The section that follows presents the research team's experiences of the informed consent process and their views on signing the consent forms; and the last section considers the experiences of SEC and CAB and their views on the volunteers' signing of the consent forms. Each of these groups of actors contributes to the informed consent is about protecting them from harm; the research teams implement the research; and the SEC and CAB members monitor the informed consent process of the research. The experiences of all the actors are important to understanding the informed consent process.

7.1 Volunteers' experiences with HIV and AIDS

The volunteers in both trials had some experience of the effects of HIV and AIDS. Those in Study 2 were affected directly and those in Study 1, indirectly. HIV has impacted the Ugandan population in various ways and has affected economic development in families where the working age group has succumbed to death due to AIDS (Seeley et al., 2009). The volunteers reported that they were prompted to participate in research because AIDS is still affecting them and families in their communities. This section examines why they took an HIV test and then discusses their reasons for joining a clinical trial; this is important for my research because in order to understand the informed consent process I needed to understand what prompted the volunteers to join the clinical HIV trials. With this background, their perceptions of the informed consent process are discussed.

7.1.1 Volunteers' reasons for taking an HIV test

For most volunteers, going for or accepting an HIV test was the result of past experience. The main reason they gave for taking the test was that they had lost a close relative, a spouse, a

parent or a close friend to HIV. A male volunteer in Study 1 reported that he decided to take an HIV test because he had lost a number of relatives, including his mother, to AIDS. A female volunteer in the same study had lost a sister who she had been very close to and looked up to; this had prompted her to take a test to learn her own HIV sero status.

The main reasons for the volunteers in Study 2 taking an HIV test included having had a sexual partner who had succumbed to AIDS and receiving information that pointed to HIV:

I had a wife I married first; that lady died. But when I went to bury her I heard rumours that her first husband had died of the same sickness [AIDS], so from there I decided [to] go and test myself on the very day of the burial ... I had started feeling that I was not leading a normal life. I was getting fevers and coughs. (Male volunteer aged 39, Study 2)

The other reason for taking an HIV test in Study 2 was ill health, particularly persistent infections:

I would get headaches and fevers. I would be fine in the morning but every evening I would be sick with fever, it kept happening ... Then I developed a skin rash and I was losing weight. After a while my brother advised me to go for an HIV test. (Female volunteer aged 40, Study 2)

7.1.2 Reasons for participating in an HIV clinical trial

The reasons the volunteers gave for joining the clinical trial were related to past and current experiences with HIV and AIDS. The effects of HIV or present HIV-infected state led them to participate. The volunteers in both studies expected that a solution to the HIV problem would be found in the future. The volunteers in Study 1 hoped that they would be protected from HIV infection and the volunteers in Study 2 expected to lead a better quality of life as a result of the trials.

There are marked differences between the two groups of volunteers as to why they continued to take part in the trials. Whereas those in Study 1 were concerned with avoiding catching HIV, the volunteers in Study 2 were seeking strategies that would help them to cope with their HIV-positive status. Their coping strategies were related to their cultural obligations, beliefs and expectations of the trial.

All the volunteers in Study 1 reported that the main reason for continuing to take part in the trial was their desire to protect themselves from catching HIV. I asked them how being in a research trial could help with this, and the majority said that the research team's HIV-prevention messages such as 'consistent use of condoms for every sexual act' were a constant reminder that the vaccine they were given did not protect them from acquiring HIV.

One female volunteer in Study 1 had a different reason for continuing to participate in the trial: to find out whether the vaccine would prevent HIV. This volunteer reported differently from the other volunteers in the trial despite the emphasis of her fellow volunteers that one of the key messages of the information session was that the vaccine does not prevent HIV. This shows that all the volunteers in a trial may not have the same understanding of the information provided.

The typical first response of Study 2 volunteers on being asked why they stayed in the clinical trial was their expectation of medical advances from the trial:

I expect we will eventually get a drug that will cure us, and I will get cured myself. (Female volunteer aged 40, Study 2)

Two male volunteers in Study 2 hoped to have a child in the future. In Uganda's patrilineal society the male is dominant and therefore having sons is important. One of the men was happy to report that his pregnant wife was still HIV-negative:

I'm still lucky; my wife is HIV-negative ... now she is pregnant, about to have a second child. And if God helps me and it is a boy then I will be one of the luckiest. (Male volunteer aged 39, Study 2)

The other male volunteer hoped that one day he would have another child and reflected on the fact that he had only one:

I have been hoping that in the near future I will be fine and be able to get a woman and have a child, probably an heir, because currently I only have one child. (Male volunteer aged 50, Study 2)

This volunteer already had a wife and one child, but after many years without another child his desire to acquire another wife and probably another child are embedded in the beliefs and values of this society (Roscoe, 1965, 1911: 82-97; Muyinda, 1997)

These two examples of male volunteers in Study 2 show the type and degree of emotional and psychological stress that people living with HIV may feel while trying to cope with AIDS. Although the volunteers in this study are on antiretroviral therapy (ARVs) and are HIV positive they have individual obligations that they feel the need to fulfil in order for them to feel happy, or 'lucky', as one of the volunteers put it. The kinds of situations such as trying to fulfil their family obligations that the volunteers have to deal with may implicitly impact on the informed consent process in the sense that they continue to participate in the trials due to personal aspirations and not necessarily for the sake of the objectives of the trials. An individual's societal obligations and norms do not change with their HIV sero status, even when a research volunteer is aware that they are HIV positive.

7.1.3 Rumours faced by the volunteers

Participation in HIV and AIDS research was not without challenges, many in the form of the rumours that the volunteers have to cope within their communities. The most challenging rumour for Study 1 volunteers was that whoever went to the MRC research station *'must have HIV'*. Even six months into my study the volunteers were still reporting the rumours they had heard in their communities, an indication that these were a source of anxiety for many of them. It is argued elsewhere that researchers should not take rumours affecting research subjects lightly (Geissler & Pool, 2006).

Other rumours reported by the volunteers were that their blood was to be sold abroad and that the researchers were injecting them with HIV. Few in the community understood the concept of a vaccine and one volunteer reported that she had been asked why the vaccines were not being tested on people already infected with HIV. The community may not understand the science of illness and disease in the same way that the researchers do (Kirwen, 2008).

Managing such rumours was critical in order that volunteers enrolled and continued to participate in the trials. The research team reinforced the trials' key messages and the volunteers had to decide whether to believe what they were told at the research clinic or what they heard in their communities.

The Study 2 volunteers heard no rumours directly relating to being infected, but were told by colleagues and family members who knew their HIV sero status that they would die quickly if they stopped taking the Cotrimoxazole. This was a concern for many of the volunteers, who reported any new symptom that they had not experienced before joining the trial to the research team. Concern about good health was clearly important for those already living with HIV.

During the focus group discussion the Study 2 volunteers had mixed information about whether they were on the placebo or the active arm of the trial. This was influenced by rumours that they had heard from other volunteers:

R1: Because we got to a point and one lady said 'I think what they are giving us doesn't contain a drug', but then I asked 'Why would they give it to us then?'

Chorus of 3: I also heard that rumour.

R1: But you know at first they told us we were going to stop using Septrin [Cotrimoxazole], and so when we came here people believed that what we are being given is a dummy (ekigumaaza).

If this kind of communication between volunteers is not fed back to the research team it can affect the progress and results of the trial. In this case Cotrimoxazole is sold over the counter in drug outlets, pharmacies and even small drug shops; a volunteer who believes s/he is being given a placebo may decide to buy the drug for her/himself. Rumours are common in this society due to close neighbourhood relationships (Nziza et al., 2011). The volunteers are part of the community and can therefore be influenced by such rumours. Rumours can contribute to potential volunteers' refusal rates. This shows the importance of the research teams having regular contact with volunteers and finding out about rumours and other issues that affect their adherence to the trial procedures and can affect the trial outcomes.

7.1.4 How volunteers understood study information

An important aspect of informed consent is the discussion of the trial information by the research team and the volunteers. As Appelbaum et al. (1987: 57) say, 'The duty of disclosure, or duty to inform, is the truly distinguishing and innovative aspect of the informed consent doctrine'. The volunteers often see the procedures that they undergo as more important than the general information provided about the trials.

While the researchers may spend a lot of time presenting the volunteers with information about the trial, this study has found that at the start of a trial volunteers may not consider all of the information important. When the different clinical procedures begin they may reflect back on information given to them at the beginning of the trial. It may be more appropriate to discuss the information piecemeal as the volunteer progresses through the trial.

The research teams and scientists were keen to provide the volunteers with information about the trial and to ensure that they understood the research aims, while the volunteers were interested in the practical procedures and the state of their health, as reported from both trials. The research team was concerned about how much of the information about the research was understood and retained by the volunteers during the trial. Providing so much information to a volunteer at the start of a trial did not necessarily bring about the expected results, as described by a counsellor:

Usually at the initial stage they tend to tell us that they have understood, but later, alone, like at visit 2 [this may be after a month], you ask them what you talked about last time and you find that they have not understood the information. (Angela, counsellor, Study 2)

A SEC member emphasized the difference between the researchers' and the volunteers' comprehension of the trial information:

The level of comprehension of the researched communities is not the same as the level of comprehension of the investigator ... because some researchers have been carrying out research in these communities for a long time. (Ken, SEC member)

The SEC emphasized the use of the guidelines even in a context that is very familiar to the research team that is continuously conducting research in the community, because a researcher routinely conducting research and a volunteer participating in the research may have different levels of understanding of the same information. The volunteer may never have experienced research before and does not know what taking part entails. These differences in understanding can affect the implementation of the informed consent process if it is not regulated by guidelines, according to my findings, raising the question of how the SEC can ensure that the investigator conducts the informed consent process appropriately as already discussed in chapter 5.

In this section I discuss the volunteers' understanding of the objectives of the trial in which they enrolled, and specifically what they understood about randomization and the side effects of the study drugs that they experienced.

7.1.4.1 Volunteers' responses about objectives and design for study 1

I asked the volunteers to describe the objectives of the trials in which they were participating. The general response from the majority of the volunteers in study 1, was that the vaccine they had been given was not to prevent HIV and that the researchers were investigating how their bodies would react to it and whether it would cause them harm. Of the 13 volunteers in Study 1, one female volunteer reported that *'they are just testing this drug on us to see if it cures AIDS, but it does not prevent it'*.

All the volunteers said that the vaccine would not prevent HIV and that they needed to protect themselves from acquiring it, but they usually referred to protecting themselves from HIV in general terms, which after probing referred to abstaining from sex or using condoms during sexual intercourse. The volunteer who said that the vaccine was to prevent HIV also said that she needed to protect herself from acquiring HIV; her mixed message reflects the need to review information presented to volunteers during the trial duration regularly with them.

In this study the use of vernacular terms that are not defined can be confusing. For example, most volunteers when they speak of HIV protection in the vernacular it can mean protection from anything and not necessarily from HIV infection. Information may be clear to the research team member providing it but make little sense in the way the research volunteer interprets it.

All the Study 1 volunteers knew that the trial involved randomization. They recalled that they had been told by the research team that some of them would be in the placebo arm and some in the active vaccine arm of the trial. During the individual interviews they said that they did not know who was on a placebo arm and who on the active drug arm in the trial. In the focus group discussion the volunteers agreed that the trial was randomized, with some volunteers on the placebo and some on the active vaccine, and they all hoped that they were on the active vaccine. This reflects the belief that they brought to the research that once one is given a drug it must be useful to them; this type of belief about research needs to be discussed and mistaken information corrected as soon as it is reported. One of the volunteers said in the focus group that he doubted that the research team were also blinded in the trial, as they had been told. The following extract from a focus group discussion illustrates the degree of doubt generated by their beliefs:

R4: They told us ... that the vaccine we are being given, they said some will get the real drug and others will get a placebo (ekyefananyiriza); anyway the vaccine is not to prevent HIV but they want to see how our bodies will react to the drug.

R7: That is the truth because the researchers (abasawo), they hid something from us ... Now among the nine of us, we cannot know whether five got a placebo or four got the right vaccine. We are looking at each other because they've kept that to themselves [all laugh], but when they look at us, I think they say 'Because of what I see, I think what we gave him works', because for them, they know.

R6: Even the researchers do not know.

R7: But for them they know the bottle types where they got the drug to inject us. [All laugh]

It is clear that the volunteers were aware of the randomization in the trial, although one discussant, who was very vocal and active, supported by the laughter of other group members, continued to insist that the research team knew the difference between the drugs they injected into each of the volunteers and were therefore not blinded.

7.1.4.2 Volunteers' responses about the objectives and design of study 2

When asked what the objectives of the trial were, Study 2 volunteers spontaneously said that it was to test what would happen to them if they stopped taking Cotrimoxazole:

They are researching so that they can see whether we can stop taking Septrin or we need to continue taking it. (Female volunteer aged 40, Study 2)

Despite all the volunteers reporting in their individual interviews that they were involved in research on Septrin and the effects of stopping to take it, only four of the ten Study 2 volunteers could immediately articulate that there was randomization in the trial and that some of the volunteers were on a placebo and others on the active drug. Of these six, two reported that they were taking a *'new drug'*; two said that they were taking *'what would be called Septrin'*; and two reported that they were on the "active or real *Septrin drug'* because they had not experienced any side effects during the trial so far.

During the focus group discussion with study 2 volunteers, two of the volunteers were clear that the trial was '... trying to find out the effects of stopping taking Septrin but continuing with *ARVs*'. The rest of the volunteers did not appear to be clear about what randomization meant for them personally.

The discussion above is an important pointer to the fact that volunteers share information via informal interactions, and randomization was not well understood by some of the Study 2 volunteers. Discussion of the trial information between the volunteers and the research team may be helpful to reinforce the correct information, as I gathered from a meeting that I attended of the Study 1 community liaison officer, senior scientist and volunteers to reinforce correct understanding of the information. If rumours in the community are not corrected by the research teams, volunteers may be influenced by them, affecting their participation.

7.1.5 Side effects reported by the volunteers

Only three female volunteers in Study 1 reported any side effects: one said that her hand had swollen after the first vaccination, another had felt dizzy on the first day of immunization and the third reported that she had experienced heart palpitations after being given the vaccine, although a test for high blood pressure was negative.

A few Study 2 volunteers reported experiencing some side effects that they related to taking part in the research. One volunteer reported having been in poor health since joining the trial:

Since I joined research my health has changed (obulamu bwekyazekyazeemu). In the past I never used to get sick frequently; I could go as long as two years without getting sick, but from the time I joined this research I've started having problems with my health. (Female volunteer aged 32, Study 2)

She had never reported this to the clinicians because she kept hoping that her health would improve. This was her seventh follow-up visit. Sometimes a volunteer will not report side effects because they expect them to end soon. According to the Uganda National Household Survey at least 46% of people who had been sick in 2005/2006 had not sought medical care because they judged their illness to be mild, and this seems to have been the attitude of some

of the volunteers, even when participating in research, because they want to remain in the study (UBOS, UNHS 2005/2006).

During the focus group discussion with the Study 2 volunteers one mentioned being told that if they got very sick they could be put back on Septrin, although it is not mentioned in the trial information sheet. She discussed this openly:

We hoped that if we left that strong Septrin and remained on the ARVs and the drug they are giving us we would survive. They also told us that if it doesn't work, and you get weak after leaving Septrin and you're getting funny effects, you can get back on the old Septrin. So we got hopeful and said 'Why don't we join – we'll probably get a cure'. (FGD, Study 2)

The quotation above opens up several issues. First, the volunteer mentions that they were told they would be put back on Septrin if they became sick. This is not on the information sheet. She also mentions that they had been taken off the 'strong Septrin', an implication that they may be on some form of drug which is not so strong, and hopes that by joining the trial that they will be cured. These statements point to how information about a trial can be interpreted in different ways. The research team should check volunteers' understanding throughout the study. The volunteers that I interviewed had all been in the research for at least six months to a year.

In the Study 2 focus group volunteers repeated information that they had received from other volunteers but had never discussed with the research team. They mentioned that they interacted with fellow volunteers who had enrolled at the same time as they did because their follow-up visits occurred on the same days.

Study 2 volunteers had more issues with the kind of information that they received about the trial than those in Study 1. Whereas the first thing they all mentioned was that the trial was about Septrin, the issue of randomization and the expected trial outcomes were mixed up with rumours that they had picked up from other volunteers. It was not easy to tease out what facts about the trial were clear to them. This points either to a gap in the way the information was presented to them or to their expectations on taking part in the research. The findings show that there is need to devise ways for research teams to pick up volunteers' daily conversations during their interactions with each other, because these conversations contribute to the understanding of the trial which is part of the informed consent process and the conversations can reveal issues that may affect the trial outcomes.

7.1.6 Reasons why potential volunteers refuse to take part or drop out of research

I was not able to interview any potential volunteers who had turned down the invitation to take part in the clinics' trials as they had been on-going for a while. In one of the volunteer focus group discussions, the volunteers reported that sometimes the inclusion criteria of the trial may lead to some volunteers refusing to participate. An example given for study 1 was the requirement that female volunteers would avoid getting pregnant and the male to avoid getting their partners pregnant during the first part of the trial. For the volunteers who needed children in the study period, some chose to decline taking part in the clinical trial.

I interviewed the counsellors in the research team about the reasons behind refusals to take part and why some volunteers drop out. I targeted counsellors because they discuss emotional and psychological issues with the volunteers during the research process. One of the reasons for refusal reported by the counsellors was misinformation, usually from the potential volunteer's peer network and particularly from peers not participating in the research. Most of those who influenced others had not read the information leaflets but instilled the fear in potential volunteers that something bad would happen to them if they participated.

The second reason for refusals is family members' opinions given during the decision-making process. As a counsellor reported:

Sometimes a client comes, reads through the information and is convinced, but when he or she goes back home a family member says 'I don't think this is right', and so [the potential volunteer] chooses to withdraw or refuses to come back (Timothy, health educator Study 2)

I interviewed volunteers about why some drop out of research trials. They gave various reasons including loss of interest in the trial, not having time for follow-up visits, and for some, difficulties finding money for transport to the clinic. While the research team refunds transport costs after a scheduled visit, some volunteers may not be able to find enough money to attend the clinic and they end up dropping out of the trial.

According to the counsellors in Study 2, volunteers dropped out due to failure to find the money to come to the clinic and discouragement from others in the community. For example they find themselves questioned by fellow community members about why they have to stop taking Septrin, and so when they begin to get sick they do not return to the research clinic because they listen to the advice of community members who tell them that they need to keep taking the Septrin. Some female volunteers are stopped by their husbands and some volunteers drop out due to relocation away from the area of the research. A few volunteers had informed the counsellors that they were experiencing problems with the trial drugs and when they were sick they could not continue to participate because they did not feel that they were benefiting from them.

The above reasons for refusal to join and dropping out of the trials were similar in the sense that they show that individual volunteers are influenced by their families or community network when making decisions about taking part in research. This influence of factors outside the research setting has implications for the informed consent process and volunteers may require on-going support in terms of receiving information updates and having key study messages reinforced.

Two participants dropped out of my qualitative study. One, in Study 1, relocated; the other potential volunteers' enrolment in Study 2 was postponed for farther investigation due to her laboratory test results and I could not continue interviewing her. I had had my first interview with her about experience with the informed consent. See Table 6 for a comparison of the volunteer responses in the two case studies

Table 6 Comparison of responses from the volunteers in the two clinical trials

Findings	Study 1 responses	Study 2 responses
Perceptions of trial	Investigating how the body	What would happen to their
objectives	would react to the study	health if they stopped taking
	vaccines and whether it would	septrin
	cause harm	
Side effects	Only 3 of 13 reported side	Only one volunteer reported that
	effects which were: a swollen	she became frequently sick since
	hand, dizzy feeling on first day	joining the trial
	of vaccination, heart	
	palpitation but not related to	
	high blood pressure	
Why join the trial	Hope to protect from HIV	Hope to get improved quality of
		life
Reasons for continuing in	Avoid catching HIV which	It is a strategy to cope with HIV
trial	information is reinforced by	
	the research team	
Why refuse to take part in	Family member's opinion at	Misinformed by the peer
research (reported by	the time of decision-making	network, those who did not take
counselors)		part in research
Why drop out	Loss of interest, no time to	Failure to get money to travel for
	attend follow-up visits,	clinic visit, discouragement from
	difficult with finding money	other members in the community
	to travel to research clinic	
*Involvement of others in	The female volunteers had to	Both male and female volunteers
decision making	inform and sometimes seek	made their own decisions and
	permission from spouses.	usually they would not share with
	A few female volunteers	their partners.
	made their own decisions.	
	The male volunteers only	
	informed spouses but were	
	not obliged to.	

* Study 1 procedures required that a sexual partner is known and also tested for HIV; Study 2 volunteers were not obliged to bring their partners to the research clinic for HIV testing.

In the next section I discuss the volunteers' reported experiences of the procedures and the implications for the informed consent process.

7.1.7. Volunteer experiences during the informed consent process

When describing the study procedures in the informed consent process at their first interviews with me, the volunteers explained the details of what happened to them from first walking into the research clinic, and the information provided to them by the research team. When I asked them about the procedures again three months later at their first follow-up interview in my study, most replied as though nothing about the trial procedures they were undergoing had changed, and I had to probe to elicit details from them. It may have been true that nothing had changed, but these responses may partly have been because the second time they saw me, I was no longer a stranger to the research and should know what was going on.

This makes me question whether volunteers going through the same procedures repeatedly end up familiar with the trial procedures and therefore see them as the 'same'. When I interviewed them about specific procedures they went through, they all mentioned that the research teams collected blood and urine samples from them, they easily described the different procedures they went through and knew what to expect at their scheduled visits. The responses at the second interview were quite short but emphasized the samples that had been collected:

They were the usual [procedures]; of course when I went they took my urine sample and a blood sample, maybe what was different was that we were told we had one more follow-up visit. (Female volunteer aged 25, Study 1)

Another female reported that she had been reprimanded by research team members because she had been sick and had not come to the clinic for treatment, as required of her as a volunteer:

I told them what I had gone through and that I had been sick but had not reported it and they told me off because they had told us to come when we are sick. They took a blood sample and then they gave me more Septrin. (Female volunteer aged 40, Study 2)

The regular clinical procedures reported in these two examples were expected by the volunteers. However as seen in the second quote volunteers may not always adhere to all that is required of them as information discussed early on with the research team. According to the volunteer, they were expected to attend the clinic when sick. She mentioned this experience to convey her sense of disappointment and lack of independence in making decisions during the trial. This volunteer mentioned that she was given Septrin at this scheduled visit; the research team was giving drug refills of the study product, which could have been the active drug or the placebo, but the volunteer referred to it as 'Septrin'. These two volunteers' responses point to their limited recall of the information provided by the research teams at the start of the trials.

Although the participant information sheet indicates that the volunteer is free to take part in a trial and to withdraw at any time, the trial procedures, as set out in the protocol, must be followed by the volunteer. They must do what is required of them by the research team once they have agreed to take part in a trial. The findings show that they may not give the same attention to issues emphasized by the research team, such as reporting to the clinic whenever they are unwell. Other options such as getting treatment from a nearby drug shop, as mentioned by the volunteer above, may be available and so volunteers may not always adhere to the research team's expectations. What is important to the research team and to the volunteers is not always the same in the informed consent process. This shows not only that the volunteers' input in the informed consent process, in terms of agreeing to adhere to the trial procedures.

An example of a divergence of interests, although this was not discussed outright in the interviews, concerned the blood samples collected from the volunteers on a regular basis by the research team, these were to enable the researchers to answer the research questions and to check for adverse effects on the volunteers. I found that the volunteers attached importance to these samples: those in Study 1 were interested in knowing whether they were still HIV negative, and in Study 2 they wanted to know their CD4 count to learn that their immunity is still fine and their levels of white blood cells is stable. Volunteers sometimes demanded to know their health status:

I wanted to know my CD4 count and I was given the information. (Female volunteer aged 45, Study 2)

I have felt very happy because every time I have come they have checked me to see if I am healthy [HIV negative], and that has helped me to protect myself from HIV. (Male volunteer aged 31, Study 1)

Such responses highlight two issues for the consideration of the bioethicists who review and develop guidelines for the informed consent process. First, if volunteers, even in long-term clinical trials, refer to research in terms of the treatment they get, what is missing from the trial information provided to them? And second, in low income settings is it possible for researchers to give the appropriate standard of care without impacting on the informed consent process? (Bull et al., 2011). The findings point to the importance of continuous communication about the research objectives between volunteers and research teams whenever the former attend for clinical procedures, particularly those related to sample collection.

The research teams set out the clinic schedules for each trial volunteer and gave them a participant card stating their next appointment at the research clinic. The volunteers reported

that they knew when their next scheduled visit was from these cards. Study 1 volunteers always expected a phone call from the research team to remind them of their next appointment. The volunteers in Study 2 usually knew when their trial drugs were running out and this reminded them that it was time to get back to the clinic. The research team behind this study only telephoned volunteers who had missed a scheduled visit.

The volunteers can be seen as dependent on the system of scheduled visits to the clinic organized by the researchers; the research team, on the other hand, have to work to keep the process going as they make phone calls to the research volunteers. This part of the process involves mobilising the volunteers to attend their clinic appointments and is dependent on the research team; the volunteer then decides whether to turn up. It shows an aspect of the power that the volunteers hold; they are sure to be contacted if they miss a visit. The informed consent process, however, is not dependent on only two key actors; the volunteer and the research team member who obtains the consent from a volunteer but on all those involved who include even the influential networks that the volunteers have in the community.

The next section in this chapter discusses how volunteers make decisions during the informed consent process and how they interpret the process of signing the screening and enrolment consent forms.

7.1.8 Decision-making by the volunteers

This section discusses how and who influence the volunteers' decisions during the informed consent process and their views on the procedure of signing the consent forms. The section ends with their suggestions for improving the informed consent process.

Most of the volunteers in Study 2 decided to join a trial in the hope that the research would eventually lead to a reduction in the number of pills they had to take, while Study 1 volunteers hoped that it would protect them from HIV infection. All the volunteers described their participation in the trial as voluntary; they had not been coerced to join. They described seeking advice from someone they trusted such as a parent, counsellor or respected community leader.

Although the volunteers had decided to join a trial, some reported difficulty in keeping to their decision and continuing in the research. Volunteers in Study 1 reported that they were discussed in the community, where it was believed that they had joined a clinical study because they were infected with HIV. There was a strong stigma attached to attending the MRC research clinic in one of the study areas because the community believed that since the MRC conducts HIV and AIDS-related research all the volunteers must be HIV positive. Thus stigma is still present in the communities despite the presence of HIV and AIDS in Uganda for over two decades. This has been reported in recent news by Uganda's National AIDS Commission

(UNGASS, 2010). The other difficulty that volunteers in Study 1 faced both before and after deciding to participate in the trial were the rumours that I have already discussed in the early section of this same chapter.

Before making the decision we talked about this research with our friends ... and got different feedback, such as 'They are going to vaccinate you and you don't know what will happen to you in ten or twenty years': 'You might grow a lot of hair like monkeys' [all laugh] or 'You will die a slow death' ... It was hard, and we actually had to think hard before volunteering. (Volunteer FGD, Study 1)

The volunteers were concerned about possible side effects of the trial, which some community members had suggested would happen a long time hence. This could worry a volunteer who had agreed to participate in a trial for the next two years. The volunteers were anxious at the start of the trial, and a number wondered why the research team were not taking part in it themselves. Volunteers in the focus group revealed a need for reassurance from the researchers that the potential harm discussed in the community would not happen to them. The research teams in both trials kept up a continuous dialogue with the volunteers to allay their anxiety.

Some volunteers' decisions, particularly regarding Study 1, were delayed because they had to inform their spouses, as encouraged by the researchers, and some spouses did not support their joining the research and even stigmatized them for it:

My husband would ask me how things had been [at the clinic] and he would tell me why [the researchers] do not try those vaccines on animals ... sometimes I got the signs that they had told us about, some feverishness and feeling cold ... Every time I felt a bit sick he would tell me that I would die in a few days. (Female volunteer, Study 1 FGD)

Whereas some volunteers met with challenges when deciding whether to join a trial, others did not, either because they had support from someone such as a parent or because they were independent in making their decisions, as was common among the men. Gender norms in this community require that married women make important decisions after informing and sometimes after getting permission from their spouse, as noted in Chapter 6. This issue of informing and sometimes getting their word to join research was reported more by the volunteers in Study 1, because a requirement for their enrolling in the trial was that their spouses must be tested for HIV.

Both male and female volunteers in Study 2 were more independent in their decision to join the trial because they felt that it was up to them to help to find a solution to AIDS, which was already a challenge in their lives, and the trial did not require that their partners were tested for HIV.

Deciding to remain in the research meant that some volunteers had to make decisions continuously, such as to refrain from sexual relationships:

You may admire someone and want to have sex with them, but because you are taking part in research you decide to wait until you are done with the research. (Male volunteer aged 24, Study 1)

Thus individual decision-making patterns differed with each volunteer according to their social context. The main reasons given for deciding to take part in a trial included the desire to make a difference in the current HIV pandemic and the desire for personal good health. The rumours that they were being infected with HIV in the trials made it hard for some of those seeking good health to decide to take part. This and their on-going decisions about their sexual behaviour throughout the informed consent process makes it clear that the researchers had to offer continuous supportive communication with the volunteers to facilitate their independent decision to join.

7.1.8.1 Who influences the decision to participate?

The volunteers' decisions to participate in the trials were influenced by various individuals who were mainly part of the volunteers' social network such as their parents, siblings, children and friends. Health workers were generally looked up to as better-informed and some of the volunteers consult them before making decisions about their health. Biological parents were the primary and most trusted confidants of many of the volunteers when deciding whether to take part in research:

Two people are very important in my life, and that is my parents, and once I have told them I don't mind what others have to say. (Female volunteer aged 19, married, Study 1)

Female volunteers confided mainly in their parents before deciding to join the trial; most of the male volunteers in Study 1 did not consult anyone, and the few who did asked the advice of friends or elder siblings. The male volunteers in Study 1 did not consult anyone before deciding to join the research because they saw them as either too old to understand the research or likely to discourage them from joining. Most married male volunteers informed their partners of the trial details to avoid conflict:

... this depends on you as an individual, but you need to inform your partner because if you do not tell them [what happens at the clinic] and yet I usually go home with leaflets with the MRC information ... It might give her the idea that you're probably HIV positive and you haven't told her. (Male volunteer aged 31, Study 1)

The above quotation reflects the stigma in the community that is attached to volunteering for research. In this society men are not obliged to consult anyone before making their decisions.

Many volunteers in Study 2 made their decision to join the trial alone, because they are living with HIV infection:

I did not seek [my husband's] advice before I joined the trial. When I heard what they told me about the research, I decided on my own to join. My husband learnt about it later. (Female volunteer aged 25, Study 2)

Two male volunteers in Study 2 who in this study were not obliged to do an HIV test with their partners communicated their decision to join the trial to their partners to avoid conflict in their relationships arising from rumours in the community.

One female volunteer did not disclose her participation in the clinical trial to anyone, including her sexual partner at the time:

I made my own decision. Although I live with a man he does not know I'm taking part in a trial. (Female volunteer aged 40, Study 2)

The volunteers' privacy was important to them even though the informed consent process might involve discussion between family members, the volunteer and other actors in the research process. This study has found that it is possible and relatively common for a volunteer to lead two lives while participating in research: one public and one hidden.

Because many volunteers often referred to consulting important others in their lives before making their final decision to join a trial, researchers should take the time to find out who these others are who influence the volunteers' decision-making and engagement with the informed consent process, as a volunteer's social network could impact on their participation in a trial.

Some of the factors discussed in Chapter 6 can play a part in the decision-making process. Who the volunteer trusts and who they involve in decision-making is influenced by other factors such as gender, sociocultural norms and power relations in their social networks. The fact that a volunteer did not inform her sexual partner that she was HIV positive and participating in research points to the concept of power within a relationship. In this example the volunteer held back important information from her spouse, perhaps because she feared his response.

7.1.9 Significance of signing and thumb printing the consent forms

I asked the volunteers what the significance of signing the consent forms was for them and how they would gauge whether someone had understood the information that the research team provided about a research trial. All the volunteers reported that it was very important that they sign or thumbprint the consent forms and that informed consent must be documented; the majority said that signing the consent forms shows that a volunteer has agreed to participate in a trial without coercion. Most volunteers discussed signing or thumb printing the consent forms matter-of-factly as a usual procedure, perhaps indicating that they were used to the way research studies are run. The volunteers in the two studies stated that there was no alternative to signing or thumb printing the consent forms in research:

Even if I've agreed to participate, you cannot know [that I have agreed to take part in the trial] until someone puts it in writing. You know things that you just talk about are not easy to accept unless you have put something in place. (Female volunteer aged 30, Study 2)

The volunteers reported that signing or thumb printing a document was not a challenge for them, and that refusal to sign the consent forms indicates a lack of interest in a study.

I asked volunteers who were able to write what they thought about being asked to thumbprint the consent forms which is a practice in research that is required before enrolling volunteers who are illiterate. In this study I use the word illiterate purely to mean someone who is unable to read or write, as I am aware that many people have a broad understanding of the world despite their illiteracy. They felt that it was not right to ask someone who could write to sign with a thumbprint. It was prestigious for a volunteer to be able to sign the consent forms, and there is stigma attached to thumb printing, which I discuss later in this chapter. A male volunteer mentioned that thumbprints may be used in banks and elsewhere, but asking a research volunteer to thumbprint the consent forms when they are able to write their name is not acceptable. To some volunteers however, it did not matter whether they signed or thumb printed the form.

Signing the consent forms is a research requirement which the volunteers accepted without question. The main reason the majority of volunteers gave for the necessity of signing was to show that they had not been coerced; they did not mention anything related to study content such as the trial's objectives and procedures as presented by the research teams at the information sessions.

7.1.9.1 Volunteer's views on thumb printing

I asked the volunteers how they compared the comprehension of trial information in a volunteer who signs the consent forms and one who is only able to thumbprint them. Most volunteers felt that it did not matter whether one signed or thumb printed; what was important was being able to understand the information given by the research team:

We need to know that both a person who has understood and one who has not understood can sign. (Female volunteer aged 31, Study 1)

The above quotation is loaded with meaning because it shows that it is possible for volunteers, whether they write or are only able to thumbprint the consent forms, to join a trial without understanding the preliminary information. My study found that the volunteers did not view signing the consent forms as a challenge, and in the quotation above the volunteer disregards literacy as a way of gauging volunteer comprehension of the study information.

If volunteers are only concerned with signing the consent forms as a prerequisite of joining a trial this could be a problem for the research team later on in the informed consent process, particularly if a volunteer forgets the objective of the research in which s/he is involved. This could be true, for example, of the volunteers who reported that they were in the group that had been given the active drug although they had been told that the study was a randomized clinical trial (see Chapter 5).

7.1.10 Volunteers' suggestions for the informed consent process

The volunteers made several suggestions about improving activities that took place during the research, all of which relate to the informed consent process. They suggested that their understanding should be gauged after they have been in a research trial for a while, as testing for comprehension of the study information soon after providing it may only show that they can recall it. Another suggestion was that the research team should give volunteers enough time to think through the study information before they assess their comprehension of it:

Questions should not be asked immediately, because sometimes we are asked questions about what we have just been told; the brain is still recalling what you read to me some ten minutes ago. (Male volunteer aged 27, Study 1)

The information given about the trials is not less well understood by illiterate volunteers, according to my findings, showing that signing or thumb printing the consent forms is not an indicator that the volunteer has understood it. The volunteers also suggested that all study information should be simple and clear.

They also suggested that the research teams should hold more than a single information session to ensure that volunteers understand the trial objectives.

Another suggestion from the same volunteer was that the research team should provide the study information in very clear terms:

When we are given information it does not tell us definitely what will happen to the baby [if a volunteer gets pregnant] – they always say the baby 'might have a problem'. Even the people who give the information are not definite. (Male volunteer aged 27, Study 1)

The consent document for Study 1 states; 'We do not know what effect the vaccine would have on an unborn child if given to a pregnant woman. If you become pregnant during the study, you will not get any more vaccinations' (p. 8, ICD version: 5.0.3 August 10). This sentence may be easily understood by the research team, but volunteer's concern was that it leaves room for the volunteer to decide whether to get pregnant or not. The information sheet for Study 2 does not refer to pregnancy.

The volunteers suggested that the research teams should come up with an adult literacy programme to support volunteers who cannot write their names, to be carried out during long-term trials so that volunteers who are not able to write their names at the start of a trial would be able to do so by the end. This was referred to as a useful benefit for a research volunteer. This suggestion points to the community stigma attached to a volunteer who is not able to sign his/her name on the consent forms. The suggestion persisted despite the fact that all the volunteers had noted that understanding the study information has nothing to do with the ability to sign the consent forms.

Some further suggestions to improve the informed consent process were personal, such as a request for more money for transport to the clinic because travel costs fluctuate. A few female volunteers suggested that research should not include females aged 25 years or less, who still need to get children and may not wait for a long time of the trial before they get pregnant because they are expected by their husbands to get pregnant when they have been married. Another suggestion related to reproductive health was that clinical trials should only enrol women who are not sexually active. These two suggestions relate to the sociocultural norms in this community; once married, a woman is expected to produce children as soon as possible. A male volunteer suggested that female volunteers should be given hormonal family planning methods such as contraceptive injections to avoid pregnancy during a trial.

A focus group discussion with the volunteers in Study 1 showed that it is important to inform them about all the activities taking place at the research clinic. For example, the research teams should explain that there are multiple research projects going on at the same time so that volunteers understand that sometimes they will have to wait for a while before being called in to see each of the research team members who carry out the scheduled trial procedures.

The volunteers' opinions about decision-making and consenting to take part in clinical trials demonstrated their active involvement in the informed consent process and they were able to comment on what they observed during the research process. Decision-making is voluntary and personal, despite the volunteers' consultation with important others in their social networks.

The next section presents the research team's experiences of the informed consent process and their views on signing the consent forms; and the last section considers the experiences of Uganda Virus research institute's (UVRI institutional review board, Science and Ethics Committee(SEC) and community advisory board (CAB) and their views on the volunteers' signing of the consent forms. Each of these groups of actors contributes to the informed consent process: the volunteers are at the centre of the process because the concept of informed consent is about protecting them from harm; the research teams implement the research; and the SEC and CAB members monitor the informed consent process. The actors are important to understanding the informed consent process.

7.2 Research team experiences of the informed consent process

This section is about the research team' positive and challenging experiences, their views on decision-making in the process, their interpretation of the process of signing the consent forms by the volunteers, lessons they have learned during the informed consent process and their suggestions for improvement.

7.2.1 Positive experiences reported by the research team

The study team members discussed their positive experiences of the informed consent process in relation to their individual roles in it. Realizing that a volunteer had understood the study information was described by all as a positive experience but was expressed differently by the different categories of team members, as shown in these examples:

When you give the information and comprehension is really good and they're scoring 10 out of 10, you discuss it and it's a good day. They have understood the study. (Susan, counsellor, Study 1)

There are some patients who understand what it takes to participate in a study; some have even gone out to talk about the study and encourage their colleagues, and some even inform you about what their friends are going through. (Timothy, health educator, Study 2)

For Susan, a volunteer gaining a high score in an assessment of their understanding of the study information is a positive experience. For Timothy, it is when he realizes that a volunteer can go out to the community members who are not in the research and talk about the trial. These differences in expression reflect what each team member believes to be important once they have provided information about the trial to a volunteer. For one research team member, short-term recall is satisfying; for the other, long-term understanding of the study information is demonstrated when the volunteer can pass the information on to others.

The clinicians reported that volunteers who understand the key study messages usually adhere to the trial procedures, with one commenting that such understanding safeguards the

researcher from outsiders interested in whether the trial is conducted without coercing the volunteers.

The community mobiliser noted that when the other members of the research team follow trial procedures listed on the participants' information sheet, such as refunding transport costs after a volunteer's scheduled visit, the volunteers trust him as a mobilizer and this makes mobilization in the community easier.

The research team also commented that because discussing the study information with volunteers was routine, with time it became easier to deal with their questions:

When you see the first patient they will ask you a question that makes your life easy to answer what the patients who follow after the first one, if they ask similar questions. Before they even tackle the problem you have given the answer so the questions become fewer along the way. (Aida, Clinician, Study 2)

All the researchers viewed working in a team as a positive experience. Volunteers are seen by different team members for different procedures, and they build on each other's information to help the volunteer to understand the trial procedures.

The research team also viewed being able to recruit the required number of volunteers for the trials as positive. The volunteers in Study 1 were HIV-negative healthy young individuals; those in Study 2 were HIV-positive and had survived comfortably for at least six months on ARVs so it was not taken for granted by the teams that they were able to recruit the required numbers.

The positive experiences discussed by the research team encouraged them during the implementation of the trials. However, they need to be understood in context; for example a volunteer scoring 10 points out of 10 for comprehension of the information supplied may be very exciting for the researcher, but as noted earlier, recalling study information does not necessarily mean that the volunteer has understood it, although it is one good indication of it. A research team member's familiarity with the information they provide about the trial can be a disadvantage if s/he takes less trouble to treat volunteers as individuals with different levels of understanding.

Teamwork within the research team, the volunteers' comprehension of the study and adherence to the trial procedures, and the research team being able to follow up and maintain a cohort of volunteers in the trial were the positive experiences that the research team recounted. The next section explores the challenges they faced.

7.2.2 Challenges in the informed consent process that were reported by the research team

Low literacy levels among the research volunteers, mainly a problem at the beginning of the trials when the study information is first given to the volunteers. This challenged the research team who wanted to ensure that they had understood the study information before enrolling on a trial. One of the research team noted that even they themselves found some of the scientific/medical terms difficult to understand, and it was equally difficult to convey them in the vernacular language:

There are a lot of medical terms that someone may fail to understand because you cannot translate them for the volunteers; for example SO1 [a component of the trial drug] ... Those terms were a challenge to me, but you [have to tell the volunteers] ... so we may not tell everything. (Sylvia, nurse, Study 1)

At the start of a study some volunteers are hesitant to join in while others are very eager. The research team reported that volunteers who are eager to participate in a study may overlook important key messages from the research team in the information sessions. Some volunteers have certain expectations about participating which can distract them from the objective of the study:

You may go through the process and everything, but at the end of the day you realize the participant had a different interest. There are some clients who want to know their CD4 count and they come for that, so even when you explain you find out later that their mind is on the CD4 count. For some, the study procedures are secondary. (Timothy, health educator, Study 2)

The quotation above shows that the volunteers may join a trial because they are interested in their health status and may see the trial objectives as secondary to their needs. This shows that study information should be integrated within the sociocultural context so that it also addresses volunteer's expectations.

The other challenges reported by the research teams are that some potential volunteers change their mind about participating after consulting important others about it; some volunteers are sensitive about participating in research and do not want to be visited at home by the research team mobilizer, even giving a false address; and that those with mobile phones may be off the network and not contactable when they are needed at the clinic for procedures. The ones without mobile phones are contacted using the details they gave the research team at enrolment.

The study information can be understood in different ways. The challenge lies mainly in helping volunteers to understand the design of the randomized trials testing drugs. The other challenge

reported has to do with handling research volunteers according to the study protocol: the participant information sheet states that a volunteer's access to medical care at the research clinic will not be affected if s/he withdraws from the study. The challenge for the research team is that they are sometimes overwhelmed by the many volunteers that they have to see as part of the trial and also have to spend time with volunteers who have withdrawn their consent and are no longer contributing to the research.

Some of the research teams' challenges during the informed consent process were technical, such as having to translate scientific terms into the local languages spoken by the volunteers, and some resulted from the differing expectations of the volunteer and the research team members. It is important to understand these challenges as part of managing the informed consent process in order to achieve genuine study results. The next section examines how the research team made their decisions during the informed consent process.

7.2.3 The research team's decision-making during the informed consent process

In this section I discuss my finding that the research team make decisions daily as they carry out their individual roles in the trial.

The structure for conducting a trial is outlined in the requirements of its protocol. One of the essential documents is the delegation log, which specifies the duties and responsibilities of each research team member and who they report to.

The research team reported that each team member can make decisions while carrying out their role during the informed consent process. Each exercises some power to make decisions that are useful to the volunteer and the study team during the informed consent process as they handle the trial procedures. A nurse who provides study information can decide that a volunteer is unsuitable for the trial because s/he has not understood certain key messages, without having to report to the clinician or principal investigator.

The research team noted that when something is not clear in the requirements of the protocol they consult together as a team, and if they cannot resolve the issue they refer to the principal investigator. While each team member can make their own decisions, these must be in line with the requirements outlined in the protocol.

The next section examines the research team's views of the process that leads to the volunteers signing the consent forms.

7.2.4 Research team's views on volunteers' consenting process

There were specific issues for the research team regarding the volunteers' consent, particularly regarding the significance of signing and thumb printing the consent forms. I explore their views on the volunteer's understanding of the study information provided to them, especially those

of illiterate volunteers; on the informed consent process in future clinical trials; about the presence of a witness to the process of providing the trial information to illiterate volunteers and to the volunteer thumb printing the consent form; the challenges they faced in obtaining consent from volunteers; and finally their suggestions for improving the informed consent process in this Ugandan context.

7.2.4.1 The significance of signing the consent forms

The research team discussed why it was important for volunteers to sign the consent forms. I have categorized their reasons into four main areas: participation without coercion, legal agreement, accountability and the protection of researchers.

The nurses, counsellors and mobilizer saw signing the consent forms as significant, in that they demonstrated that the volunteers were participating in a study without being coerced and had understood the information given to them by the research team.

The clinicians and scientists described the consent forms as evidence of discussion and an agreement between the researcher and the volunteer. It is interesting that some volunteers argued that if volunteers did not sign the consent forms it would be difficult for anyone to prove that they had agreed to participate in research. Signing the consent forms therefore protects the researchers from being suspected of having coerced a volunteer:

I think they need to sign, or else someone can easily deny that they agreed to participate in your data. If they say they did not agree, what evidence do you have to show that they actually agreed to participate in your study? (Festo, scientist, Study 2)

One of the clinicians noted that a researcher who signs the consent forms is taking on the responsibility to care of the volunteer and keep him/her from harm.

One research team member said that signing the consent forms serves both the volunteer and the researcher: for the volunteer they are a record that they can show to others, although this is not common as some volunteers keep their involvement secret; for the researcher it is a record to show that the volunteer participated freely.

The consent forms also protect the researcher in case anything goes wrong during the volunteer's participation in the study, as they provide evidence that the volunteer was informed about the risks of the trial.

One of the scientists remarked that the signed consent forms do not reveal what transpired between the researcher and the volunteer to someone outside the process:

It is a sign that something has happened. It does not tell you what happened; it does not tell you the details of what happened ... it does not tell you whether I gave the

information very well; it does not tell whether the person understood everything; it just tells you yes, there might have been a process and you know the two people signed. (Robert, scientist, Study 1)

My findings show that signing or thumb printing the consent forms as discussed by the research team is an obligation that the team must fulfil according to national and international ethics research guidelines. The reason for the consent forms, as discussed, is to protect the researcher in the long term in case a volunteer is harmed due to the trial. This seems to mean that the interaction between the two people who signed the consent forms –the research volunteer and the researcher – is more important than the documents they sign, even though the latter provide documented evidence. It is therefore of interest to note that the last scientist quoted above mentioned that seeing a signed document does not necessarily mean that the volunteer was informed about everything relevant to the trial, or that they fully understood the study as discussed with the research team.

The next section discusses the research team's views on thumb printing.

7.2.5 Research teams' views on thumb printing by the volunteers

I asked the research team how well they thought the non-literate volunteers understood the study information, and to compare that to those who could read and write. Four of the sixteen research team members interviewed reported that it was generally easier to deal with literate than with illiterate volunteers during the information sessions and consenting procedure because they did not need to find someone to witness the volunteer's thumbprint:

[Signing] shows an independence – that I have read this myself and I am signing it ... For those who thumbprint there is that traditional element: you must have a witness because you read to them and then someone has to thumbprint and the witness signs ... So it introduces another person, and you usually have to make sure they understand what this person understands, and this adds another dimension. (Robert, scientist, Study 1)

Introducing a witness for an illiterate volunteer during the consent process reduces the volunteer's autonomy because there is a third party in their discussion with the research team member. The volunteer loses some of their independence to make their own decision because the witness has to be present when they are being given information and it adds to the research team member's work load because they must ensure that the witness has understood the study information before they sign for the volunteer.

In addition to the challenge of volunteers who cannot read or write there was a problem with another group of volunteers who did not know how to read properly and yet insisted on signing the consent forms. Their signatures were different on the screening consent form and the
enrolment consent form. The protocol requires that the signature must be the same, to prove that it is the same volunteer who consented at different times. The stigma attached to not being able to read and write, as stated by some volunteers while discussing the significance of signing the consent forms, may be what makes some volunteers try to sign the form when it would have been easier for them to thumbprint it, and the stigma attached to having a witness to the consent process was one of the named drivers for some volunteers who insisted that they could write their name.

The team members indicated that although it may be easier to deal with a volunteer who can read and write those who cannot write do not always understand less well:

There are volunteers that never got the opportunity to go to school, but they have common sense and they will reason things out much better even than those who have been to school, so I do not see the difference ... (Aida, clinician, Study 2)

These findings show that volunteers' understanding is not only based on their ability to read and write. I discuss the views on having a witness for the illiterate volunteer in the next section.

7.2.6 The role of a witness during the consenting procedure

The presence of a witness is particularly required when an illiterate potential volunteer is being given information about the study by the research team (Uganda National Research Guidelines 2007). The research team saw the issue of witnesses to the informed consent process as a difficult part of the process for both the volunteer and the researcher involved in giving their consent. Some of the team members thought that volunteers might not want anyone other than the researcher to know that they cannot sign or write their name. For the researcher, involving two people the illiterate volunteer and his/her witness in the process and ensuring that both understand the study information is challenging.

Ideas about who should act as a witness to an illiterate volunteer varied among the research team. Whereas some felt it was alright to use any witness as long as the volunteer agreed, even if they did not know the witness, one felt that it should be someone with a close relationship to the volunteer:

The best would be a person close to the participant, someone who cares, a person who loves the person, has known this person for some time, or a person who benefits from the welfare of this patient to the extent that if the patient is disadvantaged due to participating in research, then this person is also disadvantaged because of that. (Timothy, health educator, Study 2)

The appropriate witness for an illiterate volunteer was described as a person who would scrutinize the study information and analyse the benefit and risks to the volunteer. Timothy

noted that a witness selected during the consenting process may not be answerable to the volunteer if the latter was harmed during the research; in such a situation the responsibility of the witness ends with the signing of the consent forms.

While the research team reported that the presence of a witness to the volunteer was common practice and expected according to the ethical guidelines that they follow, it leaves the volunteer in a vulnerable position. Volunteers are disempowered by their reliance on the study staff to pick a witness, although they may agree to or refuse the person proposed, and having to thumbprint in the presence of the witness puts them in a lower position than that of the witness. The partial loss of the research volunteer' decision-making power could have an impact on their self-determination during the process as a whole. The research team found that securing witnesses for less-literate volunteers was a challenge, especially if the witness was a fellow volunteer who, if they chose to opt out of the trial, could influence the person for whom they acted as witness. These are important issues in the informed consent process.

The signed consent forms are kept for records at the research clinic as evidence that the volunteer signed or thumb printed the form for the research team to show that the volunteer consented to take part in the trial as mentioned earlier, but this raises the question of whether it matters to the volunteer after signing or thumb printing it.

In the focus group discussions the majority of the volunteers stated that they had not looked at their copies of the forms that they had signed at the start of the trial. Only two of the twenty-three volunteers reported that they had checked back on the information sheet for some study information when they experienced some side effects. It is a good sign that two volunteers referred back to the information document, but most did not seem to consider it important. The next section presents the elements of the consent process that should continue in the research team's view.

The section below explores the challenges that the research team experienced in getting consent from volunteers.

7.2.7 Challenges during signing and thumb printing

The research teams reported some elements that can affect the trial besides getting a witness for an illiterate volunteer in the informed consent process. The first was getting thumb printing right, as noted by a clinician:

Personally I have always found thumb printing a challenge ... You roll your thumb from one side to the other, but [volunteers] become kind of stiff, they just make a small spot, and this one is kind of twisted, ... In the end when you compare their thumbprints they don't look the same. (James, clinician, Study 2) The clinician's example shows that thumb printing correctly is sometimes difficult not only for the volunteers but also for the research team involved.

Furthermore, as the research team reported, signing is viewed with suspicion by some volunteers who do not understand why they have to sign or thumbprint if they have verbally agreed to participate in a trial.

Although volunteers agree to participate in a trial they usually join for one specific procedure and it can be difficult for the researcher to get the volunteer to understand all the procedures and, after consenting, to take part in the trial:

In my experience, during the informed consent process when you give people information about what you are studying they lock onto something and ... that is what they use to join your study. You are going to tell them 'We are going to do A, B, and C' – they lock onto something, maybe A, and it is what they base joining your study on. (Festo, scientist, Study 1)

Explaining some of the factual content on the study information sheets to the research volunteers can be difficult for some research team members:

We had about four meetings ... so that we could understand ... There is a paragraph which states: '... it is not known whether your risk of acquiring HIV infection will increase, decrease or remain the same'; that statement really confused us, and the volunteers. (Sylvia, nurse, Study 1)

If the research team find it difficult to understand the information provided to the volunteers it raises the question of how much information they will be able to convey to the volunteers, particularly those who are unable to read it for themselves.

The research team face challenges at the time when the volunteers give their consent, particularly when a trial is just beginning. They must understand the study information themselves before they can discuss it with the volunteers and before the volunteers consent to take part in a research trial.

7.2.8 What procedures should be continued in the consent process?

The research team identified several activities in the informed consent process that should be continued in future trials. Although the procedure of getting a volunteer to sign or thumbprint is tedious and can take a long time, the team reported that this should continue in the same way because it is the only evidence that can protect a trial when it is audited or monitored.

The researchers also suggested that having provided study information to a group of volunteers the practice of discussing it with each volunteer should continue, because in a one-to-one

discussion the researcher can explain the information according to the volunteer's level of understanding. The advantage of holding a group session is that some volunteers may ask questions that are helpful to others who are not able to ask themselves because they cannot communicate easily in large groups.

The next section explores research team suggestions for improving the process leading up to a volunteer signing or thumb printing the consent document.

7.2.9 Lessons learned

The research team described a number of lessons that they had learned during the informed consent process, varying from how volunteers understand the study information to the activities occurring as the volunteer learns about the study and consents to participate in it.

These lessons are as follows: volunteers do not necessarily understand the study information at the start of the trial, so it should be repeated often during the course of a trial; volunteers gain confidence in the research team and understand procedures better as the trial progresses; it is important for a research team member to go through the study information with each volunteer whether they can read or not; and research teams need to be aware of the differences between volunteers and their different levels of understanding of the study information, as expressed by a clinician:

If you just give [volunteers] a sheet of paper to take home to read they will come back without having read it ... but if you take the time to explain, they may go back and read a paragraph or so. It is better to read the sheet with them. (Aida, clinician, Study 2)

Another lesson they had learnt was that volunteers' concerns must be taken seriously. A nurse reported that a female volunteer was beaten by her spouse because she got home late after being delayed at the research clinic. The volunteer's social network must be known and understood in order to be able to help them to manage conflicts caused by their participation in the research.

The lessons that the research teams learnt show that the informed consent process is a complex and on-going process that requires continuous attention to what is happening in the research setting and the volunteers' communities.

The next section considers the research team's suggestions for improving the informed consent process.

7.2.10 Suggestions made by the research team for improving the consenting process The research team made several suggestions: the first was that a literate family member should be involved in the consenting process, reading the study information with the volunteer and signing on their behalf as witness if they cannot read or write. However, volunteers who do not disclose their participation in research clearly do not want to involve their family.

It was suggested that researchers should be educated about the importance of informed consent in research with human subjects. The researchers also suggested that the SEC should conduct spot checks at the trial sites, talking to volunteers to ensure that they understand what they have consented to. This suggestion is an indicator of the value that the researchers place on the importance of a functioning SEC that protects both the volunteer and the researcher if there are ethical issues that are discovered early on in the informed consent process of a given trial.

The research teams' suggestions show that the consenting process requires the involvement of all the actors; the volunteer and their family representative, the research team, the CAB and the SEC. The latter is included to safeguard the volunteer's welfare, but according to these study findings it also safeguards the researcher. In my view this presents a challenge because the SEC is not at the research site all the time, and secondly too much involvement on their part could make it seem that they are policing the process, as one of the SEC board said.

The improvements proposed by the research team relate to their day-to-day running of activities from the start of a trial's informed consent process to its completion. One suggestion was that the study sponsors should give the site principal investigators an opportunity to offer their input during the development of the study protocols to ensure that the context of the proposed trial site was also considered.

They thought that the research teams should sensitize the community where the volunteers are picked from about the trial early enough before the trial research team starts to recruit potential volunteers. They suggested that community drama groups should be trained to highlight the key messages of a trial before its implementation so that potential volunteers' important social networks were aware of what was going to happen in the research.

Another suggestion was to tap the volunteers' resources by involving literate volunteers in providing the study information to their fellow community members in the hope that this would enable peers to discuss their concerns about the research openly. This could balance the power differential between the research team and volunteers, which can lead the former to agree to any suggestion given by the latter. It would require training for literate volunteers.

The research team suggested that volunteers should be given time to think about the study information provided to them before being asked to sign the consent forms. Ideas about how much time to give them ranged from a day to two weeks.

Another suggestion was to provide visual aids to the volunteers such as videos about the trial to enhance their understanding of the study procedures. Simple ordinary language should be used on the information sheets and consent forms, and volunteer understanding of study information should be assessed. Because a research trial must be conducted according to the guidelines and study protocol, the research team suggested that research team training should also include instructions about signing and thumb printing consistently to avoid discrepancies on the consent forms.

The investigators should plan several follow-up meetings between the volunteers and the research team so that the rumours and difficulties that the volunteers face are discussed as soon as they appear. One team member suggested that if a trial takes longer than two years the volunteers should be asked again for their consent to ensure that they still understand its objectives.

The informed consent process in the two clinical trials studied is more than an event: it is also a process. Although there are standardized guidelines and operating procedures for achieving informed consent, these depend on the individual actors' input. The perception of the actors during the process is critical to meaningful research results. If an actor thinks the process is about researcher protection that is what they will emphasize as they follow up the process; if it is about protecting the volunteer from harm during the research process that is what they will pursue.

The study findings suggest that the process requires on-going discussion between the main actors – the research team, the volunteers, SEC and the CAB – and close contact with the study sponsors, sharing experiences that may lead to an improved informed consent process. Communication gaps between actors can impact on the trial's results.

In the next section I discuss the experiences of the members of the Science and Ethics Committee (SEC) and the Community Advisory Committee (CAB).

7.3 SEC and CAB experiences of the informed consent process

This section discusses the experiences of the SEC and the CAB in the informed consent process. While these two groups of actors are not in regular direct contact with the research volunteers they do contribute to the informed consent process in the trials.

7.3.1 SEC experiences

The SEC meets once a month to review protocols. On average they review at least seven protocols per meeting. Before the meeting, each committee member receives and must read through the protocols. Two members are usually selected as the main reviewers for each protocol. SEC members reported positively that the researchers were increasingly trying to translate the participant information sheets and consent forms into the appropriate local

languages, indicating that volunteers were receiving study information in the language they understand.

The informed consent document must contain the sections stipulated in the informed consent guidelines and include the benefits and risks of the trial. When the research teams follow the standard guidelines for informed consent and fill the protocol review documents requested by the SEC, these documents are what the SEC bases on as evidence of what may have happened to the volunteers during the research.

The ethics committee members reported that increased discussion between the SEC and the researchers about ethics in research has led to the researchers ensuring that the protocols contain adequate information for the volunteers. One SEC member reported that the committee hoped that researchers followed the protocols that they had presented for review. When the committee reviews a protocol its members are encouraged to declare any links they may have to it. This leads to transparency in the protocol review process.

The challenges that the SEC members reported included having a great many protocols to review, some using very technical language:

There are a few studies [where we are completely out of our depth], like the laboratory studies; you review something that you probably don't understand because it is technical and struggle to understand the ethics involved (Bosco, SEC member)

SEC is funded by programs affiliated to UVRI that send their protocols for review. The community representative on the committee noted that this could lead to bias during the review process, because of their role in funding the SEC activities. This bias is however neutralized because the SEC members represent different research programmes on UVRI campus.

The consent forms are huge and difficult to internalize:

The consent forms are so voluminous when they come they're like legal documents ... and you do not internalize them, even if you start asking 'Is the risk described? Is there compensation? What about this?'... So these big forms are a problem for the committee, but they are also a problem in the whole continuum of things. (Titus, SEC member)

Uganda has many different local languages, which can make translating informed consent documents difficult. When committee members cannot read the translated consent forms to review it they have to source scientists who are conversant with the local languages.

Including consent to store personal samples on the consent form was reported as a potential challenge because rarely are the investigators sure what purposes they are being stored for or the future implications for the volunteers and the reviewers who approve the protocol.

Another challenge noted by the ethics committee was that the communities where the volunteers come from are poor and illiterate and ascertaining the level at which the committee could protect volunteers from any form of harm during research was difficult:

When [people] are so poor it is very difficult for the ethics committee to differentiate ethical concerns from issues like coercion. When you are trying to compensate somebody, is that coercion? ... Because if there are no services in one place and there are services at the research clinic, people want to participate in the research ... They are so desperate to get treatment and would rather have a steady supply of drugs at whatever cost. (Vicky, SEC member)

Some of the committee's challenges were technical, such as understanding the terminology in protocols outside their own field of study, but they also found it difficult to identify how best to protect volunteers who may be poor and are desperate for health services.

7.3.2 SEC s' views on gaining consent from volunteers

SEC members' views on the volunteers' consent varied, but it was important to them all because it was the only way they could audit and confirm that a volunteer had agreed to participate in the research.

The SEC did not see thumb printing as disadvantageous to the volunteer because the guidelines require that every volunteer be given study information which is read to them in a language they understand before they can sign or thumbprint their consent to participate in a trial. What is important for the SEC is that a volunteer understands the study information and is protected from any form of harm. The committee members noted that volunteers' understanding of the study information should not be linked to their ability to read and write, because even those who cannot read can understand information if it is provided to them appropriately by the research team.

They reported that because they do not supervise the informed consent process directly it is difficult for them to confirm that there was a witness who also understood the study information before signing for a volunteer. The committee has to trust the researchers' reports about consenting volunteers.

7.3.3 SEC suggestions to improve the informed consent process

The ethics committee made several suggestions for the improvement of the current informed consent process. They thought that the informed consent forms should be shorter to enable a quick review by the committee and to help the volunteers to take in the key study information.

Another suggestion by the SEC community representative was that the names given to the volunteers as contacts at the end of the consent forms should be those of site investigators who could be contacted easily. Some consent forms have contained the names of investigators who live abroad or who cannot communicate in local languages.

Study information should be provided verbally to all volunteers to facilitate their understanding before the written documents are introduced. There were similarities in how the SEC and the research team reported on the volunteers' understanding of the study information:

We might just have a diagram that shows that when you come you will begin at A and when we find you are 'blue' you go here – now this is where you are – some could be systematic or something else but it is very difficult to read all that text, so we could add some things that are simple ... We could add some spice to the process and see how it works. (Vicky, SEC member)

The SEC members suggested that researchers should protect the interests of the community because they gain from the trials by publishing their findings. Signing or thumb printing the consent forms is currently the only way the process is documented and must continue while literacy levels remain low. However, increasing numbers of local people can now read and write compared to two decades ago. However, the SEC had no control of what actually took place at the research sites when it came to the volunteer signing the consent forms and the committee was only able to monitor this on visits to the sites; therefore the SEC had to trust that the research team ran the process of signing the consent forms according to the ethical guidelines. The next section explores the experiences of the CAB and their suggestions for improving the informed consent process.

7.4 Experiences of the Community Advisory Board (CAB)

I conducted a focus group with the CAB. They laughed when I asked them about the signing of the consent forms because this was still a very fresh experience as they had all just signed their own forms consenting to participate in my study. All the CAB members were literate.

One of the main reasons given for signing the consent forms was to protect the research. They saw a signed consent form as a source of legal cover for the researcher:

... if a [volunteer] has a problem along the way they cannot take you to court because they agreed ... For example if someone in the vaccine trial got another disease they couldn't just blame the organization. (CAB FGD)

The CAB members reported that signing the consent form implies that the signatory has received the study information and agrees to be part of the study, whether the result is positive or negative. Signing the consent forms is seen as useful when following up volunteers because some may have similar names and the signatures show the difference.

Signing or thumb printing a form was compared to a land-buying transaction, which is common in this community. The document that is signed is treasured, especially by the buyer, who is given a copy with his or her signature on it. In the research the volunteer is happy that he or she is contributing to an important study and his or her copies of the signed consent forms serve as a reminder that they took part in a research.

The CAB members noted that if nothing is signed to show that there was an agreement between the researcher and the volunteer this may mean that nothing happened between the research team and the volunteer. The CAB members reported that people in rural communities are now better informed than before and if something is not signed they know that it is a fake.

A CAB member quoted a slogan commonly used in the community to express this:

We have a certain project working on quality improvement, and we have a slogan that says 'anything not documented is not done'. However much you may work, until you document it is not done. If you gave verbal consent you didn't write it [and so it is not done] (CAB FGD).

In the focus group the CAB members reported that by the time a volunteer has decided to sign the consent forms they must have understood what they have been told about the trial. A CAB member suggested the use of a photograph instead of a signature, but they all noted the disadvantage that photographs can be used by the media to misrepresent them by making inaccurate information about them public without their knowledge or permission.

CAB members noted that although the signing of the consent forms is very important to the researchers and is seen to imply that the individual has understood the study information, in this community if the influential people in the community such as religious leaders and some cultural leaders such as clan leaders and cultural kings endorse an activity, the majority of people go by what they have said. Such communal decision-making is based on the beliefs and values of these influential persons. Religious leaders were singled out by the CAB as very influential and trusted by the majority of the people in the communities.

7.4.1 Challenges and suggestions to improve the functioning of the CAB in the informed consent process

The CAB members reported some challenges in their role as advisors to the research team, noting that although they initiate contact with potential volunteers in the communities the research team do not inform them who eventually enrolled in the trial. They suggested that the research team should tell them which people in their constituencies are involved in the research so that they can follow up what happens to them in terms of effects or other concerns that the volunteers have.

They noted that their own work is not monitored, so they were less likely to be motivated to hold community feedback sessions about the research at which members of the community would expect to be given money because they represent an organisation which is conducting research and it is presumed by most community members to have a lot of money. The CAB members are not paid for being on the board but they are given an allowance when they come for board meetings.

Another suggestion was that CAB activities should be monitored and evaluated during the informed consent process:

But looking at us, I do not know whether we have a [monitoring and evaluation] system to monitor what we are really doing. I feel something could be improved in that direction, so every constituency could do something, assisted by MRC staff in preparing activities, and then you write a report on what you are doing. But now there is no reporting (CAB FGD)

CAB members suggested that they needed frequent meetings with the researchers to make them aware of what was going on in the research, as this would help them to be more proactive in their roles. They thought that the MRC should fund the activities that CAB members initiated in the communities, such as the feedback meetings.

The CAB members' experiences and suggestions pointed to a desire to be more active in the informed consent process. Their suggestions about consenting and signing the consent forms hinged on their perception of the informed consent process in terms of the legal requirement to protect the researcher. Table 7 sets out a summary of the experiences of the different actors in the informed consent process.

Actor	Role in trial/informed	Overall values	Definition of IC	Views on consent form	Views on thumb	Recommendations
	consent process				printing/witness	
Research team	Give study information to volunteer -obtain consent from volunteer -conduct study procedures	Value is to recruit and follow up according to protocol	Main emphasis is about information giving, agreement and signing of consent forms	Helping volunteer to understand design of trials not easy -signing of consent forms may be viewed suspiciously -volunteers join research for usually one specific procedure -a volunteer whether literate or not may /may not understand study information -Volunteers do not necessarily understand information at the start of a trial	-some find dealing with less illiterate volunteers difficult in communicating information -the practice of getting the thumbprint is difficult -some believe a witness can be anyone others say it should be a close relative/friend	 involve literate family members in the consenting process train research teams on the importance of informed consent SEC should do spot checks community engagement should start early in communities where volunteers are to be selected from the literate peers among the volunteers could participate in information sharing sessions volunteers need at least a day to two weeks to study the study information provided to them before they are requested to sign on the consent form need for on-going discussions between the actors(SEC, CAB, Volunteers and research team)
Volunteer	-take part in the research -inform other community members and interest them in research	-value is attached to altruism for some and for some it is about what benefits particularly related to their health well being	-main emphasis is that there are no risks to the individual and benefit of health care that may be lacking in the public health care clinics/hospitals	 it shows a volunteer has accepted to take part in research by signing a consent form it does not mean that one has understood the study -if any one refuses to sign then it is an indicator of refusal to take part 	-thumb printing is stigmatised in community	 -understanding of study information should be gauged after they have been in a trial for some time to avoid recall bias - volunteers need more than one single information session -information given to volunteers should be clear and easy to understand -interventions to support literacy and numeracy should be developed
SEC	Ensure the set national and international research guidelines are operating at the research sites -review protocols and informed consent documents -monitor what takes place at the research sites	Value is attached to the effort of ensuring volunteer do not experience any form of harm	Emphasis is on follow guidelines and safeguard volunteer from any form of harm(physical, social, emotional) -use simple and clear language in consent forms	-it is the only way to confirm that a volunteer agreed to participate in a trial -signing or thumb printing is not a problem as long as forms give full information and no harm done to volunteer -do not relate volunteer's understanding to ability to read and write	The guidelines require this to safeguard the volunteer -signing and thumb printing is currently the only way the process is documented and should continue	-consent forms should be short -contact information should reflect researchers at the sites -emphasise verbal information before you introduce documentation -introduce visual aids like flow charts to describe informed consent process -protect interests of the community
CAB/comm unity	The main link to the study population in the community -gatekeepers to the community, they support initial contact with potential volunteers	Value is attached to respect for the individual and the community	Emphasis is on free choice for volunteer to take part or refuse to take part -no coercion	 signing consent forms is to protect the research signing implies volunteer has accepted to take part in the research 	-if information is provided in a language a volunteer understand, whether one signs or thumb prints both are capable of understanding information, so it does not matter	-The activities of CAB should be monitored to encourage accountability -need frequent meetings -they want a more active involvement as stakeholders in the community

Table 7. A summary of the experiences of the different actors in the consent process

7.5 Conclusion

This chapter has examined the experiences and the views of the actors on signing and thumb printing consent forms. Most of the research volunteers reported that they were participating in the clinical trials voluntarily and knew that they could withdraw from the trial at any time. However, their specific reasons for taking part in the trial varied: some were inspired by altruism, but most hoped to benefit from the treatment package offered at the research clinics.

The volunteers argued that understanding the study information did not depend on an individual's literacy level and that consenting to take part in a trial meant that the person had understood the information. However, this view was contradicted by the research team members who noted that most volunteers understood the study information only after several interactions with them after signing the consent form. Most research team members referred to signing the consent forms as a necessary procedure, highlighting in their narratives how the aim of obtaining a signature or thumbprint on the consent forms is mainly to protect the researchers in case of adverse events resulting from the research.

The SEC reported the importance of sticking to set informed consent guidelines to protect the volunteers in research, but also noted that they do not have full control of what goes on during the trials as they are not directly involved in them. They have to trust that the researchers do what they promise in the protocols. The SEC's monitoring visits are not very frequent.

The CAB members initiate contact in the community, but seek greater involvement in the informed consent process. The CAB views monitoring the informed consent process as a key activity for them to ensure that the volunteers are protected from any harm while taking part in a trial.

The informed consent process was experienced differently by the different actors. For the volunteer the process is about the benefits of treatment and did not mention the possibility of coming to harm during a trial, yet for the research team, the SEC and the CAB it is about providing study information and ensuring that the volunteer understands it. Power, trust, belief and values are strong elements in the ways that the consent process is experienced and how the actors make their decisions.

Signing or thumb printing consent forms was reported by all the actors as very important. However the level of understanding study information does not depend on whether a volunteer is able to read and write or not. Volunteers may understand study information if it is presented in simple and clear language, using visual aids that communicate easily even to volunteers who are less literate. A witness should be a member of the volunteer's close network in order to reduce stigma attached to thumb printing on the consent form. The next chapter discusses the study findings and their implications in relation to following the standard national and international guidelines.

Chapter 8: Discussion of study findings on the informed consent process in the HIV clinical trials

In Chapter 7 I discussed my findings about the various actors' experiences of the informed consent process; in this chapter I discuss the implications of my findings for how the standardized national and international informed consent guidelines are applied in Uganda. I relate what the guidelines prescribe for the informed consent process to my findings about how the different actors' understandings and interpretations of the informed consent process affect their use of the guidelines to manage the informed consent process in these HIV clinical trials in Uganda.

I reflect on the contextual framework discussed in chapter 2 and how it relates to the findings and the implications of this study. In the first section, I briefly review the standardized guidelines on informed consent, which provide the framework within which clinical trials operate. I follow this section with a discussion about the protection of volunteers from any form of harm during research. Section 8.3 presents the discussion of the three basic principles of informed consent as outlined in the guidelines: respect for persons, beneficence and justice in the study context. In the next section I discuss the views of the respondents that emerged about written and unwritten consent and the presence of witnesses in the informed consent process. I discuss the implications of the findings of this study for managing the informed consent process in HIV clinical trials according to set informed consent guidelines.

The informed consent process is better understood as we reflect on a specific study context, in this thesis two HIV and AIDS clinical trials in Uganda. In this context, the informed consent process is influenced by both internal and external factors to the main actors. External factors include the expectations of the sponsors and funders of the research, the policy guidelines for research and clinical trials, the expectations of the relatives and families of the volunteers and the community in which the research volunteers live. The different actors in the informed consent process also had varying reasons for associating with the trials; the research team were trying to answer research questions to address the HIV and AIDS public health problem, the volunteers on the other hand took part in the trials partly because of altruism but also for what they thought were the benefits relating to their health and wellbeing since HIV and AIDS had affected their lives and the communities where they live. The other actors including the ethics committee were associated with the trial to ensure research ethics are followed by the researchers. The community advisory board was interested in knowing what went on in their community and how it would impact on the members participating in a trial.

The actors in the informed consent process were also influenced by their own beliefs and values, gender differences, the power they had to influence decisions, and the trust they had for the research and what happened during the interactions with other actors during the informed consent process of a trial. The interactions and the communication that happened between the different actors particularly between the volunteers and the research team point to how the informed consent process worked in a clinical trial. The Informed consent process is not only about the regulations, and the actors involved in a given trial but also dependent on the collaboration of all the actors.

In the sections that follow, I discuss the implications of my study findings in relation to national and international standardised guidelines for informed consent while conducting research among human research subjects.

8.1 The standardized guidelines

The research questions in this thesis aimed to understand the meaning of the informed consent process in the context of HIV clinical trials in Uganda. Researchers and scientists in Uganda are still grappling with the public health challenge of high HIV infection rates and HIV-related disease in the general population of this developing country. Clinical trials are being conducted to answer scientific questions about HIV infection. All the trials must adhere to formally-set research ethics guidelines which require researchers to obtain informed consent from all research volunteers.

As discussed in Chapters 1 and 4, the two HIV clinical trials in this research were guided by national and international ethical principles and guidelines for research among human subjects, including those of the ICH/GCP, the Belmont Report-(1978), the World Medical Association Declaration of Helsinki (1964-2008), the Council for International Organizations of Medical Sciences (CIOMS, 2002/WHO) and the Uganda National Council for Science and Technology (UNCST, 2007). These guidelines especially target the protection of human subjects involved in biomedical and behavioural research, and each outlines the procedures that must be followed in obtaining research volunteers' and patients' informed consent to participate in the research. The scientists that I interviewed in this study reported that when conducting trials they primarily refer to and are trained according to the International Conference on Harmonisation's Good Clinical Practice guideline (ICH/GCP-21 CFR 50.20, 21 CFR 50.25 (a) and (b)).

All the guidelines: ICH/GCP, CIOMS, Helsinki and UNCST, which have evolved since the Nuremberg code of 1947, state that the three basic ethical principles in conducting human research are respect for persons, beneficence and justice. In addition they outline important information that must be provided to research volunteers, including the purpose and duration of the study, the risks and benefits of participating and the contact details of the site principal research investigators. The duty to protect research volunteers from any form of harm during

the informed consent process is outlined in all guidelines. Another important element is the requirement for a witness to illiterate volunteers' thumb printing of the consent forms; written consent is imperative unless the SEC gives permission to waive it, as detailed in Table 1.

In this study, the standardised guidelines were particularly emphasised by the SEC and the senior scientists who conducted the trials and who had to ensure that the procedures research volunteers went through were aligned to what the guidelines stipulate. They emphasised the guidelines perhaps because their roles as leads in the research meant that they were responsible for what happened to the volunteers and this also meant they were to ensure volunteers would be protected from any form of harm by taking part in the trial. The research team in the field did not commonly refer to the guidelines in practice although the principles were usually discussed in the initial training of the research team by the principal investigators before a study commences.

The next section discusses the duty to protect research volunteers as an important aspect of the informed consent process.

8.2 Duty to protect volunteers

The informed consent guidelines state that the duty to protect the research volunteer lies with the researcher or study investigator and the study sponsor, not with the research subjects (UNCST, 2007; CIOMS, 2002; ICH/GCP; Declaration of Helsinki, 2008). The Declaration of Helsinki states that 'it is the duty of physicians who participate in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects' (p.2). The CIOMS guideline (2002, p.4) emphasizes that only a 'competent individual' who is able to make decisions should be involved in research because they must be able to understand the study information and, after due consideration, be able to make a decision without coercion, undue influence or intimidation. The guidelines' emphasis on protecting volunteers reflects the possibility that volunteers, for various reasons including poverty and limited literacy, may not be able to make their own decisions (RamaRao et al., 2007; ICH/GCP).

In the discussion of the roles of the various actors in the informed consent process in Chapter 5, the volunteer and the team member who obtained his or her consent were singled out as playing a very important role in the informed consent process. All the actors except the volunteers emphasized the SEC's approval of research protocols before trials are implemented as an important step in protecting research volunteers. The research guidelines prescribe that no research should be conducted unless the protocol has been reviewed by an independent research ethics committee.

The 'duty to protect volunteers' reflects the researchers and ethics committees' power over the volunteers in terms of the direction that a trial can take. The volunteer was seen as being in a vulnerable position compared to the research team and therefore must be protected from the time the SEC reviews a protocol. All the guidelines given as examples in this study highlight the importance of the SEC that approves research protocols (usually referred to as the IRB of record). The SEC guidelines required volunteers to consent to participate before enrolling in a study, partly in order to ensure that they were not coerced into joining a trial. Procedures such as asking volunteers for verbal rather than written consent need IRB approval. All the guidelines refer to the IRB as critically responsible for ensuring that research participants are protected from any form of harm. This means that the IRB can influence researchers' decisions about how they deal with volunteers during a trial if they consider that they are not being protected properly.

According to the informed consent guidelines no study should be implemented without the approval of an ethics committee, and any changes to a protocol or to request for verbal consent or expedited review of protocols must first be approved by the SEC (WHO guidelines, 2000), whether at institutional or national level. Yet although the SEC in this study had the power to protect volunteers from harm at the time of its review of protocols, it did not implement any of the two studies, but it had a mandate to monitor what went on with the research volunteers during a trial. The SEC in this study was very busy because most of its members doubled as scientists, who were struggling to cope with the demands of their research in the different programmes to which they were attached (see Chapter 2 for a description of SEC members).

Once a study was approved the site investigator or senior researcher was responsible for implementing it. I found that the investigator commanded more respect than and exercised power over the rest of the research team members, as reported in Chapter 5 in relation to the roles of the different actors. The site investigator was responsible for delegating duties to the other research team members such as obtaining volunteers' consent to participate. Apart from the site investigator exercising power over the other research team members, the team members in their turn exercise power at different points in time when carrying out their specific roles implementing the study procedures. These roles were mainly in line with their professional training, such as in counselling and nursing; the community mobilizer was charged with mobilizing potential volunteers, the counsellor with counselling the volunteers, the study nurse with carrying out physical examinations and filling out case records, providing study information and obtaining consent from the volunteers' consent forms.

In practice this shows that protecting a research volunteer is a very complex activity involving several actors in a research study. This can be an advantage, in that different research team

members encourage the volunteer to continue to participate in the research. It can also be a disadvantage if there is no specific research team member responsible for checking that each volunteer is protected from physical, emotional or social harm. I found that the nature of the trial and the setting where the research takes place may contribute to the outcome in the informed consent process. In this study, I found that in the prevention trial where the volunteers were not ill they could easily decline to join the research if they found that they spent a lot of time at the research clinic. For the volunteers who were in a treatment trial, the issue of pressing hard for time limits that they needed to be at the clinic was uncommon because they believed that good health was dependent on taking drugs and obtaining good health care from such a research clinic.

While the CAB members were not directly involved in the implementation of the studies they were the gatekeepers to the community volunteers. They noted that once the research began they were not told which volunteers the research team had recruited and reported gaps in the information they received to feed back to the community about what was going on at any given time during the research. The informed consent guidelines do not refer directly to the CAB; however, they do highlight the importance of allowing volunteers to consult family members and other important persons in the community, and this is where the CAB, as opinion leaders, held power in the community to facilitate volunteers' decision-making about joining or continuing in a trial. The findings however reflect the CAB's limited involvement in the studies and ability to protect the volunteers because they were not receiving information about which of the people they had mobilized to join the research had consented and were participating. Informing the CAB which individuals are in the trial is however a complex issue in the informed consent process because of confidentiality problems concerning how much information about a volunteer should be feed back to the CAB member.

The volunteers had some power to influence research team decisions during the trials, as reported in Chapter 6. They could choose to join a trial and decide whether to continue participating in it. In the focus group discussions the volunteers said that they wanted to be given updates and on-going feedback about the trials. They discussed how they could exercise power over the research team by not turning up for the research, meaning that the researchers would not get answers to their research questions. The findings in Chapter 6 showed that the research team's power was at times limited by the volunteers, whom they had to be careful not to coerce but were dependent on their participation in the trials. The research team saw protecting the volunteers as important in their interactions with them, but it was formally evidenced only by the signed consent forms. Beyond the signed consent forms, there was no documentation to show how the on-going interactions between the research team and the volunteers were managed to protect the volunteer and that is why the rumours from the community intimidated some of the research volunteers.

The main emphasis in the guidelines is on the investigator and the sponsor's protection of the volunteers from any form of harm in the conduct of trials and is structured through SEC's review process. The guidelines state the important role of the Institutional Review Board (SEC) but do not spell out who has the power in the informed consent process and how the different actors need to interact with each other. In this study protecting volunteers was important, but it was not a responsibility assigned just to the research teams and the SEC had the right to monitor what went on with the research volunteers. The research team's duty to protect volunteers from any form of harm during research depended on the individual research team members' interactions and the relationship with the volunteer developed over time during the trial (see also Kamuya et al., 2013).

The next section discusses the practical implications of the way the basic research principles were applied to the two case studies.

8.3 Reflecting on the Informed consent principles in the study context

The basic principles of research ethics discussed here include respect for persons, beneficence and justice that guide informed consent, how these were experienced by the actors and the implications of this for the informed consent process in HIV clinical trials. As discussed in Chapter 1, respect for persons requires that the volunteer is continually informed about what is happening to him/her throughout the research process; beneficence is about maximizing benefits and avoiding causing any form of harm to a volunteer; and justice is about distributing the risks and benefits equally among the research volunteers (Belmont Report, 1978: 8).

8.3.1 Respect for persons

Applying the principle of respect for persons means that volunteers who take part in research and their decisions must be fully respected without any form of coercion or force (Belmont Report, 1978; CIOSMS, 2002; Declaration of Helsinki, 2008). This principle addresses the volunteers' individual autonomy, allowing them to deliberate on issues that concern them and make their own choices (Belmont report, 1978).

When asked to define informed consent, the research team and SEC and CAB members all mentioned respect for volunteers and its importance in the conduct of the trials. The volunteers, however, did not mention respect; they related informed consent to the fact that they would be provided with treatment if they became ill. The research team and the volunteers viewed it in markedly different ways. For the research team, showing respect for the volunteers was protocol-driven in the sense that the team members all mentioned that giving substantial study information to each volunteer, especially at the beginning of the trial, was a key procedure to ensuring that the volunteer first understood what the research was about and then joined without being coerced.

Research team members emphasized the principle of respect for persons, mainly referring to the beginning of a trial when they were creating rapport with potential volunteers. Respect for volunteers was related especially to the research team's recruitment of volunteers and provision of study information, as required by the ethical guidelines. Therefore in essence, respect was first seen in terms of ensuring openness about the research. Their aim of giving more time to providing information was not necessarily due to the researchers' interest in the volunteers but was driven by their institution's need to recruit volunteers for the research to ensure that enough consented to take part in a trial.

The study information that a research team provides to a volunteer was already formulated and formally approved and therefore was not initiated by the individual team member who provided it to each volunteer. Respect for the volunteer in this context could be linked to the ethical requirement to use simple language that the volunteer understands. A structure was being enacted in the application of the guidelines, the protocol and the SOPs: the investigator expected the research team to respect the volunteers as part of their code of conduct, which might not have anything to do with the level of respect a team member might accord to the volunteer as an individual.

I found that respect was managed through the formal structure of the conduct of a clinical trial, and as a principle it introduced a moral aspect of treating others with respect. For example, while discussing their experiences the research team reported that when volunteers announced their intention to complete their scheduled appointments and leave the clinic in the shortest possible time, the research team would try to respect this because it was the volunteer's right to decide this. On the other hand, when a research team member realized that a volunteer was not following the expected procedures they took action to inform him/her of what was required of him/her as a volunteer. For example, in Chapter 5 I presented a volunteer who was shocked when she was blamed by a member of the research team for not reporting to the research clinic when she became ill. While this communication by the research team could have reflected concern about protecting the volunteer from possible harm, to the volunteer it clearly reflected some loss of self-determination. Respect was therefore not viewed uniformly by all the actors in the process it was not always seen as a right but was linked to the actor's responsibilities in the informed consent process

Volunteers and research team members related to the principle of respect for persons from their individual perceptions of how the procedures were conducted in the informed consent process. Communication between the research team and the volunteers was seen as crucial for the research team to realizing this principle. The process of negotiation between the research team and potential volunteers about enrolling and continuing to participate in the research reflected the principle of respect; during this process an individual volunteer's autonomy might be expressed in his or her interactions with the research team. Research team members taking the time to explain the study information to a volunteer, especially during their screening and enrolment, could be seen as a way of respecting the volunteer according to the guidelines. The way the research team communicated with them showed the extent to which they were being respectful which could only be judged by the volunteer.

The explanations that the research team members gave about the trial were guided by the study protocol and the SOP. However, the level of autonomy that a volunteer could exercise depended on what he/she thought about the information provided and how he/she had been handled by the research team. Some volunteers reported that they continued in the trial because they had been handled well by the research team (see Chapter7). When all the study information had been provided to them it was up to each volunteer to decide whether to join the trial. They had the right to withdraw from a trial when they wanted to, and according to the ethical guidelines the research team must respect this. However, although the research team did allow volunteers to withdraw at will, they did not take it well. For example, some research team members noted that volunteers who withdrew and then came back seeking treatment were a challenge to them, because although they were already busy with the volunteer visits scheduled for the day they could not ignore volunteers who had withdrawn from the research teams had to follow the protocol guidelines and provide the treatment as promised on the study information sheets.

When the volunteers in this study discussed informed consent it had nothing to do with the technical expectations laid down in the guidelines. They were not aware of the principles of documented research, but they had been provided with specific information about the trials that they had joined, and with copies of the study information sheets and the consent forms that they had signed when they were screened and enrolled. While it could be argued that this was a procedure enacted by the research team to accord volunteers respect by asking for their consent individually, it is a research ethics requirement while conducting research.

The volunteers understood the issue of respect for persons through the practicalities of how they were approached and managed by the research team when they came to the clinic. Being treated when they were ill during the trial was one of the main reasons they gave for continuing to participate. A sense of respect can be conveyed when the research team fulfils its promise to provide the volunteer with treatment when needed. A mobiliser for one of the trials mentioned that if all the research team members did as the information document promised the volunteers would respect them more and his job would be easier.

Some volunteers, however, reported that while being treated was a very important benefit for them, they wanted to minimize the amount of time they had to spend at the clinic. Although

they had agreed to take part in the research and expected to benefit from treatment when they needed it, they still valued controlling and limiting the time they spent on the trial and usually did not want to stay at the clinics for long when they came in for their scheduled visits. Therefore when evaluating respect in the informed consent process it is important to understand the context, because there is a conflict of interests between the research volunteers and the research team, which must follow the ethics guidelines to fulfil the principle of respect for persons.

A particular interpretation of this principle in terms of the volunteers' self-determination was clear in their responses about how information was communicated to them. International informed consent guidelines emphasize that participant information sheets should be in the language that a volunteer understands. However, volunteers in a focus group discussion highlighted that some words on the information documents were ambiguous even in the vernacular that they speak and understand; for example the information sheet states that the researchers do not know what may happen to the foetus if a woman becomes pregnant during the trial (see Chapter 5). The volunteers show here that respect includes the use of clear language during the trial. This came to light when they discussed why some female volunteers get pregnant during a trial in which pregnancy is a criterion for exclusion.

The volunteers again appeared to be alluding to respect-related issues when discussing their comprehension of the study information. They revealed that an illiterate individual was able to understand this information as well as a literate individual when it was discussed in their own language. Therefore whether a volunteer signed their name or they were only able to make a mark using their thumbprint on the consent forms, this did not reflect their ability or failure to comprehend study information. The guidelines emphasize that illiterate volunteers must have literate witnesses present when they receive the study information and when signing the form consenting to take part in the research. However, the viewpoints presented in this study suggest that this could actually undermine the level of respect that is accorded to the illiterate research volunteer because his understanding of information is confirmed if there is a witness in his/her consenting process. In order to safeguard respect for all volunteers, the volunteers emphasized the need for documents in the vernacular and for allowing the illiterate to consent to participate in research without a witness there to confirm that they have understood the study information. Realizing the principle of respect for persons reflects the importance of the degree to which capable subjects are allowed to choose what shall or shall not happen to them (Belmont report, 1978). In a clinical trial the issue of capability is attached to the ability to read and write; this is firmly refuted in these findings, which on the contrary highlight how such a requirement can affect the sense of respect experienced by a person who is unable to read or write her or his name on the consent form.

The way the principle of respect for persons was handled by the research team depended on each member's appreciation of this principle. They defined the research process as directed by the study protocols, and therefore the volunteers' choices in terms of what they thought should happen to them was not the main emphasis in the clinical trial. Mutual respect between volunteers and researchers was also reflected in the ways they related to and communicated with each other in giving feedback during what was seen to be a highly interactive informed consent process. I found that while the researchers might have assumed that a volunteer would follow all of what the research protocol required of them, they reported that this was not always the case. They had to make an on-going effort as they interacted with the volunteers to ensure that they gained the latter's confidence in the informed consent process this is way beyond the guidelines.

'Respect for persons' was therefore mainly realised in the on-going relationship between the researcher and volunteer and much less in the documentation. The researchers may have assumed that having been provided with the study information, the volunteer was knowledgeable about the research and was participating voluntarily (Burgess, 2007), but again this was not necessarily the case in practice. The principle of respect for persons was realized through the on-going interactions between the researcher and volunteers and included the two parties giving feedback to each other. The volunteers may not have expected direct respect from the research team but they did demand feedback about the procedures that they had undergone; and the members of the research teams were supposed to follow the structure of the informed consent process, which required that they respected the volunteers. The social norms in the study area attached respect to an individual's roles and responsibilities in the community implying that all members of a given community were expected to respect one another, and volunteers would therefore expect to find this kind of respect even in the clinical research setting.

8.3.2 Beneficence in this research context

Beneficence is a key obligation in ethical research. Researchers must not only act kindly to individual research volunteers but are also obliged to do no harm and to maximize the possible benefits and minimize possible harm (Belmont Report, 1978). In this study this principle was mainly discussed in interviews with SEC members and the research team clinicians, both of which were specifically aware of the Hippocratic maxim 'do no harm' (Belmont Report, 1978, p. 7) in their clinical practice. International ethical guidelines require that the researcher informs the volunteer about all foreseeable risks, pain, discomfort and inconvenience that they may face in a particular trial (CIOMS, 2002; Declaration of Helsinki).

When discussing the informed consent process the ethics committee members and research team clinicians mentioned that the risks and benefits of the study were part of what they

needed to flag up to potential volunteers before they could be enrolled. The participant study information sheets for both trials included a section on the risks and discomforts that a volunteer might experience during the trial and the benefits that they might gain from taking part, as discussed in Chapter 1. In Study 1 the risks were discussed under the heading 'What are the possible disadvantages and risks?' In Study 2, the relevant headings were 'Risks and discomforts' and 'Injuries'. In terms of benefits, in one of the trials the title asked 'What are the possible benefits of taking part?' In the other it was simply 'Benefits'. This key information was particularly emphasized at the beginning of the trials when volunteers were being screened and enrolled.

However, the researchers did not routinely discuss the risks and benefits during the course of a trial unless a problem cropped up that required discussion of the risks. In the HIV prevention study the 'consistent condom use' message was discussed whenever the volunteers came to the clinic as part of clinical practice but not necessarily in terms of risks and benefits. The risks and benefits of a study were seen rather than discussed when volunteers reported rumours in the community that challenged their participation in the trials. Most of these rumours were about the risks that the volunteers had taken and the side effects that they might experience in the future as a result of participating in the trials. The rumour that the Study 1 volunteers feared most about taking part in the trial was that they would eventually experience side effects from the intervention and become 'like vampires'; in a focus group discussion they reported another rumour in the community that they would grow 'abnormal hair', a long-term effect that would manifest after the study had ended, and therefore they would have nowhere to turn for help. In Study 2, a similar fear was incurred by the rumour that the volunteers might die 'before their time' because they had stopped taking the active drug. Rumours may provide an opening for discussing concerns among the study volunteers (Geissler & Pool, 2006) and because rumours can impact on a study negatively (Geissler, 2005). So beneficence was discussed by the research team in formal terms in relation to the initial stages of a study.

The volunteers were interested in being healthy, and when they discussed the reasons for their continued participation in the trials and how they had benefited the most common response related to receiving good health care with proper treatment when they got ill. The principle of beneficence was salient in the informed consent process yet it was very critical in cementing the relationship between the volunteer and a research team. Volunteers' beliefs and values can be best judged rationally through their discussion about their expectations of the study. The volunteers' expectations related to the individual; how they would be protected from foreseeable risks relating to the trial and how they might benefit from taking part in the trial. A male volunteer who had restrained from having sex with strangers noted that taking part in the research enforced positive behaviour such as consistent condom use with every sexual partner; this was a benefit according to him.

The participant information sheets for the two studies stated that there were no individual benefits for the volunteers, but that the study findings would contribute to 'better management of HIV infection in the larger population'. The risks of taking part in a trial were expressed in the information consent documents in terms of 'discomfort,' such as that of having blood drawn and the side effects that a volunteer might experience; for example those who stopped taking Cotrimoxazole (Septrin) could be at risk of fever and malaria. The information sheets, which the research team members discussed with the volunteers, also contained information about the past research findings of similar study products. They stated that no injuries were expected in the study, but if they did happen the volunteers would be treated.

This information was mainly emphasized by the research teams during the early phase of the studies, but as discussed above, the volunteers were interested in what would happen to each of them who took part in the research. These volunteers wanted to be assured that their participation would not put them at risk of contracting a disease or experiencing side effects from the trial products. Researchers have discussed how looking at the informed consent process from the bureaucratic perspective, which emphasizes following the ethical guidelines, might be helpful in correcting volunteers' assumptions that what researchers might do with them would always be for their direct or immediate benefit as individuals (Burgess, 2007).

The volunteers were keen to attend follow-up appointments and to identify what was happening to them as a result of participating in the clinical research. The two volunteers who reported referring back to the information sheets said that they did so to find out whether the side effects they were experiencing after starting on a study product were mentioned there or were unique to them as individuals and not connected with the study. This is a very small number out of the twenty three volunteers. However, because of these volunteers who referred back to the information sheets in the trial, there is a lesson that volunteers even in low income settings are able to reflect on what happens to them during research. Therefore the principle of beneficence should not be overlooked during the research process. Although the majority of volunteers never reviewed the written documents, anything unusual that happened, such as a skin irritation, nausea or loss of appetite, was usually reported as an issue of concern and was suspected of being a side effect of the study drug. Research has shown that side effects are an ethical concern in research (Kamuya et al., 2013) but the volunteers' accounts did not point to ethical concerns but to how risks to them from the study products might be reduced.

It was particularly noteworthy that some volunteers who did not experience any of the side effects mentioned on the study information sheets assumed that they were on the active study products. This is a surprising finding because it would be expected that a volunteer who does

not experience side effects would imagine that they were on the placebo, as the study information stressed that the placebo had no drug content. In Study 2 this assumption may have been due to the fact that some volunteers were not experiencing frequent illness and yet because they were HIV-positive they assumed that they were on the active study product. This is relevant to the understanding of the study risks and benefits that was constructed in practice. Some volunteers forgot the key initial message from the team that the study in which they were taking part was a randomized trial with an equal chance of a volunteer being in the active or the placebo arm of the study.

The guidelines do not prescribe how frequently volunteers should be reminded about the key messages. It was generally left to the research team to decide when, as the study progressed, they could revisit the study information and discuss the key messages with the volunteers. Fully informing the volunteers about the risks and benefits of a study, as happens at the beginning of any trial, was seen by the SEC to require a follow-up assessment later to alleviate specific fears and misconceptions about the effects of the study products. Although the informed consent guidelines emphasize beneficence, in practice this was not associated with day-to-day communication, although the research teams were aware of good clinical practice. The risks were only discussed further along in the research process when the research team heard the rumours about the volunteers.

The ethics committee emphasized the principle of beneficence in the sense that it is mentioned in the ethics guidelines. During the protocol review the committee reviewed the investigators' curriculum vitae to ensure that they were well-trained and qualified to conduct such a trial, and ensured that the study information mentioned the possible risks and discomforts and expected benefits to the volunteer. This was a formal requirement which did not automatically translate into monitoring the researchers to find out whether they were implementing the study as outlined in the protocol.

In practice, therefore, the principle of beneficence depended on how the research team members managed their relationships with the volunteers and what was laid down in the protocol, which may not mention how a researcher is required to relate to a volunteer. The different actors discussed the risks and benefits of a research study differently: the ethics committee discussed them before approving a protocol, as required by the informed consent guidelines; the research teams mainly emphasized their discussion of the possible risks and benefits at the start of a study and when volunteers opened up and told them about the rumours they were encountering, which the researchers discussed with them with the aim of dismissing them. The volunteers' main concerns during the trial were the procedures they were required to undergo and how they might benefit from them, especially if they had health problems.

8.3.3 The principle of Justice in this study context

Justice, as a principle in research ethics, is discussed by ethicists in terms of fairness in the distribution of the burdens and benefits of a volunteer's participation in a research study (Belmont Report, 1978, CIOMS, 2002). Justice refers to what is morally right and proper when researchers deal with a volunteer. As mentioned in Chapter 4, justice is important in research ethics because of the lack of it in experiments in the past (Emanuel et al., 2008).

In this study the principle of justice was not mentioned directly by the respondents in their interviews but it was brought up as an important factor by the ethics committee and the scientists. For both, justice was linked to the discussion of study design which includes randomization, which was one of the key messages mentioned on the participant information sheets. Randomization of volunteers in a trial is meant to demonstrate efficacy and safety in clinical trials (Spilker, 1991), as discussed in Chapter 1, because volunteers are allocated randomly to a trial's placebo arm or active drug arm; it is hoped that this will lead to an equal distribution of the social economic and demographic characteristics of the enrolled participants across the two arms while also distributing the risks and benefits among the volunteers without any interference by the researcher to favour or disadvantage any individual or group.

The research team may indirectly have contributed to realizing this principle to some extent when they selected the study area and target population. The volunteers in Study 1 were recruited from their homes in an already-defined study area to which the research institution has access. Volunteers interested in the study were invited to attend the information sessions, and if they met the required inclusion criteria they were invited to take part in the study.

Another aspect of justice in the clinical trials that came through is the continuation of treatment of volunteers even after they had withdrawn from the study as is stated in the information shared with the volunteers at the time of entry into the research.

To recruit volunteers for the second study, the research teams went to HIV and AIDS intervention centres – mainly hospitals and outreach clinics run by other organizations – and provided the study information to clients found there, those who became interested in joining the study were assessed and, if they met the inclusion criteria, screened and invited to enrol on the trial. The research team was obliged to provide the study information and explain how volunteers would be selected to take part in a trial (CIOMS, 2002). Although the teams had access to the information about randomization on the participant information sheets, this aspect of the research process was least understood by the research volunteers. This affected the informed consent process to the extent that the volunteers believed that they were on the active drug arm and that the trial aimed to keep them in good health, which is not necessarily true.

The volunteers in both trials did not question the process of randomization, although many did not understand it, but they did question the blinding of the research teams. The volunteers in Study 2 believed that the clinicians would change them from one study arm to the other if they became ill, forgetting that the study was randomized and blinded, and highlighting their belief that the physicians would always do what was best for them (Burgess, 2007). This may point to some tension between clinical and research ethics. The research volunteers did not refer to the principle of justice, because they did not know it, what interested them were the kind of procedures they would undergo. The principle of justice was important for the research team and SEC members, who referred to the ethical guidelines to ensure that volunteer selection was fair.

The practice of referring to the national and international informed consent guidelines was mainly demonstrated by the ethics review committee and the senior scientists. The research teams' day-to-day activities implementing a trial are directed by its protocol. The research team and volunteers never discussed justice as a research principle in practice but this was the underlying principle when the research team discussed with the volunteers how they had selected them from the larger study population; Study 1 volunteers needed to be HIV negative and those in Study 2 had to have been stable on ART for over six months.

The principle of ensuring equality and therefore fairness among the volunteers was emphasized at the time of protocol review by the ethics committee members; the volunteers based their decision to take part in the trials on the trust in the study information provided by the research team that the study would not cause them harm during the trial.

8.4 Signatures, thumbprints and witnesses

The informed consent guidelines required the volunteers' written rather than oral consent, and state that they should be given copies of their signed consent forms. The findings in Chapter 7 showed that most actors, including some volunteers, saw the signed consent forms as legal documents binding the researcher and the volunteer in a research relationship for the duration of the trial. While only two of the volunteers reported that they had referred back to their signed consent forms, the research team did return to the signed forms when a volunteer reported discomfort about certain procedures, as evidence that the volunteer had not been coerced to take part in the trial. Some senior scientists and SEC noted that while a signed consent form meets the requirements of the informed consent guidelines, it records nothing about what was involved in the discussion between a research team member and each volunteer about the procedures and other trial details , and thus gives no indication of the volunteer's comprehension of the study information.

International research ethics guidelines such as the Declaration of Helsinki allow verbal consent in some situations; Uganda's national guidelines (UNCST, 2007) do not allow these especially in

clinical trials, giving the reason that these are usually 'more than minimal risk studies'. The national guidelines prioritize written consent in clinical trials because products are mainly tested for safety and efficacy in such trials and there is a possibility of volunteers experiencing adverse events as a result of taking part.

All the guidelines state that there must be a witness when an illiterate research participant consents to participate in a trial. The Declaration of Helsinki (1964) suggests that if possible the researcher should allow participants to choose their own witness. The ICH/GCP guidelines require a researcher to show how the study information was communicated to illiterate participants in the initial stages of the informed consent process, and some informed consent guidelines suggest video-recording this interaction. The consent process was not videorecorded in the two studies that I investigated. In practice the witness was selected differently, in some instance it was a staff member not involved in that particular trial and in other instances it was any volunteer who was able to read and write. The attitude of the research teams towards what kind of witness to have for an illiterate volunteer varied. Some of the research team members preferred to involve a close friend or relative as a witness who may have prevented the volunteer from taking part in a study that would harm them. Other members of the research team did not mind who was a witness as long as the illiterate volunteer allowed them to be their witness. These different stances show that although the guidelines may have been a useful tool to guide the way informed consent was sought from a volunteer; the individual research team members could influence what happened at the time of obtaining informed consent from a volunteer. Volunteer confidentiality and privacy during the research was more questionable within circumstances that involve a witness.

The research team and ethics committee assumed that the witnesses 'understood the information better' than the illiterate volunteers, but noted that obtaining a thumbprint from a volunteer took more time than a signature and that the presence of the witness made the volunteer uncomfortable thumb printing the consent form. Signing or thumb printing the consent form was a procedure that no one, including the volunteers, debated about and the research team reported that those unable to write their name tended to feel stigmatized. Including a third party in the agreement between the research team and the illiterate volunteer violated the latter's privacy according to some of the research team members. The volunteer was relinquishing part of his/her power to make his/her own decision to take part in a trial to the witness at the signing of the consent form, even when the former had understood the study information. This requirement was seen by the research team to undermine the volunteer's self-determination.

Although signing or thumb printing was always done at the start of a trial, the majority of respondents, including the volunteers, noted that it affected the volunteer's self-determination

and autonomy, often for the duration of the study. A SEC member suggested that it might be more useful to have all the volunteers' use thumbprints rather than signatures, because no two people have the same thumbprint and there would be no possibility of forging them, while forging signatures is easy.

Of all the issues covered by the guidelines the presence of a witness when an illiterate volunteer formally consented to join the trial aroused the most controversy in the individual interviews of all the actors and during the focus group discussions, and yet this is laid down in the national and international guidelines (UNCST, 2007; CIOMS, 2000; Helsinki, 2008). Many participants saw it as failing to acknowledge the ability of illiterate volunteers to understand the study information when shared in their vernacular language.

Most respondents in my study, including the research volunteers, rejected the idea that their understanding of the study information was necessarily related to their literacy. The research team members noted that they found it difficult to translate the study terminology from English into the vernacular, but the volunteers understood it better when it was presented in the vernacular language (Luganda) in both study settings. Of the twenty-three volunteers that I interviewed for this study, only one requested to be given the information in English. The others, including university graduate, preferred information to be discussed in the vernacular. Brehault et al. (2012) review of informed consent documents from 139 trials showed that most do not meet a standard that encourages a volunteer or patient to make appropriate decisions before taking part in a trial, but that when they are translated into the local language of the volunteers it makes communication between the research team and volunteers easier. Additional resources may be needed to build the capacity of research teams to cope with this requirement (Participants, 2013). The informed consent guidelines do not prescribe assessing volunteer understanding but they do emphasize the use of simple language that the volunteers understand.

8.5 Interactions between actors

My study found that the informed consent process in the two Ugandan studies depended heavily on what transpired in interactions between the actors involved. The way the different actors built rapport through their interactions with one another affected the volunteers' decisions to take part and continue to participate in the research. My respondents did not find the issue of volunteers' individual consent to be a challenge; gender and trust, however, were cited as factors that can impact positively or negatively on a volunteer's process of consenting to take part in research. Gender differences between the research team members and the volunteers did not appear to affect the informed consent process in this context, the research team was comprised of both sexes. The decisions of many of the married women in the trial that required partner involvement were influenced by their spouses, and their final decision to join a study usually followed permission given by the husband, as discussed in Chapter 6. This was not uncommon in this setting, which other researchers have described as patrilineal with authority mainly lying with the man in a marriage (Roscoe, 1965, 1911; Muyinda et al., 1997; Wolf et al., 2000). Most of the women in the study reported informing their husbands before taking part in the trials. This reflects the expectations of women in this society, whose cultural norms give men overall authority in family decisions (Roscoe, 1965, 1911; Wolf et al. 2000). Two men in this study reported that they had informed their wives before consenting to take part in the research; this was not the usual because in this society men are not obliged to inform or even seek approval from their spouses before they make major decisions in the family, including participating in research. The rest of the men in the study had not consulted their spouses.

When discussing the role of women, for example in introducing condoms into a relationship, the CAB members (Chapter 6) reported that it would be outside the norm in their society for a woman to introduce and insist on using condoms in their marriage. If a woman cannot take part in research without their husband's permission, the principle of individual autonomy during the informed consent process stipulated in the guidelines was affected.

Trust was seen as an important factor in discussions of individual consent in this research context. Several respondents singled out trust as important, particularly in interactions between the research team and the volunteers. Despite the fact that the research volunteers would not know the end results of clinical trials studied in this thesis, they nonetheless expressed their trust that the researchers would conduct the trial well and that the outcome would benefit them. This is similar to findings from Kilifi in Kenya (Molyneux et al., 2005). The researchers, for their part, had to trust the volunteers to give them accurate feedback about what they were experiencing and to remain in the trial until the end. Trust is not highlighted in the informed consent guidelines but was demonstrated as the actors interacted with each other, showing its importance to the success of the informed consent process in these clinical trials.

Although autonomy and the freedom to choose, as recommended in the research guidelines, was emphasized in the research team's responses, in practice it was the interactions and relationships involving the individual volunteer at the clinic and at family and community level that were shown to impact on volunteer autonomy, either positively through the experience of self-determination or negatively by hindering their personal commitment to research and engagement with the informed consent process.

Some individuals' consent was affected by the stigma that the community attached to being HIV-infected. Most community members' lives were affected in some way by HIV and there was a belief in the community that whoever participated in research as a volunteer was HIV positive. The guidelines emphasize that the volunteers must understand the study, but informing the general community depends on the context of the study and the initiative of the research team. Community members who did not understand the details of the research tended to spread rumours which could create stigma for existing and potential volunteers, as pointed out in chapter 7.

The informed consent guidelines do not suggest how frequently a research team should hold study discussions with the volunteers; this activity was controlled by the research team. Study 1 held regular meetings of volunteers and research team members on the initiative of the latter. If the team did not formally organize such discussion meetings they could easily be overlooked in the need to carry out the frequent and rigorous clinical procedures required by the study. It was therefore possible to fail to address the behavioural and community challenges encountered by volunteers as individuals due to the overwhelming volume of clinical procedures planned in the protocols discussed when the research team met with the volunteers. Failure to hold frequent researcher-volunteer meetings to discuss rumours and other challenges may have affected the autonomy of individual volunteers, who might have made less well-informed decisions during the trials as a result, and increased the risk of their autonomy being affected by the important others in the community outside the informed consent process.

8.6 Implications for Informed consent in the context of an HIV clinical trial

Chapter 5 showed how each actor involved in the informed consent process in the two studies defined it from their own perspective. Whereas for some research team members it was primarily a legal process and a key marker of how things should be done, the SEC emphasized that some volunteers and research teams defined the process only in terms of an event, focusing on putting the signature or thumbprint on the consent form to prove the agreement between the research team and the volunteer. In practice, the informed consent process should be discussed in depth by the different actors to ensure that while the relevant guidelines are recognized and followed the underlying principle of volunteers' autonomy is also emphasised, ensuring understanding of the study information by the volunteers rather than the research team's interest in accomplishing a formal process. The volunteers' complaint about the lengthy consent procedures may reflect their underlying need for consent as a process rather than as an event.

All the informed consent guidelines emphasize the informed consent process as a process rather than an event, and my findings (see Chapter 5) show that this depends on the

researcher's discretion in deciding how to remain in communication with each volunteer. The regular follow-up meetings with volunteers after they enrolled were important because it was here that they brought up their concerns.

Uganda's national informed consent guidelines have integrated some local cultural-specific aspects requiring that when conducting research in the country a researcher needs, for example, to understand the roles and responsibilities of men and women in this patrilineal society. One of the research ethics team members reported that a research collaborator wanting to conduct research with pregnant mothers in Uganda would need to accommodate the sociocultural context defining such women; for example, there are rules about when it is appropriate for a mother who has delivered a baby to leave her house and engage in activities outside it and what influences her decision-making (Chapter 7).

In this society the reality of making decisions concerning issues such as taking part in a research study, which may impinge on reproductive health, involves consulting important others (Wolf et al., 2000). This may mean that apart from the informed consent guidelines, the process requires the research team to plan the informed consent process so that volunteers have time to consult their spouses or important others in their communities, since this is locally relevant.

Because most clinical trials are multi-centred and have to keep to strict timelines if they are to realize and evaluate the trial outcomes, the informed consent process is driven by the protocol requirements, which rarely take into consideration the time required to ensure that volunteers join a trial well-informed.

The guidelines prescribe what may happen during the informed consent process. However, in my study the trial protocols mainly emphasized the clinical procedures and did not consider group meetings between the research team and the volunteers. I found that it was at such meetings that the volunteers could bring up concerns not revealed to the research team in oneon-one discussions. The group dynamic at the general meetings encouraged volunteers to open up, especially about issues like possible side effects from the trial. For example some Study 2 volunteers describing their experiences equated the study product to 'real Cotrimoxazole', showing that they had forgotten that there was a chance of being put into a placebo arm. Volunteers who forget the key study information are more vulnerable to miscommunication and myths about the study coming from friends and family in their communities unless informed consent is planned as a process. Although the regulatory guidelines describe what the informed consent process should involve, in practice its implementation depends a great deal on how the actors in the process relate to each other.

The relationship between a researcher and a volunteer in a clinical research setting is different from that between a physician and a patient in a clinical setting. In the clinical relationship the

physician usually makes the final decision about a patient's treatment or procedure, and this is the case in Uganda. This may be why some volunteers reported that they would always trust the health provider to do the right thing and make the right choices for them (Chapter Six). Because of this belief, researchers discussing study information with volunteers need to clearly differentiate between a treatment situation and a research situation that may not benefit the research volunteer as an individual (Participants, 2013).

Concepts such as trust and trial terminology such as randomization become more understandable to the volunteers when discussed over time during the informed consent process. While the volunteers were given information about the trial they never argued about what the research teams discussed with them However after having experienced the informed consent process as part of the study for some time, they gained the courage to question what was happening, some reporting their disbelief that the research team members did not know which of them was on an active product and which on the placebo. This implies that more discussion about the informed consent process between the research team and the volunteers is required to manage beliefs that may impact on the research.

The regulatory guidelines set out the general requirements for discussions with volunteers about study features such as the reasons for conducting the study, the study procedures, the duration of the study, and the risks and benefits of participation. The researchers decided on the study-specific key messages to provide in the consent documents. The volunteers' decision-making process, as revealed in the context of the two trials in this case study, depended on the encouragement of a range of "important others" – not necessarily spouses – including parents, older siblings, community members and the research team members who provided the study information, all confirming that informed consent is a process and not a one-off information-giving event.

The research teams found the guidelines a useful tool as they flagged up the three key aspects of the principles of informed consent: respects for persons, beneficence and justice. However, in practice it was the principle of respect for persons that was most acutely experienced by both the research teams and the volunteers throughout the research process. The discussions of the procedures and the interactions between the research team and volunteer is what led to volunteers making the decision to take part, or not, in the trial or to continue participating. In this study context, respect for a volunteer during the trials required the research team member interacting with them to avoid putting their own personal beliefs and values on the forefront of the discussions for the sake of managing the process. An example discussed in Chapter 7 in relation to the actors' experiences during the informed consent process showed that all the principles (respect for persons, beneficence and justice) contributed to the values that a researcher may choose to integrate in their way of relating with the volunteers during the research process, which develops as they interact with volunteers. For example, as research team members said, some volunteers might not adhere to the procedures or they might decide to withdraw from a study; the researcher could not influence the volunteer's decision apart from going back over the study information with them (see Chapter 7).

The research team was bound by the agreement to provide all necessary medical care, as they told the volunteers when they signed the consent forms confirming this. The researcher was in control of clinical procedures and responsible for ensuring that the volunteer was protected throughout the research according to the informed consent guidelines. While the research team was seen not to be either formally or informally in control of the volunteers' decision-making process during the trial, they influenced volunteers through their on-going interactions, suggesting that such studies may need to explicitly address informed consent as a process and not an event.

The findings in this study show that the nature of the study and the setting in which the trial takes place influence the way the informed consent process is managed by the different actors. Concepts like actor' values and beliefs influence the process although according to the dynamics involved in the trials, these are moderated during the interactions.

The influence of the ethical guidelines, the sponsors , implementing organisation of the research are usually overtaken by what volunteers experience in the community and therefore engaging the community proactively will reduce rumours relating to the trials.

8.7 Conclusion

Although various research regulatory bodies provide guidelines for the implementation of the informed consent process, in practice factors such as the actors' values, beliefs, trust, gender and power dynamics also play a major role in how decisions are made during the process. The process therefore was defined in practice according to what the different actors saw as important. For example, some volunteers viewed the process as a one-off event and saw no reason to go back and check the consent forms once they had signed them. The research team was protective of the research and of clearly-signed consent forms as evidence that they had not coerced the volunteers to participate in the trials.

The guidelines laying down what should be done were seen to be perhaps too rigid to accurately reflect the practical requirements of the research; for example most guidelines require written consent from research volunteers, but in real life at a research clinic the interactions between the different actors in the informed consent process, how they agree to work together and their attitudes to each other can lead to genuinely informed consent in which the basic research ethics principles are realized. The documentation of consent was considered important because it proved that the guidelines had been followed, but what
appeared to be most important was the on-going communication between the members of the research teams, the volunteers and other actors throughout the informed consent process.

Getting a volunteer to listen to a lengthy information sheet being read out and to sign the consent forms was accorded great importance by the research team, as they went through the various successive trial procedures. Holding regular meetings with volunteers during the trial to discuss their experiences and dispel the rumours that they heard in the community is not included in the guidelines but is one of the ways that a research study can retain its volunteers.

Decision-making during the informed consent process was on-going throughout all the study activities. It involved the actors' beliefs and values, their trust in particular people and the reasons for it, the way they networked and interacted with others and how they affirmed their needs as autonomous beings in the informed consent process. Although autonomy is a key aspect of informed consent in the guidelines, I found that not all volunteers felt fully autonomous due to complex interactions among all the actors involved, including their spouses and family relations, which may have affected their decision-making.

The research teams confirmed that the national and international guidelines were a useful reference and guidelines on the principles involved in protecting the volunteers; however, I found that most of what goes on in the implementation of an HIV clinical trial in this Ugandan research context is decided by the different actors as they enact the informed consent process. The research teams commonly followed the specific details set out in the trial protocol rather than regularly referring to the informed consent guidelines.

Chapter 9 Conclusion

The chapter brings together the findings in the thesis, I start by reviewing the informed consent process as discussed in the event and process models outlined by Appelbaum and colleagues.

This study has investigated the informed consent process, which in this thesis refers here to all elements of the process from mobilization for the initial recruitment of volunteers, providing volunteers with information about the study, a review by the ethics committee of the informed consent documents and the signing of documents by a member of the research team with each research volunteer, and includes the various interactions that take place between the key actors over the course of a clinical trial. The study was conducted in two HIV clinical trials in Uganda and the findings are from the perspectives of the different actors involved in the informed consent process.

The ethics review process of the informed consent documents involves reading the protocol and the information sheets of the study. The English and vernacular consent forms are reviewed and discussed. The committee (SEC) pays special attention to the language used to communicate to the volunteers the information on objectives of the trial, study procedures, benefits and risks of the study among other procedures to ensure that the form is simple and clear. The committee also reviews the curriculum vitae of the principle investigators and ensures the information sheets are clear on whom a volunteer should contact in case he has a problem. The committee reviews the science and the ethical considerations in a given protocol and the pathway for a volunteer in case of a complaint relating to the trial.

Obtaining informed consent from research volunteers before they take part in clinical, biomedical and social research is one of the main principles outlined in the international standardised research ethics guidelines. The main aim of this qualitative research was to understand how the actors in the informed consent process defined, interpreted and experienced the process, and how their understandings reflect and have implications for the realization of the standardized informed consent guidelines.

The actors in the informed consent process include the members of the science and ethics committee (SEC), who approve each study protocol before the study can be conducted; the field research teams who conducted the trial and were in direct daily contact with the volunteers; the senior scientists in charge of the overall conduct of trials at the sites; the volunteers participating in the clinical trials; and the members of the community advisory board

(CAB), who acted as a link between the participating community, the research teams and the volunteers' spouses and significant others.

Research targeting human subjects must follow specific ethical guidelines. Appelbaum notes:

The existing regulations lay out the types of information that must be communicated to potential subjects. [The regulations] give no guidance about the specific information that should be conveyed [...] selection of a proper approach depends on an understanding of the differences between consent to treatment and consent to research. (Appelbaum et al., 1987, p.232)

Informed consent in both the treatment and the research setting involves challenges to ensuring that volunteers are protected from any form of harm and that they comprehend the information they are given about the study. In this study, researchers reported that they found the GCP guidelines helpful in conducting trials, but these do not provide detailed advice on how to assess volunteers' comprehension of the study information, which remained a difficult part of managing the informed consent process.

The history of UVRI's Science and Ethics Committee (SEC) shows how most research in Uganda is conducted through partnerships and collaboration. Scientists and ethics committees have had to learn to adopt important research ethics guidelines while bearing in mind the sociocultural context of the research setting in Uganda and ensuring that the research volunteers are protected from any form of harm.

Appelbaum et al. (1987) event and process models of actors' decision-making in the informed consent process was a framework for the study. The event model is about a one-time event leading to a decision taken by the volunteer which is evidenced in the signing of a consent form by both parties involved, which may be, for example, a physician and a patient in a clinic setting. The process model assumes that decision-making is a continuous process; in the research setting a research volunteer interacts with more than one actor as they consider their decision to take part and continue taking part in a clinical trial. I have shown that besides the volunteer and research team member's decision to sign the consent form, interactions in research may be affected by the various individual actors' values and beliefs and by the gender relations, trust and power dynamics among them. These two models of decision-making can contribute to understanding the decisions that the different actors' make while conducting research. The event model is limited in this setting, because some decisions were influenced by perceptions and relationships in the volunteers' communities and therefore informed consent cannot be seen as confined just to one event. The process model better explains the decision-

making patterns in the informed consent process in the two HIV clinical trials in this study, because the volunteers referred to their important social networks throughout the trial.

The research team understood and interpreted informed consent in terms of the research process that may lead to new knowledge which can be used to deal with the current HIV problem in Uganda. The research team's main emphasis in the informed consent process was on finding the best strategy for conveying information about the study to the volunteers; the critical issue was allowing as much time as possible for the informed consent process, assessing their comprehension of the study and obtaining their consent to take part in a trial and agreement to comply with the study requirements. This shows the difficulty of distinguishing consent from the wider study experiences and issues.

For the trial volunteers, the clinical procedures that they underwent and their implications for their health were important. They understood the study procedures better as they progressed through the trial than at the start, when the research team formally provided them with study information prior to their signing up to it. Motivated by their desire to find out about their health status and secure assured health care, some volunteers may have told the research team member providing them with the information that they had fully understood it in order to be allowed to sign up to the trial. However, members of the research team reported that some volunteers did not understand the study procedures even several months into a trial, and some only understood some of the procedures when they experienced side effects that they could not explain such as feeling ill most of the time, as a volunteer in Study 2 explained.

The values that the individual research team members brought to the informed consent process were influenced by the formal structure of the research institution and what it required of each of them; with 'do no harm' as an underlying element of good clinical practice. The volunteer's values, on the other hand, were mainly based on the expected trial outcome and what it meant for them as individuals. Their reasons for joining a trial were mainly linked to what they expected the trial outcome to be; for Study 1 volunteers this was continuing to prevent HIV and remaining free of it; for those in Study 2 it was about being in good health despite having HIV and taking fewer drugs than before. They persisted to the end of the trials and did not withdraw from them, mainly due to their individual beliefs about the trials and the importance they attached to the hoped-for individual results. For a research volunteer, the main factor driving their informed consent was their good health, and despite their reservations about the amount of time that they had to spend at the research clinic sometimes a volunteer did not leave the clinic until they had seen a study physician to ascertain their health status.

In this study, trust was clearly seen as an important factor of the informed consent process, and the actors demonstrated trust that the consent process would lead to positive outcomes for them although this is not necessarily a straight forward issue because it is an individual's perception of the situation. The research team trusted that the volunteers would give truthful responses during the trial and stay until it ended. Trust among the members of the research team was based on the institutional research structure and the roles assigned to each. The research team relied on the SEC to approve the trial, which provided a basis from which the team was able to inform the volunteers about the study procedures, the duration of the study and its benefits and risks. The SEC had to trust that the research team was competent enough to conduct the trial without causing harm to the volunteers, which is the main reason why any Research Ethics Committee (REC) is instituted.

The volunteers trusted that the health workers at the research institutions would provide and resolve all of their health problems; they only discussed the possibility of harm resulting from their participation if they developed side effects during the trial. In this research setting the volunteers trusted that the research was seeking a solution to the HIV problem. Trust in the research in these Ugandan communities was based on the prestige that has always been given to health workers in a clinic setting and the belief that whatever the physician decides for a patient is the right thing, as reported by a scientist and some of the volunteers. In this society the attitude to and trust of patients and carers in the clinic setting is used as a basis for the volunteers to trust the research by the research teams. The volunteers knew little about what the informed consent guidelines require of researchers and in this sociocultural context asking questions of individuals who are seen as knowledgeable, as most people perceive health workers to be, is uncommon. Trust during the informed consent process was dependent on how the interactions between the research volunteers and the research team members were managed.

The volunteers also trusted and shared the belief that by participating in the research they would be contributing to the solution to the HIV epidemic. However, they did not always see the trial results as aiming to secure a solution that was beyond their individual needs as research volunteers. While trust between volunteers and the research team was found to be vital in these research settings, some volunteers doubted that the research team were, like themselves, blinded to the research. The community belief in this society is that all the health workers are knowledgeable about health, and because they were the ones who carried out the laboratory tests and administered the study products some volunteers questioned at the point of reviewing some study concepts such as that the trials were double-blinded.

This study found that the volunteers' belief that they could not be given any product that would cause harm led to some forgetting that the trial was randomized because they did not experience side effects from the product they were given. This flags up the need for research

teams to remain in continuous discussion with the volunteers about the trials throughout their duration.

Power as a factor of the informed consent process was found to run through the interactions between actors; each group of actors had some level of power that they could exercise during the informed consent process. Each group was controlled by other actors, depending on the stage of the trial. First, the SEC had the power to approve a new study protocol. Once the trial commenced, all the actors in the process shared power because each group of actors had a specific role in the process. The power of the individual research team and the SEC members was controlled by the bureaucratic requirements of the institution they represented. The volunteers' exercised power when they decided to join a trial and agreed to the procedures that it involved. The context of clinical trials does not only involve the key actors at the research setting but clinical trials can impact more populations than just the study population.

The ethics committee and the research teams used the protocol guidelines, standard operating procedures, work policy documents and international and national research ethics guidelines to guide and control the ways in which the different groups of actors interacted with each other in conducting the study procedures with the volunteers and resolved interpersonal conflicts during the informed consent process. The guidelines also directed the ways in which the research team handled volunteers and in particular the study information that they provided, which included the risks and benefits of participating and how procedures would be carried out so that they were protected from any form of harm. With this information they would know what to expect during the trial. This had to be ensured before the research team sought the volunteers' consent to participate in the research.

The volunteers in this study, however, were not wholly or always vulnerable because they had the power to make decisions, especially about when and whether they chose to turn up for their scheduled appointments. Their power was largely not expressed overtly, but everything in the trials, including the informed consent process, depended on their cooperation with the research teams. In a focus group discussion the volunteers referred to themselves as 'heroes' for taking part in a trial, acknowledging their power to influence the research outcomes.

Autonomous decision-making on the part of all the actors is a central focus of the informed consent process. Some married women in this study gave up their own individual decisions and had to fit in with decisions made by others, particularly their husbands, in this patrilineal society. Berg et al. state:

The autonomous authorization that was informed consent also involves intent. The patient or research subject must intend to authorise the course of action consented to

or alternatively, intend to refuse such authorisation: it is in the intending that the patient or subject assumes responsibility for the decision made. (Berg et al., 2001, p. 25)

In this society autonomous decision-making was influenced and moderated by important others in the research volunteers' lives. The final decision to take part in research was eventually made by the individual, but for most it was influenced by factors such as gender relations, which position women at a lower level of authority than men, making them dependent on men even in their decision-making.

Gender relations between the research team members and the volunteers were not reported to be a problem; the main gender related challenges occurred in individual research volunteers' family setup. A few women reported incidents of psychological gender violence such as a husband who kept telling his wife, who was participating in one of the trials, that she was likely to die any time. A case was also reported of a female volunteer being beaten by her husband because she was late home from the research clinic, which is another harm which is not a trial risk as was shared in the information sheets.

Rumours in the community posed a particular challenge to the volunteers' trust in the trials. However they managed this difficulty by reporting them to the research team, who assured them by giving them correct information on the subject of the rumour. They also discussed them among themselves and advised each other during their visits to the research clinics, and some referred to important others in their lives, such as their mothers, for their views of the fears they were experiencing. The research teams managed the trial's routines and relationships during the informed consent process, mainly through weekly meetings to discuss the challenges they had met with while conducting the trial. They consulted with one another during the process as the procedures were clearly outlined in the SOPs and the trial protocols. While they did not refer directly to the informed consent guidelines to solve day-to-day problems they did refer to the ethics guidelines and good clinical practice documents for challenges related to ethics.

Relationships between the research team members and the volunteers were formal, although occasionally a volunteer divulged personal information to a research team member. These informal interactions between team members and volunteers often revealed more about what a volunteer was going through than they reported formally. The different actors developed a mutual support system over time. The ethics committee and research team relied on the guidelines and standard operating procedures set up by their institutions. The scientists and ethics committee members usually abided to the ethical guidelines. The volunteers turned to their relatives and friends for support when they experienced challenges in the trial, mainly due to rumours in the community, despite the fact that the information sheets they were given at the start of the study told them that they could report such problems directly to the ethics

committee, which was charged with ensuring that they were protected from any form of harm. As the volunteers were keen on remaining in good health, their relationships with the different members of the research team who provided medical care were most important, especially when they experienced health-related challenges during the trial.

Limitations of the study

This study has some limitations; it was limited to two HIV clinical trials targeting HIV infection, which is still a big problem in Uganda. The trials, although not similar in form – one focusing on prevention and the other on treatment – are comparable because both were guided by the same research ethics regulations and similar guidelines for the informed consent process in research.

The number of respondents in this study is small and the study results are therefore not generalisable to populations outside the Uganda context but could be used to understand the informed consent process in HIV clinical trials. The respondents were drawn from a range of actors as the study sought to learn about their experiences of the informed consent process in depth; their testimony contributed to a richer understanding of the process.

The other limitation was that I did not select the volunteers directly because my study was nested in two on-going clinical trials from which they were purposely selected via a two-stage selection process. I was not able to observe the process of obtaining informed consent as it happened for the main trials because my study took place when all the volunteers had been in the study for at least six months. The point of entry to study the informed consent process was however an advantage because volunteers discussed what they experienced in the trial process and it was not hypothetical.

I hand limited chances to observe what happened during the interactions that took place when a volunteer went into a closed room to meet a clinician, counsellor or nurse, however I was able to observe the interactions such as what happened in the corridors as volunteers waited to see the next research team member for more than half of my respondents. I also observed what happened in the main waiting rooms and how volunteers and research team members interacted with each other.

My study was not conducted at the volunteer's homes but at the clinic which could have influenced them since it was the same setting in which the clinical procedures took place. However the explanation and procedures of my study were different because the research team contacted the volunteers during the follow-up of the clinical trials and mentioned my study, and I then provided them with the study details.

It is possible that my presence as a researcher was not well understood by the volunteers since I occupied the same clinic space. I was usually referred to by the research team members who introduced the volunteers to me as a 'musawo' equated to a health worker as the research teams were commonly referred to and this could have meant that I was part of the research team, but in my explanations to the volunteers I endeavoured to clarify that I was a researcher for this specific informed consent qualitative study.

Selection bias was minimized by randomly selecting volunteers who were attending the research clinics during the season when I conducted my study, with potential volunteers hearing first from the research team and then from me about the details of the study before consenting to take part.

While this is a study of only two HIV trials in Uganda they were conducted within a well-known research programme with a functioning institutional science and ethics committee that follows both international and national research ethics regulations, and it provides findings that show what happens during the informed consent process in this context.

Conclusion

Although the informed consent guidelines are important in research ethics and are emphasized in all research processes, in practice, implementing the guidelines depends on the interactions and communications between the individual research team members and the research volunteer. The protocols for the clinical trial and the standard operating procedures were the main tools used in the daily research activities to guide the informed consent process and manage the research team and volunteers' interactions.

The three basic research ethics principles for informed consent require more than the formal documented system: the consent process requires the researchers and trial sponsors to understand the sociocultural context of the research and appreciate the volunteers' views of the process. This study has found that volunteers were interested in being given concise information about the study rather than the lengthy documents they received, because they could not retain all of the key messages in those documents in their memory. The process required continuous discussion between the research team and the volunteers about what is happening to the research volunteer even in informal situations. The informed consent process therefore should not end with the team's assessment of volunteers' understanding of the study information, usually at the start of a trial. The procedures that the volunteers undergo during the trial are recalled much more easily than some of the information they are provided with at the start. This means that study information should be provided not only at the start of a trial but throughout the trial period.

Building the capacity of the research teams to enhance their knowledge of research ethics is critical for a successful informed consent process with respect, beneficence and justice for all volunteers; ethical principles that the researchers and particularly the scientists and clinicians, who are trained in research ethics, referred to conceptually, with the intention that all the research team members managed the process with this ethical framework of research in mind.

What we learn from this study is that research teams need to go beyond the formal practice in the informed consent process of providing study information and assessing volunteers' understanding and voluntariness and getting consent forms signed. The research teams need to devise ways to keep their communication with the research volunteers and the community open and continuous as a good practice in Uganda. This however may have problems if more information is revealed informally to the volunteers than what is documented.

Clinical trial results can be affected not only by gaps in information and volunteers' failure to understand the study. Other factors, such as the amount of time that volunteers have to give up to clinical procedures, trust between the actors, interactions between the researcher and research volunteer, volunteers' relationships with their spouses and community perceptions of the trial can also affect the results. More time may therefore need to be factored in to facilitate interactions between the research team and the volunteers and to monitor what goes on in the community more closely via the community advisory boards.

The volunteer's welfare should take priority over the research teams' interest in their studies. Altruism may be an important reason for taking part in a trial for some of the volunteers, but the main reason the majority of volunteers participated was because they knew that when they were ill they would be given efficient health care. Uganda's public health services are not efficient, there are few physicians and basic drugs are not available at most health centres. Decisions made by the actors during the informed consent process were influenced by values and beliefs. The volunteers' belief that participating in a clinical trial would give them access to treatment and frequent health check-ups when they attended the research centre was an expected positive outcome for them that did not necessarily relate to the primary and secondary trial outcomes of HIV prevention and improved treatment and care but still possible. The volunteer's involvement in the research, creating the potential for finding answers to important research questions. This was a relationship forged from the need of each actor to gain from the other: the volunteer gained but the researchers also gained from the volunteer's participation in the trial.

A low level of investment in their health-care systems is one of the factors that affect the conduct of clinical trials in developing countries (Varmus & Satcher, 1997) and may contribute to the difference in understanding the consent process on the part of the research teams and

the volunteers. In Uganda the state owned healthcare services are still facing challenges in meeting the needs of the population. Given the small numbers of health workers in proportion to the population, some people have lost trust in the treatment offered at the health centres (Birungi, 1998). Although this state has improved, there are still limitations in infrastructure and services, for example outpatient care for sick children and adults with STIs, temporary family planning, antenatal care, immunisation and child growth monitoring is available in 5 of every 10 facilities (MOH, Survey Report, 2008). The guidelines for informed consent were used formally, but in practice the relationship between researcher and volunteer is what can lead to a well-developed informed consent process that is interpreted similarly by all the actors.

My research has found that managing the informed consent process is still challenging and contentious even in well-established research institutions with long term experience in conducting research. The lessons learned from this case study can be added to current understanding of the informed consent process in HIV clinical trials, and similar studies conducted in other contexts would offer further understanding for better management of the informed consent process in clinical trials.

Power was moderated through the study protocols and the informed consent guidelines. The actors in their different roles worked via specific structures: the researchers, guided by research institution requirements, drew on a set of work ethics; the ethics committee was guided by a set of standard operating procedures for reviewing and monitoring research on human subjects and referred to international and national guidelines in the process of reviewing protocols. These two groups of actors were controlled by the institutional structure in which they operated and power issues were managed depending on who had influence at which point in time during the consent process (Lukes, 2005). Similarly, while the volunteers may have had a sense of agency or independence as they joined the trials, once enrolled they had to adapt to the procedures set out in the protocol when interacting with the research teams and therefore there was a limit to how they exercised power over other actors.

Post –consent, individual agency is not emphasized in clinical trials, although most decisions concerning the specifics of handling trial procedures, managing relationships between the actors and protecting volunteers were influenced by individual values and beliefs. The interactions between the actors were generally formal, although as reported in this study, as the volunteers progressed through the trial some occasionally opened up and discussed personal concerns with research team members, some of which had nothing to do with the trial procedures.

Appelbaum notes that informed consent may encompass a legal aspect of protecting the researcher or medical professional in the clinical setting because historically informed consent has been guided by law. Informed consent is also viewed in terms of the ethical doctrine which

emphasizes individual autonomy and of the interpersonal process of interaction between a researcher and a volunteer (Appelbaum et al., 1987). The guidelines address the legal aspect of trials, ethical doctrine and interpersonal processes in general; however, in practice in this study it was repeatedly reported that implementing the informed consent process depended much more on the interpersonal researcher-volunteer relationship. In general, obtaining informed consent was treated as a one-off event by the research team, but the researchers had to prove that each volunteer had been well-informed about what could happen during the course of the trial and therefore interactions between the volunteers and the researchers were critical to the enhancement and sustainability of the informed consent process.

Some of the volunteers expected to sign the consent form because they had either seen it happening before or had been told that it must be done to show their commitment, which some respondents said could be compared to negotiations to buy a piece of land, which also involves signing an agreement between the two parties to show their commitment. The signed consent form is a sign of commitment between the doctor/researcher and patient/research volunteer (Appelbaum et al., 1987).

The informed consent process in different research contexts needs to be understood in terms of how it fits in with standard international and national guidelines on obtaining informed consent from research volunteers. The findings of this study in the context of clinical research in Uganda show that the basic principles of informed consent are not automatically translated into practice in clinical trials. Exploring and interpreting the actors' interactions throughout the research process, noting where the ethical research principles of respect, beneficence and justice were exhibited was important to understanding the informed consent process in HIV clinical trials.

This study has shown how the informed consent process was interpreted and emphasised somewhat differently by the different actors involved, particularly the research teams and research volunteers. So while greater regulation via the informed consent guidelines and the presence of SEC was emphasized this may be counterproductive if the different ways in which the actors interpret the process are not understood and some still interpret informed consent in a research setting as a one-off event rather than as a process. This research has revealed the importance of training all actors involved in research ethics on the basic research ethics principles. The senior researchers and bio-ethicists need to discuss the research ethics that involve human subjects in the Uganda context in order to gain meaningful informed consent from research volunteers in Uganda.

The implications from this study show the need to tailor informed consent processes to local contexts. There are examples of how this might be done, and documented experiences of doing this in developing countries, in the literature (Participants, 2013; Boga et al, 2011). This

how principles are interpreted and implemented in different contexts may differ by context. For instance how harm is understood, and what kinds of harm arise, might be locally specific. For example in this study, local gender relations and inequities may have contributed to a woman reportedly having been beaten by her husband for returning late home from a trial visit. The importance of supplementing consent processes with wider community engagement activities is now widely recommended for developing countries in an effort to support local tailoring of consent processes (Participants, 2013). The context related challenges might be best identified and planned for by the local researchers and the site principal investigators as they work on the local site standard operating procedures even when they have limited inputs in the research protocols and informed consent forms.

Participants have been reported to know their best interests and what may be useful to them (Nuffield council on Bioethics, 2002). They make decisions to join research within complex political, economic, and socio-cultural contexts, many of which cannot be controlled by researchers (Bull & Lindegger, 2011). It is however, important to understand how informed consent processes are understood, interpreted and experienced by the different actors, as I have done in this study in the Uganda context. This may improve the way informed consent is obtained from research volunteers in future studies.

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APPENDICES

Age (yrs)	Sex	Occupation	Marital Status	Education level
25	F	Businesswoman	Single	Primary
27	м	University Student	Single	University
31	F	Businesswoman	Married	Primary
31	М	Security Guard	Married	Secondary
23	F	Businesswoman	Married	Primary
30	м	Motor vehicle mechanic	Married	Vocational
21	М	Motor vehicle mechanic	Single	Vocational
30	F	Salon Attendant	Separated	Secondary
19	F	House wife	Married	Primary
24	м	Motor vehicle mechanic	Single	Vocational
36	М	Driver	Married	Secondary
31	F	Shopkeeper	Separated	Primary
50	М	Petty trader	Married	Secondary
32	F	Shop keeper	Single	Primary
48	М	Casual worker	Married	Primary
33	F	Food business	Separated	Primary
50	F	Casual worker	Widowed	Primary
30	F	Fishing	Married	Secondary
40	F	Housework	Widowed	Primary
26	F	Student	Single(never married)	Vocational
39	Μ	Security officer	Married	Vocational
45	F	Petty Trader	Widowed	Primary
30	F	unemployed	Single	Primary

Demographic characteristic of the research volunteers

Mean age is 32.6 (33) years

Interview guide for volunteers (understanding the informed consent process in HIV clinical trials) revised in February 2012 after piloting

- Age:
- Gender:
- Trial:
- Duration in trial:

Research process in general

- What is important for you when participating in research?
- What reasons might lead you to want to take part in research?
- What information would you need to know to help you join research?
- How do you think this information should be provided?

Experience of the informed consent process

- What do you understand by the informed consent process (the process you go through from the time you are first contacted to join a trial until you complete the trial)?
- Do you think it is important for a volunteer to be given information before he/she accepts to be involved in a clinical trial? Explain
- Describe how you joined the trial? Tell me what happened
- How were you approached to join the trial?
- What information was shared to help you decide to join the study
- What information did you find useful and what was not so useful when you first joined the trial?

Decision making

- What are the important decisions when participating in a clinical trial ?(for you as an individual and for your family)
- How did you make the decision to join the trial
- Who influenced your decision? (Spouse, family /household member, how?
- What information have you acquired during the trial that is important for you, explain
- Do you think it is important to give/share with volunteer information about a trial before they join a clinical trial? Why /Explain
- What shows that someone has agreed to participate in a trial?
- Is there any significance in signing a consent form? Explain
- From your point of view how should consent be done?
- How can the person giving information about a trial know that a volunteer has understood the information, and has voluntarily agreed to participate in a trial

Relationship/interactions

How do you relate with the different key players in the trial (counselors, nurses, clinicians) who are involved in the informed consent process?

How do you think (nurses, counselors, clinicians) contribute to the informed consent process?

How do you influence the other key players in the informed consent process?

What is the role of trust in the informed consent process, how is trust practiced in the process?

Can you describe any challenges you have met during the informed consent process while involved in the trial?

Scenarios

1. A certain lady joined a clinical trial which was finding out about the safety of a certain drug. She was told that she should avoid getting pregnant while in the trial. However just a few months after she joined the trial she finds herself pregnant.

What do you think about that situation, what should she do?

Do you think she understood why she joined the study? Explain.

What would you advise her and the study staff who have been giving her information and taking her through the study procedures to do?

2. A man joined a twelve month follow up research study because he wanted to know his HIV sero status and after that he withdrew quietly from the study.

What do you think about the issue of the issue of withdrawing quietly from the study by this volunteer?

What should he have done in relation to the study since he knew it was going to be a twelve month study?

Do you think you would stay in a trial even when your initial aim has been achieved?

What factors would keep you in a trial even when you think your initial aim has been achieved?

3. Martha was very interested in joining an HIV clinical trial in their village because it was to do with preventing HIV infection using a microbicide gel (a gel that is inserted into the vagina to test whether it will prevent HIV from an HIV positive sexual partner).

What do you think are the decisions she has to make before enrolling, why?

Who may influence her decisions to join the trial?

What information will she require to know before she joins the trial?

4. Martha was later able to meet the research staff and they gave her a lot of information and asked her to sign a consent form. But she couldn't write so she was told to use a thumb print.

What do you think went through her mind at the point of signing the form?

If you were in her place, what would you have wanted to know at that time in relation to signing a form?

Is there any other way, one can give consent without having to sign a form? Describe

How can the researcher be sure you have accepted to participate in the study of your own free will?

Thank you very much for participating in this discussion.

Question guide for senior scientists and ethics committee in the study on understanding the informed consent process in HIV clinical trials in Uganda.

Topic one: Ethics in research

Discussion of history of ethics in research in Africa, and specific issues in Uganda (Probe how have these evolved, what debates, progress, current thrust and concerns, collaboration/partnerships,)

Discussion of informed consent as one of the principles in research ethics (Probe for main guidelines, importance of this principle, How has this principle been understood over the years, what has changed and why, what is the main aspect of this principle, opportunities and challenges in putting this principle in practice in Uganda context)

Discussion of main key players/actors in the informed consent process (probe for who and the roles attached and implications of their roles in practice)

Topic two: The informed consent process

Probe for meaning and interpretation of the informed consent process

Probe for understanding and how it is implemented (practice) in relation to standard guidelines

How informed consent is achieved in HIV clinical trials, what is critical in the process for scientists, study team, volunteers and ethics committee members

Topic three: Experience in the informed consent process

Discuss experience in being part of a trial and following up on the informed consent process.

Probe for specific role, how it works in practice in this trial, what relationships and interactions happen and their importance/contribution to the process.

Probe for involvement in information sharing, signing of consent, ensuring voluntariness.

Probe for significance of signing or thumb printing a consent form, what works out easily, what is challenging in the process.

Probe for suggestions and recommendations for participation and follow- up of the process in the local setting of the clinical trials.

Topic four: Decision Making

Probe for how decision making takes place in the informed consent process. Who makes what decisions and why

As a scientist/ethics committee member what decisions do you have to make to ensure the informed consent process is conducted appropriately, what decisions are crucial by other key players in your view? How are the interactions and relationships managed in the informed consent process?

Topic five: Interactions

Probe for power dynamics, who influences who during the process why, what drives the interactions with the other key actors in the informed consent process?

Do you influence the other actors in decision making, how and why? what are the benefits if any?

Discuss the role of trust, beliefs, values and gender in the informed consent process

Focus group discussion guide for trial volunteers in the study on understanding the informed consent process in HIV clinical trials in Uganda.

Ask for permission to record the discussion/interview, introduce study aim, give ground rules for the discussion and emphasise confidentiality.

Topic one: The informed consent process

What is important for you when participating in research? Probe for activities, information, relationships, procedures

Probe for meaning and interpretation of the informed consent process.

Probe for understanding and how the informed consent process is implemented (practice) in the trial they are involved in, what is the main aspect of the process and why?

What is your specific role in the process, what is critical in the process for scientists, study team, and you as volunteer/s

Topic two: Experience in the informed consent process

Probe for what they went through before consenting to join the trial (how was he/she approached, by who? what information was shared, what was useful and what was not so useful, who shared the information with you, what was clear at the start, what has become clear along the way and why

Discussion of other key players/actors (field study team-mobilisers, clinicians, counselors, interviewers,) in the informed consent process, probe for the role of each category and perceived contribution in the informed consent process)

Probe for relationships and interactions with other key players (research team, fellow volunteers, community leaders,) and their importance/contribution to the informed consent process. Which relationships have been very useful and why?

Probe for significance of signing or thumb printing a consent form, what happened, what was easy or challenging, what is the importance of signing a consent form. Suggestions of how they think consent should be done

Probe for suggestions and recommendations for participation in and follow- up of the informed consent process in the local setting of the clinical trials. What in the informed consent process would you want to see done differently from what you went through?

Topic three: Decision Making

Probe for how they made the decision to join the trial, who influenced their decisions and why (study team, spouse/ household member or any other person)

Probe for what they think are important decisions when participating in a clinical trial, for them and for their families/spouses.

Vignettes/scenarios for farther discussion

A certain lady joined a clinical trial which was finding out about the safety of a certain drug; she was told that she should avoid getting pregnant while in the trial, but just a few months in the trial she finds herself pregnant. What do you think about that situation, what should she do? Do you think she understood why she joined the study? Explain. What would you advise her and the study staff who have been giving her information and taking her through the study procedures?

A man joined a twelve month follow up research study because he wanted to know his HIV sero status and after that he withdrew quietly from the study, what do you think about this, what should he have done in relation to the study since he knew it was going to be a twelve month study, do you think you would stay in a trial even when your initial aim has been achieved? What factors would keep you in a trial even when you think your initial aim has been achieved?

Martha was very interested in joining an HIV clinical trial in their village, it was to do with preventing HIV infection using a microbicide gel, what do you think are the decisions she had to make before enrolling, why? Who may influence her decisions to join the trial?

Martha was later able to meet the research staff and they gave her a lot of information and asked her to sign a consent form but she couldn't write so she was told to use a thumb print, what do you think went through her mind at the point of signing the form? If you were the one, what would you have wanted to do at that time in relation to signing a form? Is there any other way, one can consent without having to sign a form? How can the researcher be sure you have accepted to participate in the study voluntarily?

Thank you very much for participating in this discussion/interview.

Question guide for field study team in the study on understanding the informed consent process in HIV clinical trials in Uganda.

Topic one: Ethics in research

Discussion of informed consent as one of the principles in research ethics (Probe for main guidelines, importance of this principle, How is this principle understood, what is the main aspect of this principle, opportunities and challenges in putting this principle in practice)

Discussion of main key players/actors in the informed consent process (probe for who and the roles attached and implications of their roles in practice)

Topic two: The informed consent process

Probe for meaning and interpretation of the informed consent process.

Probe for understanding and how it is implemented (practice), what is the main aspect of the process and why?

How informed consent is achieved in HIV clinical trials, what is your specific role in the process, what is critical in the process for scientists, study team, volunteers and ethics committee members.

Topic three: Experience in the informed consent process

Discuss your experience in being part of a trial and the informed consent process.

Probe for specific role, how it works in practice in the trial, you are involved with, what relationships and interactions happen and their importance/contribution to the process.

Probe for involvement in information sharing, signing of consent, ensuring comprehension and voluntariness of volunteers.

Probe for significance of signing or thumb printing a consent form, what works out easily, what is challenging in the process.

What have been the positive experiences in managing the informed consent process (communication, decision making, information sharing, follow up, and timing/duration of procedures).

Probe for challenges in the informed consent process, and how they have been managed.

Probe for lessons learnt in the informed consent process.

Probe for suggestions and recommendations for participation in and follow- up of the informed consent process in the local setting of the clinical trials. What would you do differently or in the same way in future and why?

Topic four: Decision Making

Probe for how decision making takes place in the informed consent process. Who makes what decisions and why?

As a field study team member , what decisions does he/she make to ensure the informed consent process is conducted appropriately, what decisions are crucial by other key players ?What interactions occur in the informed consent process among the key players? Probe about relationship with other team members, volunteers and community leaders. How are interactions and relationships managed in the informed consent process?

What is the role of trust in the informed consent process(for the study team, volunteers and the other key players)

Interview guide for spouses or household member of a volunteer in the study on understanding the informed consent process in HIV clinical trials in Uganda.

Topic: decision making

What do they think is important information for a volunteer being requested to participate in research?

Probe for what they think are important decisions when participating in a clinical trial, for them and for their spouses

Probe for how their spouses/ household members made the decision to join research/clinical trial, who influenced their decisions and why, what was their role in the decision made by volunteer to participate in research?

Probe for what they think are benefits and importance of spouse/ household member being involved in research. Probe for suggestions on how to ensure continued voluntary involvement of their spouses/household member in a clinical trial

Vignettes/scenarios for farther discussion

A certain lady joined a clinical trial which was finding out about the safety of a certain drug; she was told that she should avoid getting pregnant while in the trial, but just a few months in the trial she finds herself pregnant. What do you think about that situation, what should she do? Do you think she understood why she joined the study? Explain. What would you advise her and the study staff who have been giving her information and taking her through the study procedures?

A man joined a twelve month follow up research study because he wanted to know his HIV sero status and after that he withdrew quietly from the study, what do you think about this, what should he have done in relation to the study since he knew it was going to be a twelve month study, do you think you would stay in a trial even when your initial aim has been achieved? What factors would keep you in a trial even when you think your initial aim has been achieved?

Martha was very interested in joining an HIV clinical trial in their village, it was to do with preventing HIV infection using a microbicide gel, what do you think are the decisions she had to make before enrolling, why? Who may influence her decisions to join the trial?

Martha was later able to meet the research staff and they gave her a lot of information and asked her to sign a consent form but she couldn't write so she was told to use a thumb print, what do you think went through her mind at the point of signing the form? If you were the one, what would you have wanted to do at that time in relation to signing a form? Is there any other way, one can consent without having to sign a form? How can the researcher be sure you have accepted to participate in the study voluntarily?

Thank you very much for participating in this interview.

Focus group discussion guide for community advisors and leaders in the study on understanding the informed consent process in HIV clinical trials in Uganda.

Welcome and Introduction of all,

Ask for permission to record the discussion, introduce study aim, give ground rules for the discussion and emphasise confidentiality.

Topic one: The informed consent process

This topic is a discussion about the informed consent process.

Probe for meaning and interpretation of the informed consent process.

Probe for understanding and how it is implemented (practice), what is the main aspect of the process and why?

How informed consent achieved in HIV clinical trials, what is your specific role in the process, what is critical in the process for scientists, study team, volunteers and ethics committee members.

Topic two: Experience in the informed consent process

Probe for specific role for community leaders in the informed consent process, how it works in practice in the trial they are involved in,

Discussion of other key players/actors in the informed consent process (probe for who and the roles attached and implications of their roles in practice)

Probe for relationships and interactions that take place and their importance/contribution to the informed consent process.

Probe for involvement in follow up of study information as shared by the research team and how they think voluntariness is ensured

Probe for significance of signing or thumb printing a consent form

Probe for positive experiences in following up the informed consent process (communication, decision making, information sharing, follow up, and timing/duration of procedures)

Probe for challenges in the informed consent process from their point of view

Probe for suggestions and recommendations for participation in and follow- up of the informed consent process in the local setting of the clinical trials.
Topic three: Decision Making

Probe for what decisions community leaders/advisors make following up clinical trials and the informed consent process. Why?

Probe for what they think are important decisions when conducting a trial, for them and for other key players such as research team, volunteers and volunteer families/household.

Vignettes/scenarios for farther discussion

A certain lady joined a clinical trial which was finding out about the safety of a certain drug; she was told that she should avoid getting pregnant while in the trial, but just a few months in the trial she finds herself pregnant. What do you think about that situation, what should she do? Do you think she understood why she joined the study? Explain. What would you advise her and the study staff who have been giving her information and taking her through the study procedures?

A man joined a twelve month follow up research study because he wanted to know his HIV sero status and after that he withdrew quietly from the study, what do you think about this, what should he have done in relation to the study since he knew it was going to be a twelve month study, do you think you would stay in a trial even when your initial aim has been achieved? What factors would keep you in a trial even when you think your initial aim has been achieved?

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Martha was later able to meet the research staff and they gave her a lot of information and asked her to sign a consent form but she couldn't write so she was told to use a thumb print, what do you think went through her mind at the point of signing the form? If you were the one, what would you have wanted to do at that time in relation to signing a form? is there any other way, one can consent without having to sign a form? How can the researcher be sure you have accepted to participate in the study voluntarily?

Thank you very much for participating in this discussion.

Second interview guide for volunteers

1. How have you been since the last time we met? (probe health if not mentioned)

2. Tell me what has happened today at the clinic from the time you came in?

3. Who invited you to come for this visit? Explain

4. Have you had any information in the community concerning the research you are involved in? (ask about any rumours)

5. How have your interactions been with the study staff to day, what have you gone through, please explain

6. What is the value of the clinical research you are involved in?

7. How do you think the research will help in future?

8. Add any issues that were not exhausted in interview one

Third interview with volunteers

1. Confirm age, education level and occupation of volunteer

2. What do you have to say about the informed consent process according to today's visit?

3. Why are you participating in the clinical trial (ask about objectives and aim of trial, values, interests, preferences)

4. How long is it before you complete your taking part in the clinical trial?

5. What do you expect at the end of the trial? What are you looking forward to?

6. What is the reason you have kept coming for this long time? What keeps people/ volunteers interested in research?

7. What do you think of people who are continually involved in research, move from one research to another? What motivates you to continue in research?

8. Do you have additional information that you want to share about the informed consent process?



Uganda Pational Council for Science and Technology (Established by Act of Parliament of the Republic of Uganda)

Our Ref: SS 2673

12th March 2013

Mrs. Agnes Ssali MRC/UVRI Uganda Research Unit on AIDS Uganda Virus Research Institute Entebbe

Dear Mrs. Ssali,

RE: RESEARCH PROJECT, "UNDERSTANDING THE INFORMED CONSENT PROCESS IN HIV CLINICAL TRIALS IN UGANDA: A CASE STUDY"

This is to inform you that on 6th March 2013, Uganda National Council for Science and Technology (UNCST) reviewed and approved your request to continue with the above study.

The approval will expire on 6th March 2014. If however, it is necessary to continue with the study beyond the expiry date, a request for continuation should be made to the Executive Secretary, UNCST.

Yours sincerely,

Jane Nabbuto for: Executive Secretary UGANDA NATIONAL COUNCIL FOR SCIENCE AND TECHNOLOGY

LOCATION/CORRESPONDENCE

Plot 6 Kimera Road, Ntinda P. O. Box 6884 KAMPALA, UGANDA COMMUNICATION

TEL: (256) 414 705500 FAX: (256) 414-234579 EMAIL: info@unest.go.ug WEBSITE: http://www.unest.go.ug



Uganda Virus Research Institute

Plot 51-59, Nakiwogo Road, Entebbe P.O. Box 49, Entebbe-Uganda Tel. *256 414 320 385 / 6 Fax: *256 414 320 483 Email: directoruvri@uvri.go.ug



Our Ref: GC/127/12/11/06

Your Ref:

12th November 2012

Mrs. Agnes Nanfuka Ssali,

RE: UVRI SEC review of progress report titled "Understanding the informed consent process to HIV Clinical trials in Uganda: A case study."

Thank you for submitting the progress report dated 12th October 2012 for the above study to the UVRI Science and Ethics Committee (SEC).

This is to inform you that after review of your report, UVRI SEC continuation approval has been granted for you to continue with this study for another one year up to 14th October 2013.

At that time, SEC would expect you to submit a progress report and request for renewal, prior to the expiry date, to allow timely review.

Yours sincerely,

Dr. Ben Kikaire For Chair UVRI SEC

C.C Secretary, UVRI SEC

Amawulire eri abaneetaba mu kunoonyereza , "okutegeera omutendera gw'okukiriza okwenyigira mu kunoonyereza ku kawuka akaleeta siliimu nga kukolebwa mu Uganda".

Anoonyereza: Agnes Nanfuka Ssali (muyizi mu yunivasite ya East Anglia mu Bungereza)

Abalondoola engeri gye naakolamu okunoonyereza: Pro. Janet Seeley ne Dr. Fiona Poland (okuva mu kitongole kya MRC ne yunivasite ya Anglia mu Bungereza)

Enyanjula

Nkulamusiza! Okunoonyereza kwe njagala okukola kutunuulidde omutendera omuntu mwayita okukiriza okwetaba mu kunoonyereza mu kifo okunoonyereza n'okugezesa ku kawuka akaleeta siliimu gye kukolebwa.

Nkusaba owulirize ebikwata ku kunoonyereza kuno nga mbi kusomera oba oyinza okubyesomera ku lulwo okusobola okubitegeera obulungi. Oli wa ddembe okubuuza ebibuuzo singa waliwo ekitategeerekese.

Lwaki okunoonyereza kuno kukolebwa?

Okukiriza okwetaba mu kunoonyereza na ddala nga kukwata ku kugezesa, kiba kikulu olw'ensonga nti abantu okwetaba mu bateekeddwa okuba nga bafunye amawulire gona agakwata ku kunoonyereza okwo. Era balina okutegeera obulungi olwo ne bewayo okwetabamu. Omutendera gw'okukiriza okwetaba mu kunoonyereza nga kulimu n'okugezesa, kuyinza okwenyigiramu abantu okusuka ku ba biri n'okusuka ku mulundi ogumu ng'ekigendererwa ye nkola ennungamu mu kunoonyereza nga n'abenyigiddemu besaliddewo awatali kukakibwa.

N'olwekyo, okunoonyereza kuno kuluubirira okumanyisibwa okuva mu bantu ab'enjawulo (betuyise abakola ku bintu eby'enjawulo) nga benyigira mu mutendera ogw'okukirizisa omuntu okwetaba mu kunoonyereza nga bano mwe muli: banasayaansi, abakola ku kunoonyereza mu byalo, abaakakiiko akakwasisa empisa mu kunoonyereza, abawi b'amagezi mu bitundu okunoonyereza gye kukolebwa n'abetaba mu kunoonyereza, okwetaba mu konoonyereza kitegeeza ki gye bali era ne bye bayiseemu nga bikwata ku mutendera ogw'okukiriza okwetaba mu kunoonyereza wano mu Uganda. Amawulire aganaakunganyizibwa gajja kuwa ekifaananyi ku ngeri ebintu gyebikolebwabwamu wano mu Uganda okusinziira ku mutindo oguliwo kati ogugobererwa mu nsi yonna na wano mu gwanga era n'engeri amateeka agagobererwa bwe gayinza okukozesebwa mu mbeera ya wano okugezesa wekukolebwa. Okukunganya amawulire mu kunoonyereza kuno kujja kumala emyezi nga kumi n'ebiri (12).

Lwaki olondeddwa okwetaba mu kunoonyereza kuno?

Olondeddwa okwetaba mu kunoonyereza kuno olw'ensonga nti oli mu kunoonyereza nga kulimu n'okugezesa nga nakyewa. Omulimu gw'okola mu mutendera gw'okukiriza okwetaba mu kunoonyereza mukulu nyo mu kugezesa era y'ensonga lwaki olondeddwa okuwa ebirowoozo byo na biki bye wayitamu.



Nja kusaba omuwendo gwa bantu 45 okwetaba mu kubuuzibwa ebibuuzo n'okukubaganya ebirowoozo okwawamu nga kwetabiddwamu abakola ku bintu eby'enjawulo. Nja kukusaba okwetaba mu kubuuzibwa ebibuuzo bya kinoomu emirundi esatu mu bbanga lya mwaka gumu nga twongera okulondoola omutendera gw'okukiriza okwetaba mu kunoonyereza okulimu n'okugezesa kwewetabyemu.

Kiki ekinabaawo bw'osalawo okwetabamu?

Bw'onakiriza okwetaba mu kunoonyereza kuno, nja ku kubuuzayo ebibuuzo nga bikwata ku mutendera omuntu gwayitamu okutuuka ku kkukiriza okwetaba nokumbera mu kunoonyereza ebbaga lyona era nkusabe owe n'ebirowoozo ku mutendera ogwo mu ku kubaganya ebirowoozo mu bulambulukufu. Ebibuuzo bino bijja kutwala eddakiika 45-60. Ebibuuzo eby'engeri eno bijja kukolebwa emirundi esatu mu bbanga ery'emyezi e 12. Ebibuuzo bino bijja kukwatibwa ku katambi okusobola okukendeeza ku budde era n'okukakasa nti tewali mawulire gonna gasubwa ng'era gasobola okuddamu ne gawulirizibwa mu biseera by'okugekeneenya. Era nja kukusaba wegate ne mu kukubaganya ebirowoozo okwa wamu n'abantu abalala nga mukaaga nga nabo betabye mu kunoonyereza. Okukubaganya ebirowoozo bino nakwo kujja kukwatibwa ku katambi. Amawulire gonna aganaakwatibwa ku butambi tegajja kusiimulwako okuk<u>t</u>uu<u>k</u>ta ng'okunoonyereza kuwedde mu myaka ebiri oba esatu. Singa oba okkirizza okwetabamu, nja ku kusaba omwagalwawo oba omuntu omulala yenna mu makaago abuuzibwe ebibuuzo nga bikwata ku mutendera omuntu gwayitamu alyoke akirize okwetaba mu kunoonyereza.

Nsobola okugaana okwetaba mu kunoonyereza kuno oba mu kintu kyonna ekikwata ku kunoonyereza kuno?

Kiri gy'oli okusalawo okwetaba mu kunoonyereza kuno oba nedda. Era osobola okulekerawo okwetaba mu kunoonyereza kuno w'oyagalidde. Bw'osalawo obutetaba mu kunoonyereza kuno, tekijja kukosa kwetabamukwo mu kunoonyereza kulala kwe wenyigiddemu era n'okuganyulwa kw'ofuna okuva ku ddwaliro awali okunoonyereza.

Kabi ki akayinza okuva mu kwetaba mu kunoonyereza kuno?

Obuzibu butono nyo obuyinza okuva mu kwetaba mu kunoonyereza kuno naye buyinza okubaawo nga buva ku mawulire g'onawayo mu ku buuzibwa ebibuuzo n'okukubaganya ebirowoozo okwa wamu n'abantu abalala nga by'ogeddwako awalala mwabo abatenyigidde mu kunoonyereza kuno. Erinnyalyo terijja kuteekebwa ku kiwandiiko kyonna okujjako enaamba eyo yokka enakuwebwa. Abanetaba mu kukubaganya ebirowoozo okwa wamu bajja kusabibwa obutoogera ku bikubaganyiziddwako birowoozo n'abantu abalala abatali mu kunoonyereza kuno. Amawulire gonna aganakunganyizibwa, gajja kukuumibwa nga ga kyama awatali kutekebwako linnya lya muntu lyonna.

Waliwo engeri yonna gye naaganyulwamu nga netabye mu kunoonyereza kuno?

Gwe ng'omuntu, oyinza obutaganyulwawo. Naye ng' amawulire aganaakunganyizibwa gajja kweyambisibwa okunyonyoka abantu bwe bategeera era ne bye balowooza ku mutendera gw'okukiriza

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okwetaba mu kunoonyereza. Kino kiyinza n'okwongera okutangaaza n'okutegera omutendera ogwo era nga kino kya mugaso mu kuteekateeka n'engeri esaniidde okukozesebwa okusinziira ku mbeera wano mu Uganda nga bategeka okunoonyereza okulimu n'okugezesa mu biseera by'omumaaso.

Amawulire gempaayo mu kubuuzibwa ebibuuzo ganakuumibwa nga gakyama?

Buli ekinaayogerwako kijja kukuumibwa nga kya kyama. Ebinaaba bivudde mu kunoonyereza bijja kwanjulwa mu kifaananyi ekikwata ku mutendera ogw'okukiriza okwetaba mu kunoonyereza so ssi ku bantu abetabye mu kunoonyereza.

Ku nkomerero y'okukunganya amawulire, ebinaaba bivuddemu mu bufunze bijja kwa njulwa eri abo abanaaba betabye mu kunoonyereza. Ku nkomerero y'okunoonyereza kwange kuno, amawulire gona gajja kuwandiikibwa mu bitabo ebikwata ku by'okunoonyereza okuliwo kati ku mitendera omuntu gyayitamu okutuuka lw'asalawo okwetaba nokumalako ebbaga mu kunoonyereza.

Ani gwe nyinza okutuukirira singa nina ekibuuzo?

Nalyagadde okuddamu ebibuuzo byamwe byonna kati, naye singa ofuna ekibuuzo kyonna gye bujjako mu maaso, oyinza okunkubira ku naamba eno ey'essimu 0772 454775. Era oyinza okukubira omu kubagoberera engeri gye nkolamu okunoonyereza kuno ayitibwa Prof. Janet Seeley, owa MRC/UVRI Uganda Research Unit on AIDS e Entebbe, ku ssimu naamba 0414770400.

Singa ofuna okwemulugunya kwonna nga kukwata ku ddemberyo mu kunoonyereza kuno, tukusaba otuukirire akulira akakiiko ka UVRI Science and Ethics Committee, ku UVRI P. O. Box 49, Entebbe ku ssimu 0414 321962.

Ekitongole kya Medical Research Council/UVRI Uganda Research Unit on AIDS kye kitaddemu sente okulaba ng'okunoonyereza kuno kukolebwa.

Bw'oba oyagala okwetaba mu knoonyereza kuno, nali yagadde ojjuze foomu okukakasa okusalawokwo.



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Kala ankulu	ingo ku Veo ob	a Nedda
Kola enkult	ingo ku tee ob	aneuud
Nsomye oba baansomede olulapula omuli amawulire ku kunoonyereza	Yee	Nedda
okutegeera omutendera omuntu gwa yitamu nga tanakiriza kwetaba mu		
kunoonyereza		
Nzikiriza okwetaba mu kubuzibwa e bibuuzo	Yee	Nedda
Nzikiriza okwetaba mu kukubaganya ebirowoozo	Yee .	Nedda
Okwetabamu kwange kwa kye yagalire era ndi wa ddembe okuva mu		
kunoonyereza wenjagalidde, awatali kuwa nsonga zonna era nga kino tekijja	Yee	Nedda
kukosa kwetabamu kwange mu kugezesa bikwata ku bulamu		
Nkuwa olukusa okujja mu bimu ku bibuuzo ebya mbuuzibwa amawulire	Yee	Nedda
gakozesebwe ku kigendererwa ky'okunoonyereza (nga mw'otwalidde okug	gafulumya	
mu biwandiiko ne alipoota) bwe biba nga tebiraga nti bikwata ku nze		
Erinnya ly'eyetabyemu Ennaku z'omwezi On	nukono	
	•.	
Erinnya ly'oyo ateekesezaako omukono		
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ETHICS COMMITTEE		

Information sheet for the field study team members in the study "understanding the informed consent process in HIV clinical trials in Uganda: A case study".

Researcher: Agnes Nanfuka Ssali (student at University of East Anglia, UK)

Supervisors: Prof .Janet Seeley and Dr. Fiona Poland (MRC and University of East Anglia, UK)

Introduction

Greetings! The research I want to carry out is looking at the informed consent process in a research setting of HIV clinical trials.

Please listen to the details of this research as I read it out or you can read it on your own to understand it. You can ask any questions if anything is not clear.

Why is the research being done?

Informed consent in clinical trials is considered crucial because people must only be involved in any form of research after they have been given all the information about it. They then must understand and voluntarily agree to participate. The process of informed consent in clinical trials may involve more than two people and more than one event with the aim of ensuring proper conduct of a trial with voluntary participation of those involved.

This research is therefore interested in learning from all the different people (termed as key players) involved in the informed consent process who may include: scientists, field study team members, ethics committee members, community advisors and volunteers in the trials, what they understand about the process and how they experience it in the Uganda context. Data collected will provide information on how appropriate or applicable the current international and national standardized informed consent guidelines for conducting research are in the Uganda context and how best the guidelines can be tailored to the local context in which the clinical trials are taking place. The research will take at least 12 months of data collection.

Why have you been chosen to take part in this research?

You have been selected to participate in this research because you are already involved in a clinical trial as a member of the study team. The role you play in the informed consent process is critical to the trial and therefore you have been selected purposely to give your understanding and experiences.

I will be asking a total of about 45 people to participate in interviews and focus group discussions who will include the different key players.

What will happen to you when you decide to take part?

If you agree to take part in this research, I will ask you some questions about the informed consent process and request for your suggestions about the process in the Uganda context in an in-depth



interview. The interview will take between 45-60 minutes. The discussion will be tape recorded to save on time during the discussion and to ensure information is not missed and can be referred to when analyzing the data. The recorded information will not be deleted until the study is completed in 2-3 years.

Can I refuse to be in this research or refuse to participate in any aspect of it?

It is up to you whether or not to take part in this research. You can also stop being in this research any time you want. If you choose not to participate in this research, this will not interfere with your current role as a study team member in the clinical trial you are involved in.

What risks can I expect from being in this research?

The risk in this research is minimal but can only come as a result of information you give being shared out to others not directly involved in this research and attaching your name to information collected with your names. This is not going to happen, all the information will be kept confidential without attaching respondent's names.

Are there benefits for me for being in the research?

As an individual there are no direct benefits. However the information collected will be helpful in understanding what people understand and think about the informed consent process. This may contribute to better understanding of the informed consent process and will be useful in planning and tailoring informed consent appropriately in the Uganda context while planning future trials.

Will the information I give during the interview be kept confidential?

Everything we talk about will be kept confidential. The findings of the research will be shared in relation to what is reported about the informed consent process and not about the individuals involved in the research.

At the end of data collection, a brief summary of the preliminary findings will be shared with those who would have participated in the research. At the completion of my study this information may be written in research journals to contribute to current research work on the informed consent process.

Whom can I contact if I have a question?

I would like to answer all your questions now, but if you have questions in future you can contact me at the following number 0772 454775. You can also contact my supervisor Professor Janet Seeley at the MRC/UVRI Uganda Research Unit on AIDS, phone number 041770400.

If you have concerns about your rights in this research, please contact the chairman of the UVRI Science and Ethics committee, UVRI, P.O. Box 49, Entebbe. Contact phone number is 0414 321962.

The research is sponsored by Medical research Council/UVRI Uganda Research Unit on AIDS.

Field study team



If you are willing to participate in this research, I would like you to complete a consent form to confirm your agreement. SRESEARCH INSTITU SCIENCE & ETHICS COMMITTEE 2 0 JAN 2012 BOX 49 ENTER Field study team Page 3

Consent form

Consent form for the research	on understanding the	e informed consent prod	cess in HIV cli	nical trials
			Circle Yes	or NO
I have read or had read to me	the information sheet	of the research on		
understanding the Informed co	onsent process		Yes	No
I agree to participate in the in-	depth interview		Yes	No
My participation is voluntary a	nd I am free to withdra	aw from the research,		
any time, without giving reaso	ns and this will not affe	ect my role		
in the clinical trial			Yes	No
I give permission for short ext	racts from my interviev	w to be used for		
Research purposes (including	publications and repor	ts), so long as		
they are strictly anonymous			Yes	No
Name of participant	Date	Signature		
Name of person taking				6
Consent				
Field study team	(5)	URUS RESEARCH INSTITU SCIENCE & ETHICS COMMITTEE		Page 4

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BOX 49 ENTEBBE (U)

Information sheet for the ethics committee members and senior scientists' in the study "understanding the informed consent process in HIV clinical trials in Uganda: A case study".

Researcher: Agnes Nanfuka Ssali (student at University of East Anglia, UK)

Supervisors: Prof Janet Seeley and Dr. Fiona Poland (MRC and University of East Anglia, UK)

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Why have you been chosen to take part in this research?

You have been selected to participate in this research because you are already involved in a clinical trial as a senior researcher who is overseeing a trial/ethics committee member who is involved in approving and monitoring of research studies.

I will be asking a total of about 45 people to participate in interviews and focus group discussions who will include the different key players.

What will happen to you when you decide to take part?

If you agree to take part in this research, I will ask you some questions about the informed consent process and request for your suggestions about the process in the Uganda context in an in-depth interview. The interview will take between 45-60 minutes. The discussion will be tape recorded to save



on time during the discussion and to ensure information is not missed and can be referred to when analyzing the data.

The recorded information will not be deleted until the study is completed in 2-3 years.

Can I refuse to be in this research or refuse to participate in any aspect of it?

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The research is sponsored by Medical research Council/UVRI Uganda Research Unit on AIDS.

If you are willing to participate in this study, I would like you to complete a consent form to confirm your agreement.



Consent form

			Circle Yes	or NO
have read or had read to me	the information sheet o	f the research on		
inderstanding the Informed c	onsent process		Yes	No
agree to participate in the in	terview		Yes	No
My participation is voluntary a	and I am free to withdra	w from the research,		
any time, without giving reaso	ons and this will not affe	ct my role		
in the clinical trial			Yes	No
give permission for short ext	racts from my interview	to be used for		
Research purposes (including	publications and report:	s), so long as		
hey are strictly anonymous			Yes	No
Name of participant	Date	Signature		
Name of person taking				
Consent				
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Amawulire eri abagalwa/ab'omu maka g'abaneetaba mu kunoonyereza , "okutegeera omutendera gw'okukiriza okwenyigira mu kunoonyereza ku kawuka akaleeta siliimu nga kukolebwa mu Uganda.

Anoonyereza: Agnes Nanfuka Ssali (muyizi mu yunivasite ya East Anglia mu Bungereza)

Abalondoola engeri gye naakolamu okunoonyereza: Pro. Janet Seeley ne Dr. Fiona Poland (okuva mu kitongole kya MRC ne yunivasite ya Anglia mu Bungereza)

Enyanjula

Nkulamusiza! Okunoonyereza kwe njagala okukola kutunuulidde omutendera omuntu mwayita okukiriza okwetaba mu kunoonyereza mu kifo okunoonyereza n'okugezesa ku kawuka akaleeta siliimu gye kukolebwa.

Nkusaba owulirize ebikwata ku kunoonyereza kuno nga mbi kusomera oba oyinza okubyesomera ku lulwo okusobola okubitegeera obulungi. Oli wa ddembe okubuuza ebibuuzo singa waliwo ekitategeerekese.

Lwaki okunoonyereza kuno kukolebwa?

Okukiriza okwetaba mu kunoonyereza na ddala nga bikwata ku kugezesa, kuba kukulu olw'ensonga nti abantu okwetaba mu bateekeddwa okuba nga bafunye amawulire gona agakwata ku kunoonyereza okwo. Era balina okutegeera obulungi olwo ne bewayo okwetabamu. Omutendera gw'okukiriza okwetaba mu kunoonyereza nga kulimu n'okugezesa, kuyinza okunyigiramu abantu okusuka ku ba biri n'okusuka ku mulundi ogumu ng'ekigendererwa ye nkola ennungamu mu kunoonyereza nga n'abenyigiddemu besaliddewo awatali kukakibwa.

N'olwekyo, okunoonyereza kuno kuluubirira okumanyisibwa okuva mu bantu ab'enjawulo (betuyise abakola ku bintu eby'enjawulo) nga benyigira mu mutendera ogw'okukirizisa omuntu okwetaba mu kunoonyereza nga bano mwe muli: banasayaansi, abakola ku kunoonyereza mu byalo, abaakakiiko akawasisa empisa mu kunoonyereza, abawi b'amagezi mu bitundu okunoonyereza gye kukolebwa n'abetaba mu kunoonyereza, okwetaba mu konoonyereza kitegeeza ki gye bali era ne bye bayiseemu nga nga bikwata ku mutendera ogw'okukiriza okwetaba mu kunoonyereza wano mu Uganda. Amawulire aganaakunganyizibwa gajja kuwa ekifaananyi ku ddaala n'omutindo e gwanga Uganda kweriri okusinziira ku mutindo oguliwo kati ogugobererwa mu nsi yonna na wano mu gwanga era n'engeri amateeka agagobererwa bwe gayinza okukozesebwa mu mbeera ya wano okugezesa wekukolebwa. Okukunganya amawulire mu kunoonyereza kuno kujja kumala emyezi nga kumi n'ebiri (12).

Lwaki olondeddwa okwetaba mu kunoonyereza kuno?

Olondeddwa okwetaba mu kunoonyereza kuno olw'ensonga nti oli mwagalwa w'oyo eyenyigidde mu kunoonyereza nga kulimu n'okugezesa nga nakyewa. Omulimu gw'okola ng'omwagalwa weyenyigidde

Abaagalwa	QUS RESEARCH INSTITUTE	Page 1
	ETHICS COMMITTEE	
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mu mutendera gw'okukiriza okwetaba mu kunoonyereza mukulu nyo mu kugezesa era y'ensonga lwaki olondeddwa okuwa ebirowoozo byo na biki bye wayitamu.

Nja kusaba omuwendo gwa bantu 45 okwetaba mu kubuuzibwa ebibuuzo n'okukubaganya ebirowoozo okwawau nga kwetabiddwamu abakola ku bintu eby'enjawulo.

Kiki ekinabaawo bw'osalawo okwetabamu?

Bw'onakiriza okwetaba mu kunoonyereza kuno, nja ku kubuuzayo ebibuuzo bitono nga bikwata ku mwagalwawo okwetaba mu kunoonyereza. Ebibuuzo bijja kutwala eddakiika nga 30 oba 45.

Ebibuuzo bino bijja kukwatibwa ku katambi okusobola okukendeeza ku budde era n'okukakasa nti tewali mawulire gonna gasubwa ng'era gasobola okuddamu ne gawulirizibwa mu biseera by'okugekeneenya. Amawulire gonna aganaakwatibwa ku butambi tegajja kusiimulwako okukuuta ng'okunoonyereza kuwedde mu myaka ebiri oba esatu.

Nsobola okugaana okwetaba mu kunoonyereza kuno oba mu kintu kyonna ekikwata ku kunoonyereza kuno?

Kiri gy'oli okusalawo okwetaba mu kunoonyereza kuno oba nedda. Era osobola okulekerawo okwetaba mu kunoonyereza kuno w'oyagalidde. Bw'osalawo obutetaba mu kunoonyereza kuno, tekijja kukosa mulimogwo ng'omwagalwa w'oyo eyeyabye mu kunoonyereza era n'okuganyulwa kw'ofuna okuva ku ddwaliro awali okunoonyereza.

Kabi ki akayinza okuva mu kwetaba mu kunoonyereza kuno?

Obuzibu butono nyo naye buyinza okubaawo nga buva ku mawulire g'onawayo mu ku buuzibwa ebibuuzo n'okukubaganya ebirowoozo okwa wamu n'abantu abalala nga by'ogeddwako awalala mwabo abatenyigidde mu kunoonyereza kuno. Erinnyalyo terijja kuteekebwa ku kiwandiiko kyonna. Amawulire gonna aganakunganyizibwa, gajja kukuumibwa nga ga kyama awatali kutekebako linnya lya muntu lyonna.

Waliwo engeri yonna gye naaganyulwamu nga netabye mu kunoonyereza kuno?

Gwe ng'omuntu, oyinza obutaganyulwawo. Naye ng' amawulire aganaakunganyizibwa gajja kweyambisibwa okunyonyoka abantu bwe bategeera era ne bye balowooza ku mutendera gw'okukiriza okwetaba mu kunoonyereza. Kino kiyinza n'okwongera okutangaaza n'okuteera omutendera ogwo era nga kino kya mugaso mu kuteekateeka n'engeri esaniidde okukozesebwa okusinziira ku mbeera wano mu Uganda nga bategeka okunoonyereza okulimu n'okugezesa mu biseera by'omumaaso.

Amawulire gempaayo mu kubuuzibwa ebibuuzo ganakuumibwa nga gakyama?

Buli ekinaayogerwako kijja kukuumibwa nga kya kyama. Ebinaaba bivudde mu kunoonyereza bijja kwanjulwa mu kifaananyi ekikwata ku mutendera ogw'okukiriza okwetba mu kunoonyereza so ssi ku bantu abetabye mu kunoonyereza.

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Ku nkomerero y'okukunganya amawulire, ebinaaba bivuddemu mu bufunze bijja kwa njulwa eri abo abanaaba betabye mu kunoonyereza. Ku nkomerero y'okunoonyereza kwange kuno, amawulire gona gajja kuandiikibwa mu bitabo ebikwata ku by'okunoonyereza okuliwo kati ku mitendera omuntu gyayitamu okutuuka lw'asalawo okwetaba mu kunoonyereza.

Ani gwe nyinza okutuukirira singa nina ekibuuzo?

Abaagalwa

Nalyagadde okuddamu ebibuuzo byamwe byonna kati, naye singa ofuna ekibuuzo kyonna gye bujjako mu maaso, oyinza okunkubira ku naamba eno ey'essimu 0772 454775. Era oyinza okukubira omu kubagoberera engeri gye nkolamu okunoonyereza kuno ayitibwa Prof. Janet Seeley, owa MRC/UVRI Uganda Research Unit on AIDS e Entebbe, ku ssimu naamba 0414770400.

Singa ofuna okwemulugunya kwonna nga kukwata ku ddemberyo mu kunoonyereza kuno, tukusaba otuukirire akulira akakiiko ka UVRI Science and Ethics Committee, ku UVRI P. O. Box 49, Entebbe ku ssimu 0414 321962.

Ekitongole kya Medical Research Council/UVRI Uganda Research Unit on AIDS kye kitaddemu sente okulaba ng'okunoonyereza kuno kukolebwa.

Bw'oba oyagala okwetaba mu knoonyereza kuno, nail yagadde ojjuze okekakasa okusalawokwo.

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Consent form

Foomu ey'okukiriza okunoonyereza ku kutegeera omutendera gw'okukiriza okwenyigira mu kunoonyereza ku kawuka akaleeta siliimu nga kukolebwa mu Uganda

	Kola enkul	ungo ku Yee ob	a Nedda
Nsomye oba baansomede olula	pula omuli amawulire ku kunoonyereza	Yee	Nedda
okutegeera omutendera omun	tu gwa yitamu nga tanakiriza kwetaba mu		
kunoonyereza			
Nzikiriza okwetaba mu kubuzib	wa e bibuuzo	Yee	Nedda
Okwetabamu kwange kwa kye	yagalire era ndi wa ddembe okuva mu		
kunoonyereza wenjagalidde, av	vatali kuwa nsonga zonna era nga kino tekijj	a Yee	Nedda
kukosa kwetabamu kwange m	u kugezesa bikwata ku bulamu		
Nkuwa olukusa okujja mu bimu	ku bibuuzo ebya mbuuzibwa amawulire	Yee	Nedda
gakozesebwe ku kigendererwa	ky'okunoonyereza (nga mw'otwalidde okuį	gafulumya	
mu biwandiiko ne alipoota) bw	re biba nga tebiraga nti bikwata ku nze		
Erinnya ly'eyetabyemu	Ennaku z'omwezi On	nukono	
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Amawulire eri abagalwa/ab'omu maka g'abaneetaba mu kunoonyereza , "okutegeera omutendera gw'okukiriza okwenyigira mu kunoonyereza ku kawuka akaleeta siliimu nga kukolebwa mu Uganda.

Anoonyereza: Agnes Nanfuka Ssali (muyizi mu yunivasite ya East Anglia mu Bungereza)

Abalondoola engeri gye naakolamu okunoonyereza: Pro. Janet Seeley ne Dr. Fiona Poland (okuva mu kitongole kya MRC ne yunivasite ya Anglia mu Bungereza)

Enyanjula

Nkulamusiza! Okunoonyereza kwe njagala okukola kutunuulidde omutendera omuntu mwayita okukiriza okwetaba mu kunoonyereza mu kifo okunoonyereza n'okugezesa ku kawuka akaleeta siliimu gye kukolebwa.

Nkusaba owulirize ebikwata ku kunoonyereza kuno nga mbi kusomera oba oyinza okubyesomera ku lulwo okusobola okubitegeera obulungi. Oli wa ddembe okubuuza ebibuuzo singa waliwo ekitategeerekese.

Lwaki okunoonyereza kuno kukolebwa?

Okukiriza okwetaba mu kunoonyereza na ddala nga bikwata ku kugezesa, kuba kukulu olw'ensonga nti abantu okwetaba mu bateekeddwa okuba nga bafunye amawulire gona agakwata ku kunoonyereza okwo. Era balina okutegeera obulungi olwo ne bewayo okwetabamu. Omutendera gw'okukiriza okwetaba mu kunoonyereza nga kulimu n'okugezesa, kuyinza okunyigiramu abantu okusuka ku ba biri n'okusuka ku mulundi ogumu ng'ekigendererwa ye nkola ennungamu mu kunoonyereza nga n'abenyigiddemu besaliddewo awatali kukakibwa.

N'olwekyo, okunoonyereza kuno kuluubirira okumanyisibwa okuva mu bantu ab'enjawulo (betuyise abakola ku bintu eby'enjawulo) nga benyigira mu mutendera ogw'okukirizisa omuntu okwetaba mu kunoonyereza nga bano mwe muli: banasayaansi, abakola ku kunoonyereza mu byalo, abaakakiiko akawasisa empisa mu kunoonyereza, abawi b'amagezi mu bitundu okunoonyereza gye kukolebwa n'abetaba mu kunoonyereza, okwetaba mu konoonyereza kitegeeza ki gye bali era ne bye bayiseemu nga nga bikwata ku mutendera ogw'okukiriza okwetaba mu kunoonyereza wano mu Uganda. Amawulire aganaakunganyizibwa gajja kuwa ekifaananyi ku ddaala n'omutindo e gwanga Uganda kweriri okusinziira ku mutindo oguliwo kati ogugobererwa mu nsi yonna na wano mu gwanga era n'engeri amateeka agagobererwa bwe gayinza okukozesebwa mu mbeera ya wano okugezesa wekukolebwa. Okukunganya amawulire mu kunoonyereza kuno kujja kumala emyezi nga kumi n'ebiri (12).

Lwaki olondeddwa okwetaba mu kunoonyereza kuno?

Olondeddwa okwetaba mu kunoonyereza kuno olw'ensonga nti oli mwagalwa w'oyo eyenyigidde mu kunoonyereza nga kulimu n'okugezesa nga nakyewa. Omulimu gw'okola ng'omwagalwa weyenyigidde

SCIENCE &

Abaagalwa

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Name of applicant:	Agnes Nanfuka Ssali
Student ID no. (if applicable)	4587243
Supervisor (if	Professor Janet Seeley
applicable)	Dr Fiona Poland
Project Title:	Understanding the informed consent process in HIV clinical trials in Uganda: a case study

Accept	
Request modifications	
Reject	

Reviewers' checklist	Delete as a	ppropriate	
Risks and inconvenience to participants are minimised and not unreasonable given the			
research question.			
All relevant ethical issues are acknowledged and understood by the researcher.			
Procedures for informed consent are sufficient and appropriate			
Reviewers' Comments			
This is an in-depth application, with the researcher having thought in detail about	the key iss	sues	
involved. The applicant is clear about her research focus and methodology, and se	ensitive to	the	
needs of the participants – of which there is a range from scientists to local level clinical trial			
volunteers.			
The dates (end date) for the duration of the project (section 19) need amending.			
Committee's recommendation:			
Ethical approval granted.			

Signature (Deputy Chair of the International Development Ethics Committee)	
Date	26 th June 2011