

A survey of researchers' Ethics, Law, and Human Rights dilemmas, resources and needs in
HIV vaccine trials (HVTs) in Africa.

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DECLARATION

Unless specifically indicated to the contrary, this thesis is the result of my own work

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Acronyms and abbreviations

AAVP	African AIDS Vaccine Programme
AIDS	Acquired Immune Deficiency Syndrome
ARVs	antiretroviral drugs
ARASA	the division of AIDS and rights alliance for Southern Africa
AVAC	AIDS Vaccine Advocacy Coalition
AVERT	AIDS Virus Education and Research Trust
BONELO	the Botswana Network on Ethics, Law and HIV/AIDS
CAB	Community Advisory Board
CEBESA	the Centre for Bioethics in Eastern and Southern Africa
DAIDS	Division of AIDS
ELH	Ethics, Law and Human rights
GCP	Good Clinical Practice
HAVEG	HIV/AIDS Vaccine Ethics Group
HDSS	Holographic Data Storage System
HIV	Human Immunodeficiency Virus
HSRC	Human Sciences Research Council
HVT	HIV Vaccine Trials
HVTN	HIV Vaccine Trial Network
IAVI	International AIDS Vaccine Initiative
IC	Informed Consent
ICH	International Conference on Harmonisation
IVR	Initiative for Vaccine Research
MRC	Medical Research Council
NCST	National Council for Science and Technology
NGO	Non-Governmental Organisation
NHREC	National Health Research Ethics Committee of Nigeria
NIH	National Institute of Health
OHRP	Office for Human Research Protection
REC	Research Ethics Committee
RSA	Republic of South Africa
SAAVI	South African AIDS Vaccine Initiative

SARETI	South African Research Ethics Training Initiative
SOP	Standard Operation Procedures
TASO	The AIDS Support Organisation
UN	United Nations
UNAIDS	the joint United Nations Programme for HIV/AIDS
UNCST	Uganda National Council for Science and Technology
UNDP	United Nations Development Programme
UNICEF	United Nations International Children's Fund
US	United States
VCT	voluntary counselling and testing
WHO	World Health Organisation

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Abstract

This study investigated the Ethic, Law, and Human rights (ELH) dilemmas of researchers involved in preparing for and/or conducting HVTs in African countries. Furthermore it investigated availability of ELH material resources and infrastructure necessary for the successful conduct of HVTs. The study employed both qualitative and quantitative research methods.

The main ethical challenges that researchers face when conducting HVTs include; high seroconversion rates, determining social value, working collaboratively with participants and communities, and paying trial participants. Legal challenges faced by researchers included; termination of participants who meet study inclusion criteria due to demands to do so from their parents and/or male partners, and in some countries lack of support from health care service providers when it comes to caring form trial participants. Understanding of consent age in African countries by communities was reported as a human right concern for researchers.

The study concludes that researchers conducting or preparing to conduct HVTs in African countries face different ethics, law and human rights challenges when conducting HVTs at their sites and these challenges need to be addressed in order to improve the conduct of HVTs in Africa.

1. Introduction

1.1 Statement of the problem

Researchers play a critical role in the conduct of HIV vaccine trials (HVTs) and face a variety of ethics, law and human rights (ELH) challenges at their sites. However, these challenges are not sufficiently documented. This study was thus conducted with an aim to explore and identify them in order to improve the conduct of HVTs in Africa. The study investigated the ELH dilemmas of researchers involved in preparing for and/or conducting HVTs in African countries. Furthermore it investigated availability of ELH material resources and infrastructure necessary for the successful conduct of HVTs.

1.2 Objectives of the study

The main objective of the study was to elicit ELH dilemmas and challenges that researchers face while conducting HVTs in African countries. Another objective was to give researchers the opportunity to respond to questions regarding availability of resources at their research sites. In addition to these two objectives, this study also evaluated the appropriateness and relevance of legal frameworks and ethical guidelines adopted at selected trial sites. Its findings will be used to make recommendations to the World Health Organisation – the joint United Nations programme for HIV/AIDS – African AIDS Vaccine Programme (WHO-UNAIDS-AAVP) ELH working group on how to improve the conduct of HVTs in Africa. The study received financial support from the WHO-UNAIDS-AAVP - ELH working group.

1.3 Theoretical frameworks

This study investigated three domains namely ethics, law, and human rights. Each of these domains was constructed upon a different theory or framework. These are outlined below.

1.3.1 Ethics

This research project was based mainly upon the Emanuel, Wendler and Grady (2008) ethical framework. This framework was chosen because it focuses on the ethical issues in clinical trials in developing countries and covers a wide range of ethical issues namely:

- Collaborative partnership
- Social value
- Scientific validity
- Fair subject selection
- Favourable risk-benefit ratio
- Independent review
- Informed consent
- Ongoing respect for participants.

In addition the study refers to the UNAIDS 2000 and 2006 special guidelines on HVTs.

1.3.2 Law

A theoretical framework that is applicable to all countries is not feasible since countries have different laws. The appropriateness of the conduct of trials was examined with regard to the laws of each country, with the assistance of an inventory of African laws developed by the ELH working group of the UNAIDS AAVP (University of KwaZulu-Natal, 2009).

1.3.3 Human Rights

With regard to human rights, the study referred to the Universal Declaration of Human Rights (UN, 1948). The Universal Declaration of Human Rights was adopted in 1948 (Singh, Govender & Mills, 2007). This declaration was put in place to encourage global respect for human rights. Investigation

of human rights relevant to HVTs, such as the right to privacy and the right to health, was based on reference to the Universal Declaration of Human Rights (UN, 2009).

1.4 Questions the study seeks to answer

1. What ELH dilemmas do researchers in HVTs in African countries experience?
2. What do researchers identify as their ELH needs?
3. What resources help researchers deal with ELH problems at their site?
4. Which ethical guidelines and legislative frameworks do researchers in HVTs in African countries find most appropriate or most inappropriate? Why?
5. Are there any laws governing the conduct of HVTs, which researchers find useful or problematic?

2. Literature review

This section explores the HIV/AIDS pandemic in Africa, including HIV/AIDS research and the conduct of HVTs in the continent. The literature review also outlines theoretical frameworks and related studies that informed this study.

Africa remains the continent worst affected by the HIV/AIDS pandemic (UNAIDS, 2009). As a result HVTs are being conducted in the continent to try and find a successful HIV/AIDS vaccine. Available literature reviewed indicates that researchers in HVTs face a variety of barriers when conducting HVTs.

2.1 HIV/AIDS in Africa

The first HIV/AIDS infections in Africa were reported in the early 1980s (IVR, 2005). Since then more than 25 million people around the world have died from AIDS-related disease (AVERT, 2010) and 33 million are presently thought to be infected with the HI virus (UNAIDS, 2008). In other regions of the world, HIV/AIDS is mostly prevalent among gay men, intravenous drug users, commercial sex workers and their partners (UNAIDS, 2008). However, in Africa the virus has rapidly spread in the general heterosexual population (Epstein, 2007).

In South Africa, the country with the most HIV/AIDS infected population, an estimated 5.4 million people are living with HIV/AIDS (UNAIDS, 2008). An estimated 74% of people currently living with HIV/AIDS are in Sub-Saharan Africa (UNAIDS, 2008). Roughly 40% of all people living with the HI virus live in eleven countries, situated in eastern and southern Africa, home to less than three percent of the world's population (Epstein, 2007). HIV/AIDS related deaths have contributed to the dramatic fall in life expectancy in these countries. For example, at one point in Botswana and

Malawi life expectancy for those who are HIV positive fell to as low as less than 40 years while life expectancy was 47 years for the whole continent (Poku & Whiteside, 2004).

Since the beginning of 2002, Botswana has taken the front stage in the fight against HIV/AIDS in Africa. It was the first African country to provide free anti retroviral therapy to all citizens infected with the HI virus (“Botswana Country Report”, 2010). There has since been improvement in life expectancy in Botswana which is now at 54 years from less than 40 years (“Botswana”, 2010). Life expectancy in Malawi and Uganda is 53 years old while life expectancy is 52 for South Africa (<http://www.unicef.org>).

Sub-Saharan Africa, having an estimated 74% of all the HIV infected people worldwide, is more heavily affected by HIV/AIDS than any other region of the world (UNAIDS, 2008). “In 2005, an estimated 3.2 million people in the region became newly infected, while 2.4 million adults and children died of AIDS” (UNAIDS, 2006, para. 2). In 2007, the number of new infections decreased to 2.7 million and 2.0 million died from the disease (UNAIDS, 2008). HIV/AIDS related deaths have left 12 million children under the age of 18 orphaned in Sub-Saharan Africa (UNAIDS, 2008).

The spread of HIV/AIDS in Africa has been so rapid that before countries were even aware of the threat posed by this pandemic, their communities were deeply penetrated (Poku & Whiteside, 2004). As a result, many African countries are just now becoming aware of the seriousness and lethality of the HIV/AIDS pandemic as more and more HIV positive individuals become ill (<http://www.avert.org/history-aids-africa.htm>). This sudden awareness of the seriousness of the pandemic has resulted in more HIV research being conducted in African countries and an increase in the number of African countries conducting HVTs. The number of African countries conducting HVTs has increased over the years. By 2008 at least eight African countries; Botswana, Kenya,

Malawi, Rwanda, South Africa, Uganda, Tanzania and Zambia had conducted or/and were conducting HVTs (<http://www.hvtn.org/>; IAVI, 2007). Funding for HIV/AIDS research and treatment increased and more and more African countries carried out HIV/AIDS prevention campaigns. However, in recent years there was evidence that funding for HIV prevention was decreasing in some areas (UNAIDS, 2009). Funding for HIV vaccine research was seen to have decreased by 10% in 2008 and it now remains stable (<http://www.iavi.org>).

The crisis of HIV/AIDS is evidenced by the way this disease has rapidly spread across the African continent over the years (UNAIDS, 2008). The African productive sector has been deeply impacted by the HIV/AIDS pandemic as mostly healthy and productive populations are getting sick and dying in increasing numbers (Poku & Whiteside, 2004). The impact of the HIV epidemic has already negatively affected not only the health sector but also education, transport, industry, human resources, agriculture and the economy at large (UNAIDS, 2006).

2.1.1 Why is HIV/AIDS worse in Africa?

In 1985, virtually no-one in Botswana was infected with the HI virus (Epstein, 2007). By 1992, ten percent of Botswana adults were living with the virus and by 2005 nearly 40 percent of adults carried the virus (Epstein, 2007). In South Africa the HIV prevalence rates rose from 0.76% in 1990 to 10.44% in 1995 and 22.4% in 2000 (Abdool Karim & Abdool Karim, 2002).

These rates are very high compared to most of the rest of the world. For example, in North America HIV rates remain less than 1 percent (UNAIDS, 2009). Furthermore, adult HIV prevalence in every country in Asia, except Thailand, is less than 1 percent (UNAIDS, 2009). In East Asia rates are as low as < 0.1% (UNAIDS, 2009). Even with its thriving sex and drug trade, Thailand's national rates only peaked at 2.1 percent in the mid 1990s and have fallen to 1.4 percent (UNAIDS, 2009).

Although HIV rates were predicted to spread rapidly in the general population of Asia and Eastern Europe, this has not happened despite the fact that the virus has been present in these parts of the world for decades (Epstein, 2007). Extensive spread of HIV/AIDS in these regions has never happened; instead the virus remains prevalent among those with well-known risk factors such as sex work, drug use, and homosexuality (Epstein, 2007). On the contrary, HIV/AIDS in Africa has spread extensively and prevalence is highest among heterosexual individuals.

Early analysis of HIV infection focused on the practice of multiple partners, among other things, as a key driver of HIV/AIDS in African communities (Caldwell et al., 1989). However recent scholars such as Epstein dismiss these claims arguing that Africans are not more promiscuous than other heterosexual populations in other parts of the world (Moore, 2007). Instead, some theorists and researchers focus on people's sexual behaviour as a key risk factor for HIV and AIDS in Africa. This will be discussed further below.

Other scholars suggest that HIV/AIDS is worse in Africa than anywhere else in the world because Africa has the least developed economies (Hunter, 2003). This is coupled with poor agricultural output due to the geographical situation of the continent. According to Hunter (2003), Africa is almost entirely tropical with 80 percent of the continent lying between the Tropic of Cancer and Tropic of Capricorn (Hunter, 2003). Food production in countries that lie within this zone is more difficult because of the notoriously poor quality of tropical soils that are leached by rains (Sanchez, 2002). Africans therefore rely on wage economy as a main source of livelihood. This however creates problems because in most African countries jobs are scarce. Studies have shown how, due to unemployment, women may resort to transactional sex as a means of survival (Hunter, 2003; Setel, 1999). This approach enables an understanding of HIV risk that takes into account the socio-economic environment of an individual instead of locating risk solely within an individual. While

recognising the impact of socio-economic circumstances on HIV risk behaviour, this section proceeds by looking specifically at sexual behaviour as a risk factor for HIV. In particular it discusses sexual mixing, multiple concurrent partners, early sexual debut and migrant labour as key drivers of HIV (Parker, Makhubele, Ntlati & Connolly, 2007; Soul City, 2008,2009); Stock, 2004). These are each discussed more fully below.

2.1.1.1 Sexual mixing

Some theorists maintain that the epidemic is worse in Africa because of what they call ‘sexual mixing’ (Stock, 2004). It is not the number of sexual partners but the nature of the partners – for example, people who engage in risky sexual behaviour [have unprotected sex with their sexual partners; have multiple concurrent partners], people in the high HIV prevalence age range - that causes the rapid spread of the disease. “In Africa sex crosses social boundaries more than in the West. It occurs between rich and poor, urban and rural, old and young” (Epstein, 2007, p.53). This according to Epstein (2007) sexual mixing has given rise to the extensive spread of the HI virus through the population in Africa. These patterns of sexual relationships are often a result of the poverty and socio-economic inequalities. For example younger women get involved with older richer men for monetary and other material gain. The poor get involved with the rich for monetary and other resources gain as well. As a result of this mixing, individuals from high HIV prevalent populations build sexual networks with individuals from low HIV prevalence populations and this allows the disease to spread rapidly across all populations.

2.1.1.2 Multiple concurrent partners

According to the South African National HIV prevalence, incidence, behaviour and communication survey (HSRC, 2008), multiple concurrent sexual partnerships increases the spread of HIV infection because they add to sexual networks that allow rapid HIV transmission. The term ‘concurrent

partnerships' refers to having more than one sexual partner at the same time or starting a sexual relationship before ending another one (Parker et al., 2007). Concurrent unprotected sexual contact with multiple partners increases the risk of HIV infection. "In such interlinked networks, where a single individual contracts HIV and has a consequent high viral load, there is a higher likelihood of infecting other individuals in the network" (Parker et al., 2007, p. 12). There are different forms of multiple concurrent partnerships namely; steady partner and the 'other' side partner, intergenerational sexual relationships, transactional sexual relationships and polygamy (Soul City, 2008). All of these forms are commonly practiced in some African countries (Soul City, 2008).

Steady partner and the 'other' side partner is a situation where an individual has a steady partner but also has other partners on the side who the steady partner does not know about (Soul City, 2008).

Different societies across Africa have invented names for the 'other partner'. In Zimbabwe the other partner is referred to as 'small house' (Chingandu, 2007), in South Africa referred to as '*makhwapeni*' (a Zulu word that means an armpit used to refer to sexual partners kept as a secret) (Parker et al., 2007) and referred to as '*Nyatsi*' (a Tswana word that means extramarital partner) in Botswana. The 'other' partner/s is often kept secret and is kept for sexual, material and at times for emotional gain (Soul City, 2008). There are also intergenerational sexual relationships. These relationships are those that happen between young people and much older partners (HSRC, 2008). Youth who have sexual partners who are five or more years older than themselves expose themselves to HIV because of being sexually involved with individuals in a higher HIV prevalence age group (HSRC, 2008).

Transactional sexual relationships are similar to intergenerational sexual relationships in that they both have monetary gain attached. However unlike intergenerational sexual relationships, transactional sexual relationships can also happen between partners of narrow age differences.

Another form of concurrent sexual relationships is polygamy. Polygamy refers to having more than one wife and it is still practiced in some African cultures. In a study conducted by Soul city (2008) in ten African countries, participants indicated that polygamy was a cultural institution that permits multiple partners. This was especially stated by male participants who used polygamy to validate having multiple sexual partners (Soul City, 2008). Polygamy is not inherently a risk factor for HIV infection and it continues to be practiced by some African societies. Polygamy does however become a risk for HIV infection if one of the partners is not faithful.

2.1.1.3 Sexual debut

Sexual debut age is the age at which an individual has his or her first sexual act. Sexual debut age “remains a crucial factor in vulnerability of youth to HIV infection” (HSRC, 2008, p. 64). A study of early sexual debut found that some individuals have their first sexual act as early as before the age of 15 (Harrison, Cleland, Gouws & Frohlich, 2005). This is as a result of a variety of factors including sexual abuse, and exposure to sexually explicit materials at an early age (Phalane, 2010). Children who are exposed to sexually explicit materials such as pornography, or seeing parents engaging in sexual acts (common where parents share their bedroom with their children) are more likely to seek to experience the sexual behaviour they witnessed (Phalane, 2010). Secondly, children and youth who are victims or survivors of sexual abuse are more likely to practice risky sexual behaviour (HSRC, 2008). Individuals who engage in sexual activities at an early age, as a result of a variety of factors including those mentioned above, are less likely to use barrier protection hence increasing the likelihood of HIV infection (Geary et al., 2008).

2.1.1.4 Migrant labour

Migrant labour refers to a situation where someone works outside their home village, home town and even home country. Historically it was often men who left their families to work in the mining,

agricultural and other economic activities in urban areas (Kalipeni, Craddock, Oppong, & Ghosh, 2004). The fact that individuals, especially men, spend long periods of time away from home exposes them to potential multiple partner relationships and subsequently HIV infection. These individuals leave their homes and countries in search of employment. When they get to urban areas, these individuals are often exposed to conditions that promote risky sexual behaviour (Louw, 2005). For example, in South Africa, it is reported that miners stay in same sex hostels and have easy access to alcohol and sex workers with very little provision of condoms (Louw, 2005). These living environments increase chances of multiple sexual acts, and unsafe sexual behaviour. Migrant workers who get infected with HIV, take the infection back home to their spouses and in so doing spread the disease.

The main mode of HIV/AIDS transmission is multiple concurrent sexual partners. This sexual behaviour creates sexual networks that enhance the spread of HIV/AIDS rapidly amongst people of different ages, gender, and socio-economic status. With rising HIV/AIDS mortality every day (UNAIDS 2008), the need for a successful vaccine to prevent HIV/AIDS is clear. Vaccines have proven to be a single most effective preventative strategy for many infectious diseases in past years and the search is on for a successful HIV/AIDS prevention vaccine (Abdool Karim & Baxter, 2005). Other interventions that have been implemented to stop the epidemic include voluntary counselling and testing, the use of microbicides to prevent infection in women, and male circumcision. These programs have however not made much impact as HIV infections continue to increase in Africa.

2.2 HIV/AIDS vaccine research in Africa

The high HIV/AIDS statistics in Africa have highlighted the need for preventive clinical research to be done speedily (Marais, 2006). As a result, Africa has become a site for such research where most people at risk of being infected with HIV can be included as participants in clinical research (IAVI,

2007). People at risk of HIV/AIDS are perceived to be those in areas with high HIV/AIDS incidence and prevalence rates. Involving people at high risk of HIV/AIDS in HVTs allows for better assessment and monitoring of the success of the vaccine in decreasing HIV infection. A successful HIV/AIDS vaccine is identified as an “important hope for the control of HIV/AIDS” especially in developing countries (Abdool Karim & Baxter, 2005, p. 226). HVTs were identified as a way of carrying out investigations to find an effective, preventive HIV vaccine that “would provide the best method for controlling the catastrophic HIV/AIDS pandemic, especially in less developed countries” (Abdool Karim & Baxter, 2005, p.227).

HVTs, like other clinical trials, involve different trial phases. According to HVTN (<http://www.hvtn.org/science/phases.html>) a vaccine must effectively complete *three* stages of testing in people before it can be approved. These three stages are referred to as phases. The first phase of clinical trials entails the first administration of the study drug to trial participants to determine the safety of the drug and investigate vaccine related side effects (<http://clinicaltrials.gov/ct2/info/understand#Q19>). This phase usually enrolls about 20 to 100 HIV-negative participants (<http://www.hvtn.org/science/phases.html>). A Phase I trial on average lasts 12 to 18 months (<http://www.hvtn.org/science/phases.html>).

Once safety of the vaccine has been determined, the investigation moves to phase II clinical trials for further safety testing (<http://clinicaltrials.gov/ct2/info/understand#Q19>). Phase II trials enroll more participants than phase I - up to several hundred individuals - with the intention to collect more in-depth information about the human immune response and further data on the most effective dosage and administration schedule (<http://www.hvtn.org/science/phases.html>). A Phase II trial can last two to three years (<http://www.hvtn.org/science/phases.html>).

Thousands of HIV negative participants are enrolled for phase III clinical trials. These trials are conducted to test if the most promising experimental vaccine – investigated in phase II - is effective in preventing HIV infection (<http://www.hvtn.org/science/phases.html>). A Phase III trial can take three to five years to complete (<http://www.hvtn.org/science/phases.html>).

Vaccine development to fight HIV/AIDS started in developed western countries. Subsequently HVTs have been conducted in these countries for more than 15 years with most early phase clinical trials involving human participants been done in the USA and Europe (Abdool Karim & Baxter, 2005). Only “thirteen years ago, WHO recommended developing vaccine trial sites in developing countries including Thailand, Rwanda, Uganda, and Brazil” (IVR, preface para. v., 2005). Four African countries – Kenya, South Africa, Tanzania and Uganda - are currently preparing for or conducting HVTs (<http://www.avac.org/ht/a/GetDocumentAction/i/3436>; <http://www.hvtn.org/about/sites.html>). However at the time of data collection eight countries were preparing for or conducting HVTs. According to Wassenaar and Barsdorf (2007), the development and distribution of an effective HIV vaccine remains Africa’s best hope to end the AIDS pandemic, given the poor uptake of known effective methods such as abstinence and condoms.

Successful implementation of HVTs involves sponsors, researchers, trial participants, host communities and other stakeholders (WHO-UNAIDS, 2004). Of all these people, trial site researchers occupy a critical position – they act as intermediaries between sponsors on one hand, and research participants and their communities on the other hand. However, HVT researchers often have to overcome significant dilemmas and/or barriers when conducting HVTs in developing countries. Researchers face a variety of ELH challenges such as; minimising risks and maximising benefits, complying with multiple laws and guidelines that protect the welfare of trial participants, and respect for basic human right (c.f. Elsayed & Kass, 2007; Grinyer, 2001; Keith-Spiegel, Koocher &

Tabachnick, 2006). It is crucial to investigate and understand these challenges, and find out what researchers' needs are in order to maximise the ethical protection of trial participants and to enhance the success of work done by researchers.

2.3 Theoretical frameworks

When investigating researchers' dilemmas, needs and resources, this study involved three main domains, namely ethics, law, and human rights. Each of these domains is based on a different theoretical framework as detailed below.

2.3.1 Ethics

The ethics domain of this study was based on the Emanuel et al. (2008) ethical framework and to some extent on the special UNAIDS 2000 and 2006 guidelines on HVT. The Emanuel et al. (2008) framework was chosen because it focuses on ethical issues in clinical trials in developing countries and covers a wide range of ethical issues namely collaborative partnership, need for social value, scientific validity, fair subject selection, favourable risk-benefit ratio, independent review, informed consent and ongoing respect for participants. These principles are discussed in relation to the manner in which research participants should be treated. This study investigated whether the ethical dilemmas and needs of researchers in HVTs can be understood in terms of these principles, or whether researchers face ethical dilemmas not anticipated by the Emanuel et al. (2008) framework.

There have been many debates about the ethics of clinical research in developing countries (Emanuel et al., 2004). The debate includes "the standard of care that should be used in research in developing countries, the reasonable availability of interventions that are proven to be useful during the course of research trials and the quality of informed consent" (Emanuel et al., 2004, p. 930). Research conducted in developing countries often raises concerns about possible exploitation of research

participants and host communities (Hawkins & Emanuel, 2008). The possibility of exploitation in developing countries is increased by “poverty, limited health-care services, illiteracy, cultural and linguistic differences, and limited understanding of the nature of scientific research...” (Emanuel et al., 2004, p. 930). Emanuel et al. (2008) propose guidelines for minimizing exploitation of research participants and for conducting clinical research that is ethical.

2.3.1.1 UNAIDS 2000

The UNAIDS (2000) is a guidance document that outlines ethical considerations in HIV preventive vaccine research. The document discusses eighteen guidance points namely:

- HIV vaccine development
- Vaccine availability,
- Capacity building
- Research protocols and study participation
- Community participation
- Scientific and ethical review
- Vulnerable populations
- Clinical trial phases
- Potential harm
- Benefits
- Control group
- Informed consent
- Informed consent – special measures
- Risk-reduction interventions
- Monitoring informed consent and interventions
- Care and treatment

- Women
- Children

(UNAIDS, 2000).

Some of these areas – such as HIV vaccine development, community participation, vulnerable populations and informed consent - were referred to in shaping the ethical domain of this study.

2.3.1.2 UNAIDS 2006

UNAIDS (2006) is a revised version of the UNAIDS (2000) guidelines and has technical and procedural recommendations for creating effective partnerships for HIV prevention trials. The document highlights the need for effective partnerships between researchers and civil society in HIV prevention trials. Some of the recommendations highlighted include: the involvement of community in study design, implementation and monitoring; communication and dialogue among stakeholders – including researchers, activists, ethicists, government officials, sponsors and funders, civil society and trial participants; dealing with vulnerable populations and building human and physical capacity through research.

2.3.2 Legal frameworks

A legal theoretical framework applicable to all countries is not feasible since countries have different laws. The appropriateness of the conduct of trials was therefore examined with regard to the laws of each African country currently conducting or planning to conduct HVTs, with the assistance of an inventory of laws developed by the ELH working group of the UNAIDS AAVP (Grant, Lewis & Strode, 2005). Some examples of country specific legal frameworks are given below.

Botswana

Botswana has no national legislation guidelines regulating the conduct of HVTs in the country. The country however does have ethical and legal structures such as the Ministry of Health that play a role in regulating the conduct of HVT in Botswana (Grant et al., 2005). The Ministry of Health regulates and monitors clinical trials through the health research committee (Grant et al., 2005). Botswana also has national HIV testing guidelines which incorporate ethical considerations on confidentiality consent and counselling; age of consent (<http://www.moh.gov.bw/>). The Botswana Network on ethics, law and HIV/AIDS (BONELA) also provides a legal approach to the country's response to HIV/AIDS (<http://www.bonela.org/>).

BONELA highlights the need to support the public health systems to create an environment that allows people to protect themselves and others from HIV infection without violation of their human and legal rights (<http://www.bonela.org/>). Secondly, BONELA emphasises that punitive action must not be used as a legal tool to address the HIV/AIDS epidemic. These are also applicable to those involved in HVTs.

Kenya

Kenya has national guidelines for research and development of HIV/AIDS Vaccines (“Kenya National Guidelines”, 2005). These outline different policies relating to the conduct of HVT such as:

- The roles of government, regional and sub-regional intergovernmental organizations
- The African AIDS Vaccine Programme
- WHO
- UNAIDS
- Vaccine manufacturers
- Funding organizations

- Investigators
- Collaborating institutions

According to these guidelines, a candidate vaccine must undergo a thorough regulatory process – including testing for safety in animals - before it is approved for testing in humans. The guidelines also detail the involvement of organisations such as the National Council for Science and Technology (NCST) in this regulatory process. Other regulatory and executing institutions include the Ministry of Education, Science and Technology; public research institutes; commodity-based research institutes, institutions of higher learning; and semi-private non-governmental organizations” (“Kenya National Guidelines”, 2005).

Organisations that oversee research in Kenya are the NCST and the Ministry of Education, Science and Technology through the Department of Research Development. In 2005 the NCST published Kenya’s guidelines for the ethical conduct of biomedical research involving human subjects (NCST, 2005). These guidelines outline issues such as: research ethical clearance procedures and guidelines, and guidelines for determining whether clinical research conducted in Kenya is ethical (NCST, 2005). Some of the frameworks outlined in these guidelines include: value, scientific validity, fair subject selection, favourable risk-benefit ratio, independent review, informed consent and respect for potential and enrolled subjects (NCST, 2005).

Malawi

Like Botswana, Malawi does not have specific guidelines for the conduct of HVTs. The country however has drafted policies that are intended to play a role in regulating the conduct of HVTs in Malawi (Grant et al., 2005). These include the National HIV and AIDS policy which was drafted in 2004, the national HIV and AIDS bill and the public health act (Malawi Government, 2009). These laws are aimed at promoting the welfare of citizens and at promoting provision of accessible health

care to all citizens (Malawi government, 2009). These laws also promote and safeguard the human rights of all citizens such as the rights of people living with HIV and those affected by HIV.

The Centre for Bioethics in Eastern and Southern Africa (CEBESA) is an NGO in Malawi committed to promoting research ethics (UKZN, 2009). The centre promotes among others, operations of RECs and safety monitoring (ARASA, 2008).

South Africa

South Africa has national ethics guidelines (Strode et al., 2005) which inform the conduct of research involving human participants. All researchers conducting health research in South Africa should follow these guidelines to ensure that human participants' rights are protected. The National Health Act (61 of 2003) also informs the conduct of research involving human participants.

Furthermore, the South African Medical Research Council (MRC) published specific guidelines on the ethical conduct of HVTs (Strode et al., 2005). These guidelines are informed by the UNAIDS (2000) *Ethical considerations in HIV Preventive Vaccine Research*. These guidelines cover topics such as: research protocol, study population, IC, community participation, scientific and ethical review, vulnerable populations, clinical trials phases, potential harm, benefits, control groups, HIV risk reduction interventions and care and treatment (MRC, 2003).

The South African constitution guides the contents of all laws and policies through the Bill of Rights (ARASA, 2008). When conducting HVTs, study protocols and all guidelines and documentation to inform the research must comply with the demands of the constitution. There are fundamental rights that are applicable to the development and implementation of health policies that must be realized

(ARASA, 2008). These are rights such as right to privacy, right to dignity and right to an environment that is not harmful to the health of an individual (ARASA, 2008).

Institutes in South Africa such as the Steve Biko Centre for Bioethics, South African Research Ethics Training Initiative (SARETI)

(<http://web.up.ac.za/default.asp?ipkCategoryID=4264&subid=4264&ipklookid=8>), HIV/AIDS

Vaccine Ethics Group (HAVEG) (<http://www.saavi.org.za/haveg.htm>) and the Centre for Applied

Ethics, to mention just a few, are working to promote necessary ethical, legislative and human rights practice in HVTs (<http://elh.ukzn.ac.za/InventoryofEthicsCentres>).

For example HAVEG promotes the establishment of sound IC process, a fair risk/benefit ratio for participants and their communities and adolescents' participation in clinical trials (<http://elh.ukzn.ac.za/InventoryofEthicsCentres>).

Uganda

Uganda also has statutory bodies such as the national drug authority and the Uganda National council for Science and Technology (UNCST) to regulate clinical trials (Grant et al., 2005). The national drug authority is responsible for the regulation of drug trials while the UNCST is responsible for guiding, coordinating and monitoring research (Grant et al., 2005).

Uganda also has national guidelines for the management of HIV/AIDS (ARASA, 2008). These guidelines are used to provide a framework for the conduct of HVTs in Uganda. Published by the Ministry of Health these include national guidelines for the implementation of ARVs, and national guidelines for HIV counselling and testing (<http://www.avert.org/>). Appropriate HIV counselling and testing must be provided to all people (<http://www.avert.org/>). Uganda national guidelines address issues such as management of people living with HIV/AIDS, IC process, monitoring and provision of adequate health care (ARASA, 2008).

In addition there is The AIDS Support Organization (TASO) which works to promote the quality of people living with HIV, their families and communities affected by HIV/AIDS (<http://www.tasouganda.org/>). In doing so this organisation, promotes the ethical and legislation requirements stipulated in the national guidelines on the management of HIV/AIDS in Uganda.

2.3.3 Human rights

The Universal Declaration of Human Rights (UN, 1948) provides a useful conceptual framework for considering human rights in HVTs. The Universal Declaration of Human Rights was adopted in 1948 (UN, 1948). This declaration was put in place to encourage global respect for human rights.

The Universal Declaration of Human Rights (UN, 1948) informs the national Constitutions of many African countries. For example, the Bill of rights is contained in chapter eleven of the constitution of Botswana, chapter four of the constitution of Malawi and Uganda and chapter two of the South African constitutions (UN, 2009). Some of the rights relevant to HVTs include: the right of access to public service, the right to education, the right freely to participate in the cultural life of the community, to enjoy the arts and to share in scientific advancement and its benefits, the right to life and security of person (UN, 2009). The HIV vaccine trial network (HVTN) published participants' Bill of rights and responsibilities to ensure that participants in HVTN vaccine trials are always aware of their rights (<http://www.hvtn.org/community/rights.html>). Some of the rights stipulated in this document are: right to all information about the study, right to refuse joining and withdrawing from the study, right to be in a discrimination free study, right to all the necessary treatment and care and right to confidentiality. The documents contains responsibilities of trial participants which include adhering to study requirements and processes, respecting research staff, keeping the confidentiality of others' participation, reviewing and comprehending the study material.

In investigating human rights challenges, the study also refers to guidelines compiled by UNAIDS (2000). According to these guidelines trial participants, involved in the same type of trials, have the right to be provided with the best current treatment at all times and to be protected from harm at all times (UNAIDS, 2000). If a successful vaccine is created through the trials this must be provided to trial participants who received placebo (UNAIDS, 2000). Researchers should strive to maximise benefits and minimise risks and should at all times avoid discrimination against women and other marginalised groups (UNAIDS, 2006). These guidelines cover issues such as ensuring the full enjoyment of all human rights and fundamental freedoms by people living with HIV and members of vulnerable groups; promoting availability to HIV education and information; ensuring confidentiality and informed consent; encouraging responsible sexual behaviour, promoted access to VCT; and developing strategies to combat stigma and social exclusion connected with the epidemic (UNAIDS, 2006).

2.4 ELH issues and barriers to the conduct of HVT in Africa

Large clinical trials are needed to provide reliable evaluation of interventions designed and implemented to improve health (Duley et al., 2008). Researchers play a crucial part in the conduct of these trials. It is thus very important that they are provided with all the necessary resources, ethical and legal support to carry out trials that will provide reliable findings to implement change in the health sector. In recent years more and more clinical trials, including HVTs, have been conducted in Africa. In this context, clinical trials must be simple and affordable and widely applicable to the context within which they are conducted, given the developing and diverse nature of the researched populations. However this is not always the case. As a result, researchers face a variety of barriers when conducting HVTs in African countries. These barriers include ethical, legal, human rights and resource related barriers. These are discussed below.

2.4.1 Ethical issues and barriers

Collaborative partnership

For successful clinical research to be conducted there must be collaborative partnership between all stakeholders. These include the research staff, funders, policy makers, and host communities (Emanuel et al., 2008). This collaborative partnership is essential for ensuring that host communities are involved in deciding and determining what is acceptable and relevant to the community's health problems and in so doing minimises possibility of exploitation of host communities (Emanuel et al., 2008). Involving all stakeholders in the research poses challenges for researchers in that it is often impossible to meet the expectations of all stakeholders. Although working in partnership with host communities helps to establish a two-way communication needed to achieve mutual understanding of research intended to be conducted (Woodsong & Abdool Karim, 2005), researchers are sometimes pressured to meet the expectations of the funders over those of the host communities. Finding a balance as far as whose contribution to employ into the research can also be a challenge.

In conducting HVTs the research team must work with the communities to establish a collaborative partnership that would yield research that is responsive and that addresses communities' needs and priorities (UNAIDS, 2006). Researchers should recognise, acknowledge and respect the host community's culture, values, and social norms and practice (Emanuel et al., 2008). This can be achieved by adopting research methods that do not conflict with cultural beliefs, norms and practices of the host community. Researchers must always make an effort to incorporate and be informed by these aspects because these reflect the realities of participants' local context (Woodsong & Abdool Karim, 2005). However, in incorporating these aspects into the design of the study, researchers face a challenge of making sure that their initial aims of the proposed study are not altered (Woodsong & Abdool Karim, 2005).

Therefore although working collaboratively with all stakeholders may be beneficial to the product of the research, researchers face challenges in achieving this.

Social value

According to Emanuel et al. (2008) clinical research must have social value to be recognised as ethical. A research study without social value is unethical in that participants are exposed to possible risk without any potential direct or indirect benefit (Arnason & Van Niekerk, 2009). Research without social value also wastes resources (Emanuel et al., 2004). For research to take place there is need for the necessary material resources; clinical equipment, laboratory equipment, stationary, and personnel add costs to the conduct of HVTs. Therefore it is very important that research has social value to avoid wasting these resources, capital and person power.

A clinical research project can demonstrate social value in the form of information or knowledge generated that can subsequently give rise to improvements in health service (Emanuel et al., 2008; Lairumbi et al., 2008). Translating study results into benefits is a complex process for researchers. Usually studies that generate information that informs future research or information that may lead to improvements in health service are considered valuable (Emanuel et al., 2008). Apart from knowledge generated from research, other determinants of social value are often difficult to identify. Identifying social value determinants of research is made more difficult by study priorities that may change during the conduct of the study (Emanuel et al., 2004). Researchers in developed countries, where research is well established and health care is well supported, face the dilemma of imperfectly incorporating research results into clinical practice (Emanuel et al., 2008). This problem is more complex in developing countries where research and health care facilities are not well established

and funding is not well supported (Callier, 2005). As a result, “the social value of research for the host community must be explicitly specified and enhanced” (Emanuel et al., 2004, p. 932).

Scientific validity

Scientific validity is the third ethical requirement in clinical research according to (Emanuel et al., 2008). Scientifically valid research is that which produces reliable and valid information (Atici, 2008). To start with, research studies must be planned with the aim to generate results that will be useful in the context of the health problem in the developing country (Emanuel et al., 2008).

Achieving results that will be useful and ensuring that the research design is useful in identifying successful and/or suitable interventions is a challenge for researchers because these factors cannot be guaranteed. Moreover, researchers are challenged by the need to select interventions that ensure implementation of culturally, socially and economically appropriate changes in the health care system and/or provide reliable groundwork for conducting subsequent research (Emanuel et al., 2008).

One of the critical parts of any research is to have a sample that is large enough to produce scientifically valid conclusions. “The belief is widespread that studies are unethical if their sample size is not enough to ensure adequate power” (Bacchetti, Wolf, Segal & McCulloch, 2005, p.105). It is for this reason that Emanuel et al. (2004) list scientific validity as one of the ethical requirements in clinical trials. Bacchetti et al. (2005) argue that there should be a balance between “the burdens that participants accept and the clinical or scientific value that a study can be expected to produce” (p. 105). Therefore, a study that has low power is more likely to produce unacceptably low scientific value hence it is unethical to ask study participants to accept the risk, inconveniences and/or discomforts of participating in such a study (Bacchetti et al., 2005). There are cases where studies with small sample size are regarded as unethical (Prentice, 2005). “If there is no projected net

burden, then any sample size is ethical, and sample size can be determined entirely by other considerations” (Bacchetti et al., 2005, p. 106). A particular sample size is ethical if the study’s expected value outweighs the total risks to be accepted by the study participants (Prentice, 2005).

Fair subject selection

Research is often criticised for targeting vulnerable populations such as prisoners, women and poor individuals to mention just a few (Grady, 2004). In the past, vulnerable populations were targeted for high-risk studies because they were powerless to defend their interest (Emanuel et al., 2008). Historically this was mainly criticised because promising research results were preferentially accessible to more privileged persons (Emanuel et al., 2004). Subject selection is a challenge for research in developing countries (Grady, 2004). Researchers are faced with the challenge of selecting the target tribes, villages or towns from which research participants will be recruited. Emanuel et al. (2008) propose four benchmarks to achieving fair subject selection.

Firstly, the sample of the study must be selected to ensure valid data. Target communities are often chosen because of high prevalence of infection of disease in that particular community. For example, HVTs are often conducted in communities with high prevalence and incidence rates of HIV infection. Secondly, minimising risk is essential for subject selection. HIV/AIDS is a highly stigmatised disease in most communities. As a result, researchers face a dilemma in that individuals who take part in HVTs may face discrimination from such communities. In an attempt to minimise risk, a community that does not discriminate against HIV/AIDS, or any stigmatised disease being studied, will be preferred over a community that does discriminate against such infections to minimise risk in the form of social harm (Emanuel et al., 2008).

Thirdly, communities that have legitimate representatives in terms on community advisory boards (CABs) and/or those that are able to establish such representation are preferred. Such communities are preferred because they provide a sustainable platform for collaborative partnership between all parties including the community (Grady, 2004). However this preference may exclude other communities and result in biased selection of host communities. Researchers therefore face a challenge in achieving fair subject selection. Finally, only scientific reasons, such as high prevalence of infection, must be used to determine the target population of study. Researchers face a dilemma of making sure that target populations for research are not selected because of social subjugation such as political powerlessness and/or social marginalisation (Emanuel et al., 2008).

Favourable risk-benefit ratio

For a study to be ethical in its design its expected value must be more than the expected risks to those participating in it (Grady, 2004). Researchers are faced with a challenge of always offering a favourable risk-benefit ratio (Grady, 2004). In most studies, the risks outweigh direct benefits to those participating in the study. Where potential risks outweigh benefits, researchers are challenged by showing that social value of the study must give good reason for the risks (Emanuel et al., 2004).

When communicating the risks and benefits of the study, the researcher is obliged to make clear to the potential participants that there may be unanticipated or unknown risk (Macklin, 2009). By doing so, researchers face the risk of losing potential trial participants who might not feel comfortable with knowing that there might be unanticipated risks in the study.

Researchers must always bear in mind that the underlying potential risks vary from society to society. Therefore, in determining a favourable risk-benefit ratio, local perspectives on the overall risks and benefits of the research must be considered (Killen, Grady, Folkers, & Fauci, 2002).

Considering local perspectives on the overall risks and benefits of the study will promote a reliable determination of risk-benefit ratio in relation to the context in which the research is intended to take place. However doing so and achieving this is a challenge for researchers.

Independent review

All proposed biomedical HIV trial protocols should be reviewed by a Research Ethics Committee (REC) located in the respective countries the research will take place in (UNAIDS, 2008). The AAVP has compiled an inventory of RECs in Africa (AAVP, 2009). A study on RECs' ELH challenges by Milford, Wassenaar and Slack (2006), found that 38% of REC's reported that they had reviewed protocols for HVTs while 66% reported that they would be reviewing HVTs protocols in the future. The study included RECs from 72 RECs from 15 African countries (Milford et al., 2006). RECs reported that they face a variety of challenges to independent review of protocols. These challenges included pressure from funders, pressure from political powers, biased committee members, and lack of transparency of RECs (Milford et al., 2006).

Independent review of protocols by research ethics committees is necessary to minimise concerns associated with researchers' conflict of interest and ensure that participants are not harmed and are treated with dignity and respect (Emanuel et al., 2004). In a study conducted by Milford et al. (2006), 6% of African ethics committees surveyed reported that lack of transparency of RECs is a challenge. Transparency in research is fundamental because it ensures enhances liability by assuring the host community that research conducted is not exploitative (Emanuel et al., 2004). It is therefore, very important that researchers have their protocol reviewed by independent research review committees to ensure public accountability.

Informed consent

HIV prevention research in Africa, as in other developing countries, gives rise to ethical issues, especially the issue around the process and quality of informed consent (Woodsong & Abdool Karim, 2005). Informed consent (IC) serves to ensure that voluntary agreement to take part in trials is obtained from potential participants and to ensure that adequate information about the research is disclosed to trial participants before agreeing to take part in the research (Sreenivasan, 2003). Informed consent according to Woodsong and Abdool Karim “is the bedrock of bioethics, the tangible evidence of respect for individuals and for autonomous decision-making” (2005, p. 413). Often the informed consent process, however, is reduced to signing a form by a potential study participant at the beginning of a study.

IC documents vary in length with some being as short as 2 pages and some being over 10-15 pages long (DAIDS training, 2008). Some researchers prefer short IC forms because they believe that the longer the IC the higher the possibility that the participant would be overwhelmed with information and subsequently fails to comprehend important aspects of the study (DAIDS training, 2008). Duley et al. (2008) suggest that shorter consent forms, maximum 2 pages, outlining key information are a good alternative. However, the consent form should not simply be a checklist but be complemented with open-ended measures, especially for significant concepts that, if misunderstood, could have serious consequences for trial participants (Lindegger et al., 2006). Additional information can be provided for participants who want more information about the study.

It is not only the length of the IC that may be a cause for concern; language may also be a barrier to the IC process. In African communities, local languages often do not have local words for ‘placebo’, ‘randomisation’ and other HVT concepts (Abdool-Karim, 2000). This contributes to the inability of trial participants to understand the trial. The validity of the individual’s consent depends on the

person's level of understanding of the information disclosed by the research staff (Sreenivasan, 2003). Existing data shows that sometimes research participants may not comprehend information outlined in the IC document (Flory & Emanuel, 2004). Therefore researchers have a major task to ensure comprehension of the protocol and the research as a whole on the side of trial participants. Comprehension is also necessary for valid consent by trial participants. For example, most participants in HVTs fail to appreciate the meaning of randomised trials, the concept of study product, and placebo (Sreenivasan, 2003). As a result trial participants often believe that they are on the active arm and not in the placebo. This has serious ethical implications such as risky sexual behaviour leading to HIV infections that could have been avoided had the participant fully comprehended the research. It is very important that the researchers implement recruitment plans that outline the necessary steps to be followed to ensure that the information given to trial participants is fully comprehended. For example, having educators who conduct one-on-one talks with potential participants is an effective way of enhancing research participants' understanding (Flory & Emanuel, 2004). Where trials take place in communities with high illiteracy, inability to comprehend the study process through the IC process may be a major barrier to the conduct of trials in that particular setting.

Another ethical issue that is brought about by the IC process is voluntariness. Sometimes consent to participate in trials is not voluntary. This is due to factors that make some individuals vulnerable to undue influence and coercion (Appelbaum, Lidz, & Klitzman, 2009). These include being a child, a woman, a prisoner and economically disadvantaged to mention only a few (Appelbaum et al., 2009).

Respect for enrolled participants

Ongoing care and respect for participants must be ensured from the time participants are enrolled to after the completion of the trial. Respected for enrolled participants is ensured through continuous

assessment and monitoring of their welfare and by putting in place procedures that are followed to maintain confidentiality of the private information collected (Emanuel et al., 2004; Grady, 2004). However researchers face a challenge of losing potential participants when participants are alerted to the fact that “despite researchers’ best efforts, there is no guarantee of absolute confidentiality” (Emanuel et al., 2004) or that trial participants are allowed to withdraw at any point without any penalty (Grady, 2004).

Researchers must continue to monitor trial participants after the completion of the trial and this can be a challenge due to factors such as limited funding and participants lost to follow-up.

2.4.2 Legal issue and barriers

Overly complex regulations

A number of regulations and guidelines for the conduct of clinical trials have been introduced over the last fifteen years (Macrae, 2007). For example, the good clinical practice (GCP) guidelines published by the International Conference on Harmonisation (ICH) and the Standard Operating Procedures (SOP) documents (Gajic, Herrmann, & Salzberg, 2004). The introduction of these tools, also used by researchers to inform the conduct HVTs in Africa , has resulted in increased quality of clinical trials and have promoted measures to ensure trial participants’ care (Gajic et al., 2004). Duley et al. (2008) writes that current regulations and guidelines for the conduct of clinical trials have also increased the complexity of trials, now becoming barriers to the design and conduct of trials.

Restrictive interpretation of privacy laws

Although some argue that having restrictive interpretations of privacy laws is good for the public, this may be a barrier to the conduct of successful, good quality research (Armitage et al., 2008).

Firstly, regulatory bodies sometimes present conflicting interpretations of the law and this affects the conduct of clinical trials (Armitage et al., 2008). Secondly, restrictive interpretation of privacy laws may be a serious hindrance to a variety of HVT processes (Gable, Gamharter, Gostin, Hodge, & Puymbroeck, 2007). It may be a hindrance to the identification of potential participants for a trial, access to participants' charts to confirm events, continuous follow-up of participants after the trial has been concluded, and secondary use of the HVT data to inform future trials or for other useful purposes not directly related to the original purpose of the study (Armitage et al., 2008). Although these processes are aimed at ensuring participants' legislative right to privacy, they may cause delays and prevent identification of eligible participants for clinical trials.

Stigma and discrimination

Some legal issues that apply to HVTs relate to stigma and discrimination against individuals assumed to be HIV positive because of their participation in HTVs (Shapiro & Stein, 2004). As a result of participating in HVTs, some participants may suffer social harm in the form of being stigmatised and being discriminated against. These participants are stigmatised for a variety of reasons: they are assumed to be HIV positive or at high risk of HIV infection because of their participation in HVTs by other community members (Shapiro & Stein, 2004). In some instances participants who are screened out are assumed to be screened out as a result of their HIV positive status. As a result, these screened out individuals may be stigmatised.

Disclosure

Stigma and discrimination related to HIV are associated with lack of HIV status disclosure (Simbayi et al., 2006). According to Gorbach et al. (2004), one of the factors driving the spread of HIV in Africa is failure to disclose HIV infection by infected individuals. Simbayi et al. (2006) report that in anonymous surveys which were completed by 413 HIV-positive men and 641 HIV-positive women

sampled from HIV/AIDS services, the findings showed that HIV – positive individuals who did not disclose their status to their partners were more likely to have multiple sexual partners. This finding further illustrates how lack of disclosure of HIV – positive status is one of the factors driving the continuous spread of the HIV and AIDS. Medical practitioners are often faced with the dilemma of having to practice their legal duty to maintain confidentiality (Mae, 2009) of all patient information even where they realised that someone – for example a sexual partner of their HIV – positive patient – may be at high risk of infection. As the privacy of people living with HIV is upheld by the need to maintain confidentiality of their HIV – positive status, some believe that this will only make the disease continue to be secretly and privately transmitted (Mae, 2009).

Provision of medical care to volunteers

Many researchers, especially in developing countries, report that care must be given to trial participants when necessary (Belsky & Richardson, 2004). However some have pointed out that the aim of research is to produce knowledge, not to provide treatment and care for patients (Belsky & Richardson, 2004). Therefore provision of health care to trial participants is one of the legal dilemmas researchers are facing in HVTs. Researchers have the obligation to provide adequate health care and other benefits to trial participants who have adverse reactions to the vaccine (Shapiro & Stein, 2004). It is critical for researchers to anticipate any ancillary care responsibilities (Belsky & Richardson, 2004) and to do everything in their ability to prevent any suffering and harm to trial participants. Failure to do so, and failure to assure trial participants of their safety in the trial would result in poor adherence from participants because participants who are not confident that their well being and health is a priority are less likely to participate in trials and less likely to adhere to the trial procedures and follow-up (Shapiro & Stein, 2004).

2.4.3 Human rights issues and barriers

Lack of training of research staff

Every individual working on a clinical trial has the right to be provided with all the necessary information and training to be able to execute their responsibilities. Staff members with insufficient training are prone to make mistakes during the course of the trial. All staff involved in clinical trials requires training on the scientific principles on which key aspects of the trial are based. Staff should also be aware of their rights and the rights of trial participants. For example Godwin and Csete (2005) explore the different rights that must be considered and protected in the conduct of clinical trials. These rights are elaborated below.

Right to information

People have the right to information about everything that concerns them. In HVTs, trial participants have the right to information about HIV, AIDS, about the trial, study product/s and all other aspects of the trials. Given that HVTs often take place in vulnerable communities in Africa, communities that are usually poor and illiterate, it is crucial that all the information concerning the research and the trial is provided to the community and the trial participants. The research staff has the responsibility to help vulnerable populations learn about their human rights (Godwin & Csete, 2005).

The research team also has the duty to educate community leaders about the trial and about how protecting people's human rights may enhance the effectiveness of the trial. Failure to educate the community and trial participants and to ensure that all involved fully comprehend all aspects of the research could result in exploitation.

Right to informed consent

Potential trial participants have the right to informed consent. Information given during the informed consent process should include risks and inconveniences involved, potential benefits of being involved in the trial, what it means to be a trial participant and what is expected from one as a trial participant and elaboration of the trial, trial procedures, the purpose and description of the study product (Rights, 2005). Once this information is provided, potential participants must be given time to reflect on this information and to voluntarily decide to give consent. Most importantly, individuals must be told about their right to not enrol in the trial if they do not want to do so and they must be informed about their right to withdraw from the trial at any time without penalty (Edwards, 2005).

Researchers must ensure that trial participation is voluntary. Factors that may limit individuals' ability to exercise their rights, such as voluntarily participating in HVTs may include poverty and desperation for money (Appelbaum et al., 2009). Trial participants in African HVT sites are often unemployed and come from poor families. The reimbursement they get from participation in trials is much needed money (Appelbaum et al., 2009). As a result, their ability to exercise their right to voluntarily give consent may be compromised and cannot be ensured.

Right to prevention and care

As stipulated in Article 12 of the International Covenant on Economic, Social and Cultural Rights, and other treaties, all people have the right to the highest attainable standard of health (UN, 2009). Trial participants also have the right to quality health care (Macklin, 2003). Services such as regular provision of condoms, HIV testing, counselling, medical assessments and physical assessments must be accessible to all HVT participants. "Even though it may hinder the ultimate goal of the trial to test the vaccine's effectiveness in preventing HIV infection, it is unethical and disrespectful of people's

human rights to deny them the possibility to protect themselves from HIV just because they are in a vaccine trial” (Godwin & Csete, 2005, p. 19).

One of the challenges that researchers are facing in African HVTs is the high rate of seroconverters in HVTs. People who become infected with HIV during their participation in the trial must be provided with the required treatment and the necessary care and support (Slack et al., 2005). Individuals screened out because of their HIV positive status also have the right to adequate medical care (Godwin & Csete, 2005). However these individuals are seldom followed-up.

Confidentiality

Researchers must at all times keep participants’ information confidential. To demonstrate the importance of ensuring the right to privacy and confidentiality of trial participants’ information UNAIDS recommends that HVTs should be carried out where confidentiality of trial participants’ information such as sensitive information about a person’s drug use or sexual behaviour can be ensured (Godwin & Csete, 2005).

It has emerged however that sometimes absolute confidentiality cannot be achieved. For example, where focus group discussion is a methods of data collection – other participants may share contents of the discussion with individuals who did not take part in the discussion - and in instances when the law requires researchers to disclose participants’ information especially where failure of disclosure may result in harm to others (Galletly, DiFranceisco, & Pinkerton, 2008).

Women and HIV

One of the factors that make people vulnerable to HIV infection is being a woman (UNAIDS, 2008). Amongst other factors, gender inequality in economic, social, educational and political life increases

women's risk and prevents them from accessing treatment and care services (Wassenaar & Barsdorf, 2007). Therefore there is need for a focus on gender when preparing for trials and it is especially crucial to find women initiated prevention measures. To achieve this, women's participation in HVTs is important (Wassenaar & Barsdorf, 2007).

Participation of women in HIV trials has been difficult for a variety of reasons (Godwin & Csete, 2005). These include the fact that women have more fear of being stigmatised than men with regard to HIV-related issues. As a result, they face possible abuse and violence (Godwin & Csete, 2005). Women have more fear of being stigmatised than men because often they are blamed by their male partners for their infection. Women who are believed to be infected with HIV are called names such as 'sfebe', 'lebelele', 'phatlha' 'magosha' to name only a few all referring to a woman who sleeps with many men (S. Mfecane, personal communication, June 28, 2010). As a result, women fear being perceived as unfaithful by society and therefore not good wives according to social standards.

Men, on the other hand, side do not get the same harsh treatment. There is a Setswana/SeSotho (African language) old saying that '*monna selepe o a adimangwa*'. This translated into English means 'a man is like an axe, he can be borrowed'. This saying was used to describe how men worked in the fields and at times had to help other families with ploughing the fields. Men would leave their own families to plough for other families hence the expression 'borrowed'. Once they were finished working in the farms of other families, they would go back home. However over the years this saying has been used differently. The saying has been used to describe that 'men can be borrowed or shared with other women'. As a result some men have used the saying to give reason for having multiple female sexual partners. Furthermore, there are widespread beliefs in some communities that men are biologically programmed to want more than one sexual relationship at a time (Leclerc-Madlala, 2005). These beliefs were expressed by young people in townships around Durban, South

Africa – in research conducted by Leclerc-Madlala (2005) – and they [beliefs] were reported to be common amongst societies who were traditionally polygamous. Consequently some men continue to use practices such as polygamy to justify their multiple sexual relationships. As a result HIV infected men face less social harm than women.

Secondly, women sometimes feel that they have to be permitted by their husbands or parents, to participate in trials (Godwin & Csete, 2005). Most women (87.6%) who participated in a preliminary study - conducted in Harare, Zimbabwe – to investigate the potential impact of relationships on decision-making and autonomy of women reported that they were ready to check with their husbands before participating in health research (Nyika, Wassenaar & Mamotte, 2009). Approximately forty six percent of the surveyed women said they would talk to their relatives before deciding to take part in health research. Consequently women often make decisions that do not necessary make them happy but that please their male partners, parents or/and relatives. Likewise, some women who want to participate in HVTs end up not participating in HVTs because they were not permitted to do so, hence their rights are compromised.

2.4.4 Resource related barriers

Lack of funding for clinical trials

Clinical trials have become enormously costly (Fee, 2007). One reason for this is the fact that most clinical trials involve some degree of complexity such as need for multiple ethics approval which adds to cost of the trials (Duley et al., 2008). Independent low cost clinical trials are increasingly becoming impossible to do. Duley et al. (2008) identified inadequate funding to be a barrier to the conduct of successful clinical trials. Although HIV/AIDS research is well funded, less funding is provided for HVTs in developing countries than in the United States of America (Ijsselmuiden, 2007). “A relative lack of appreciation in the scientific and lay communities of the importance of

clinical trial research compared to basic science research” (Duley et al., 2008, p. 41) may be suggested by this limited availability of funding in developing countries.

Due to the increase in regulatory complexity of trials, more funding than before is now required for the conduct of clinical trials (Kermani, Rouse & Mosqueira, 2005). This is because it has become harder to satisfy regulations and to secure funding for multi-centre clinical trials. Therefore it is critical to design and conduct simple HVTs and keep cost low to enable maximum return but this must not in any way compromise the quality and ethical standards of the trials (Kermani et al. 2005).

Researchers in developing countries face challenges resulting from the increased complexity and cost of clinical trials. The increasing cost of conducting clinical trials in developed countries and the increase in regulatory complexity makes it harder to secure funds and recruit large numbers of study participants. Despite this, there is increasing interest in conducting HVTs in developing countries where the pandemic is more prevalent (Duley et al., 2008). Although low cost trials may be affordable in developing countries, the trials might lack scientific validity and may not reflect the priorities of the host country. Many trials in developing countries are conducted in collaboration with researchers from developed countries. This is because investigators in developing countries seldom have access to sufficient funding, adequate infrastructure, skills and reputation to secure funding from international agencies or pharmaceutical companies (Duley et al., 2008).

Where drugs are shipped into the country of research, highly qualified individuals are needed to approve the materials. This may not only be costly but may cause delay “especially for investigator initiated studies where commercial support for this activity has to be purchased” (Duley et al., 2008, p. 44). Furthermore, import duties charged by some countries add significant additional costs to the

conduct of trials and this can be a barrier in low cost studies dependent on external funding (Duley et al., 2008).

2.5 Related studies

Many studies on HVTs examine the ELH needs, concerns and welfare of trial participants (c.f. Lindegger, Milford, Slack, Quayle, Xaba, & Vardas, 2006; Strode, 2005; Wassenaar & Barsdorf, 2007; Wassenaar & IJsselmuiden, 2007). It is felt that a preoccupation with the needs and concerns of research participants has resulted in the neglect of empirical studies on researchers, in general, and researchers' needs and concerns in particular. This study aims to address this oversight and determine and examine researchers' ELH needs. Such information may inform the improved ethical conduct of HVTs. While there is a clear lack of empirical studies on the ELH dilemmas, needs and concerns of HVT researchers, studies on researchers' dilemmas and needs in other studies and settings may provide some insight into the ELH dilemmas and needs faced by HVT researchers. Some of these are reviewed below.

Grinyer (2001) examined different ethical challenges that professional and academic researchers encounter in the health field in both non-clinical and social research. She found that some of the ethical dilemmas that researchers face include unexpected challenges or problems that may occur when conducting covert studies, the ethical dilemma of causing alarm or distress, and ethical challenges in relation "...to researchers' ability to maintain confidentiality, their commitment to welfare of respondents, and the tensions that arise from undertaking research for an employer" (Grinyer, 2001, p.123). In another study Hyder et al. (2004) surveyed 670 health researchers in developing countries to investigate researchers' "concerns and opinions regarding ethical review processes and the performance of developing countries' and US international review boards" (p. 68). This study found that researchers have concerns about inadequate ethical review by host countries

RECs. According to Hyder et al. (2004, p. 68) these results highlighted the need to have “ethical review of collaborative research in both the US and host countries”.

Keith-Spiegel et al. (2006) sampled 886 experienced biomedical, social and behavioural scientists to determine what scientists/researchers want from RECs. Participants rated 45 descriptors of REC actions and functions as to their importance. As predicted, scientists rated justice issues as more important than competence or other issues. Scientists gave procedural and interactional justice the highest importance. Scientists indicated that they experience an ethical challenge negotiating their legal rights and working collaboratively with RECs.

A more recent study conducted by Elsayed and Kass (2007) investigated one of the common challenges faced by researchers: obtaining informed consent from study participants involved in health research. They interviewed 95 researchers in Sudan and found that one of the ethical challenges that researchers face is obtaining informed consent from study participants. Factors that result in researchers not getting informed consent from study participants include “...cultural diversities, lack of communication due to language barriers and a high illiteracy rate among Sudanese citizens” (Elsayed & Kass, 2007, p. 95).

Although very limited in relation to the present study, the above studies highlight some of the ELH issues that may emerge. For example, some of the challenges that researchers face – as presented later on in this thesis - include the challenge of maintaining confidentiality, their commitment to welfare of respondents, difficulties obtaining informed consent, negotiating their legal rights and working collaboratively with RECs.

Of particular relevance to this study is Milford et al.'s (2006) investigation of the ELH concerns, resources and needs of Research Ethics Committees (RECs) in 15 African countries that have conducted or are planning to conduct HVTs: Uganda, Kenya, Botswana, South Africa, Tanzania, Code d'Ivoire, Ethiopia, Senegal, Zambia, Zimbabwe, Malawi, Cameroon, Gambia and Burkina Faso. They found that members of these committees needed assistance with understanding the scientific design of the vaccines, had variable support infrastructure, had difficulty making phase determinations and were unaware of local laws impacting on clinical trials. Several RECs indicated that they lacked funding and material resources (Milford et al., 2006). Only a third of RECs had adequate funding and most of these were from Southern Africa. The study also showed that RECs that had access to computers, email and the internet had this access through institutions and personal support. Furthermore, not all RECs had access to infrastructure (Milford et al., 2006). Forty percent of the participants in the study did not have dedicated REC office space. Lastly, Milford et al. (2006) found that 67% of the respondents rated UNAIDS (2000) guidelines on HVTs as very appropriate, while the Belmont Report was rated least appropriate.

Although the study by Milford et al. (2006) investigated RECs, not researchers, conducting HVTs, it gives an indication of what might be the most needed resources, ethical dilemmas and concerns of researchers in HVTs in African countries. This study however provides some information on ethics, law and human rights issues that RECs face.

A review of the literature reveals that research on ELH issues in HVTs has been dominated by the study of research participants. Drawing on the literature available on researchers, in general, this study aims to shift the attention from researching trial participants to researching vaccine trial researchers and explore their ELH dilemmas and the resources that they use for solving these problems.

2.6 Literature review summary

HIV/AIDS infections remain highest in Africa, especially Sub-Saharan Africa. South Africa has the highest HIV infected population at an estimated 5.4 million. The high HIV prevalence in Africa has been attributed to sexual behaviour amongst heterosexual African populations. As a result of the alarming numbers of HIV infections and deaths in the African continent, the need for a successful HIV preventive vaccine is vital. A variety of HVTs are currently being conducted in different African countries to continue the search for a successful vaccine. In conducting these trials, researchers face a number of challenges. These come in the form of ethics, law and human rights dilemmas. In some cases researchers also lack the necessary material resources needed to conduct successful trials.

Previous related studies have shown that some of the challenges researchers may face in conducting HVTs include ability to maintain confidentiality and obtaining informed consent from participants. Barriers to the conduct of trials are reported to include lack of adequate funding for trials and lack of trained research staff. Ethical guidelines play a crucial role in promoting ethically sound research. Some researchers have expressed that the UNAIDS (2000, 2006) guidelines are the most appropriate in providing requirements for the conduct of ethically sound research. Ethical and legal issues in HIV vaccine research must be comprehensively identified and analysed and appropriately resolved to assure the scientific success of trials and the protection of individual and community interests.

3. Methodology

3.1 Aims

Aim 1

To investigate ELH dilemmas, challenges and needs of researchers in HVTs in different African countries conducting and/or preparing for HVTs.

Rationale

According to Keith Spiegel et al. (2006) the welfare of all personnel participating in and conducting research should be safeguarded. This study is based on an argument that participants' needs may be better met if researchers' ELH concerns are identified and addressed. Therefore researchers can better take care of trial participants if researchers' ELH challenges are identified and addressed. An investigation of researchers' ELH concerns will hopefully make a contribution to the lack of data on this topic, inform remedial actions, if necessary, and remove some of the possible barriers to researchers' successful implementation of HVTs in Africa.

Aim 2

To establish which resources are available to researchers and which resources researchers have no access to.

Rationale

Availability of resources is essential if HVTs are to be successful. HVTs are well funded by various international organisations such as the National Institutes of Health (NIH) in the United States of America through the HIV Vaccine Trial Network (HVTN). Although HIV vaccine research is well funded, less funding is provided for HIV vaccine trials in developing countries than in the United States of America (IJsselmuiden, 2007). Results from this study regarding the availability of resources to HVT researchers, and researchers' perceptions of their appropriateness will hopefully reveal what the resource needs of trial site researchers are. This information will hopefully inform the relevant stakeholders for limited funding to be allocated appropriately.

Aim 3

To investigate which ethical guidelines and legislative frameworks researchers in HVTs in African countries find most appropriate or most inappropriate in addressing their ELH needs and concerns.

Rationale

Mattingly (2005) suggests that predetermined ethical guidelines are not always appropriate due to the context-specific nature of ethical dilemmas that arise in research in developing countries. It is therefore important to find out how researchers in HVT sites in Africa perceive the different ethical and legislative guidelines adopted at their sites.

3.2 Research design and methodology

This study used both quantitative and qualitative research methods. Qualitative research is subjective in that it entails getting involved in people's lives and getting the insider perspective (Breuer, Mruck, & Roth, 2002). The idea is that to learn more about a phenomenon, it is impossible to be impartial, detached and/or uninvolved completely (Silverman, 2004). As its name suggests, this kind of research method is concerned with the quality of the phenomena investigated. Qualitative research tries to interpret phenomena exactly as they are experienced in a given context, and as constructed by the people.

In contrast, quantitative research is not as flexible as qualitative research but is 'objective', distant and concerned with 'facts'. The response category from quantitative items from which respondents may choose is closed-ended (Mack, Woodsong, MacQueen, Guest, & Namey, 2005). The advantage of quantitative research method is that it allows for meaningful comparison of responses across respondents (Mack et al., 2005). In so doing, quantitative researchers seek to present findings in a scientifically balanced way.

It is for the above-mentioned strengths of quantitative and qualitative designs that this survey employs both qualitative and quantitative research design. The study attempts to draw on strengths of both designs to give a deep analysis and understanding of the research questions. The aim of the study was not only to generalise research findings to other settings around Africa but to also to provide qualitative analysis to provide contextual understanding. The questionnaire which was used as a method of data collection was a mixture of both quantitative and qualitative items.

3.3 Procedures and data collection

The first step in the sampling process was to identify countries that were currently preparing to conduct HVTs or/and conducting HVTs. HVT sites in countries identified were then located. These sites were located via internet searches, IAVI newsletters and snowball sampling. Once trial sites were located, contact information of contact persons at the sites was obtained. All contact persons at the different trial sites identified were telephoned and briefly told about the study. The study cover letter, giving a brief description of the study, and the ethical clearance letter were then emailed to each contact person. Contact people, who in most cases were study coordinators, were asked to inform the Principal Investigator (PI) about the study. Letters were then emailed to the PI of each site to request permission for the study to be conducted at their sites.

Data was collected using a specially constructed questionnaire (as informed by the literature reviewed) consisting of four domains namely: Resources, ELH dilemmas/problems, ELH needs/gaps and laws/guidelines (See Appendix 3). This study employed both quantitative and qualitative research methods. Open-ended questions served to allow respondents freedom to indicate which ELH dilemmas they are facing to compliment the closed-ended questions which may have been too restricting, limiting responses from researchers.

The questionnaire, study cover letter and informed consent were emailed to trial sites once local permission was granted to conduct the study. Both the study coordinators and sometimes PIs informed the research staff about the study and encouraged participation. To ensure confidentiality, the questionnaire and informed consent were emailed to the contact persons who then forwarded the two documents to their respective research teams. Sending the documents to individuals would have jeopardized individual confidentiality because staff email addresses often bear individuals' names or surnames and sometimes both.

An email survey was used because it is cheap and fast (Robson, 2002). Unlike focus groups and interviews the researcher does not have to be in a face-to-face dialogue with respondents.

Respondents can also answer the questionnaire at a time that suits them and then email back their responses. Follow-up emails and phone calls were made to ensure that the participants received the questionnaire. Although very costly, follow up calls are necessary to increase the response rate given that the response rate of e-mail surveys is about 30% (Robson, 2002).

3.4 Sampling

At the beginning of data collection seven African countries were currently preparing or conducting HIV vaccine trials. These were Botswana, Kenya, Rwanda, South Africa, Tanzania, Uganda and Zambia (IAVI, 2007). Malawi was also indicated to be conducting HVTs by the HVTN website (2008). Researchers from 14 HVT sites in these African countries were sampled via snowball sampling. A database of all identified sites was created to keep track of sites contacted and those still to be contacted (Appendix 6). This database was updated regularly as sites were contacted and as sites gave permission. The database also indicated reasons given by some sites to not take part in the study, when spontaneously provided.

Snowball sampling was used because although identifiable and clearly located, the sample for this study was scattered (Galloway, 1997). Snowball sampling was also used to allow identified contact people from research sites to identify other HVT sites in their area or country. Sites that reported not being involved in HVTs were asked if they knew of trial sites that are conducting or preparing to conduct HVTs.

3.4.1 Response rate

Table 1 Trial sites contacted

Region	Country	Number of sites contacted	Total number of sites accessed	Total number of trial sites never accessed.		Total number of sites conducting/preparing to conduct HIV vaccine trials	
				Did not get through telephonically	Never got to speak to an appropriate contact person	yes	no
East Africa	Kenya	2	*	*	*	*	*
	Rwanda	1	*	*	*	*	*
	Uganda	2	*	*	*	*	*
Southern Africa	Botswana	2	*	*	*	*	*
	Malawi	1	*	*	*	*	*
	South Africa	5	*	*	*	*	*
	Tanzania	1	*	*	*	*	*
	Zambia	2	*	*	*	*	*
	Total	16	12	2	2	8	4

*¹ This information has been omitted to protect the confidentiality of individual trial sites as specified in the consent and ethical clearance

Table 1 above illustrates that sixteen HVT sites in eight African countries were contacted, two of which were follow-up sites. These sites, from East and Southern Africa, were identified through internet searches and snowball sampling. No HVT sites were identified in Western, Central and

¹ [*] used to maintain confidentiality

North Africa. Four of the sites identified could not be accessed after numerous attempts. A total 12 of the 16 trial sites contacted were accessed. Questionnaires were emailed to nine of the twelve HVT sites – that gave permission for the conduct of the study. Completed questionnaires were received from six of the nine HVT sites. Reasons given for not completing the questionnaires by sites who did not return any completed questionnaires included lack of time to complete the questionnaire while other trial sites did not give reasons for not completing the questionnaire. Not all researchers at the HVT site that participated in the study completed the questionnaire. The highest number of researchers who returned completed questionnaires from a single site was 12 and the lowest was one. A total of 34 completed questionnaires were returned (Questionnaires were emailed to each site's contact person who then forwarded the questionnaires to relevant site staff. It is for this reason that the exact number of site staff who received the questionnaire at each site is unknown). Only 31 of these were correctly completed. Responses were received from HVT sites in Botswana, Malawi, South Africa and Uganda.

3.4.2 Sample characteristics

The sample consisted of researchers from Eastern and Southern Africa. Approximately 94% (n=29) of researchers indicated that they were currently conducting HVTs while approximately 65% (n= 20) reported that they were preparing to conduct HVTs. Nearly Sixty-five percent (n=20) of researchers reported that they were currently conducting HVTs and preparing for HVTs. It must be noted that some researchers indicated that they were conducting HVTs and also preparing for new HVTs. The sample consisted mostly of research nurses and clinicians/medical officers with approximately 26% (n=8) each, having completed the questionnaire. Following research nurses and medical officers were study coordinators 13% (n=4), research educators 10% (n=3), principal investigators 10% (n=3), and program director, research assistant, pharmacist and data officer all at 3% (n=1).

3.4.3 Distribution of the sample

Most of the respondents – approximately 52% (n=16) - in this study were from HVT sites in South Africa followed by Uganda with approximately 39% (n=12) as illustrated in figure 1. The least number of respondents – nearly 6.5% (n=2) - were from HVT sites in Botswana and nearly 3.5% (n=1) from Malawi. The low response rate from Botswana and Malawi is attributed firstly to the fact that the two countries had fewer HVT sites than South Africa and Uganda. Secondly, the sites in Botswana and Malawi were follow-up sites that were not currently conducting any HVTs.

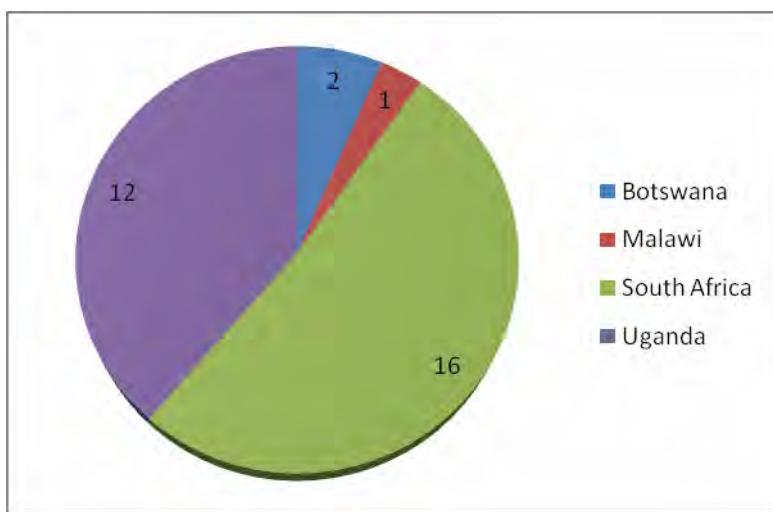


Figure 1. Distribution of respondents by country

Figure 2 depicts the distribution of the research staff who took part in this research. These included around 10% (n=3) principal investigators, approximately 26% (n=8) research nurses, about 26% (n=8) clinicians, research counsellor 3% (n=1), around 10% (n=3) recruiters/educators, data officer 3% (n=1), research assistant 3% (n=1), Country Program Director 3% (n=1), Pharmacist 3% (n=1) and approximately 13% (n=4) study coordinators.

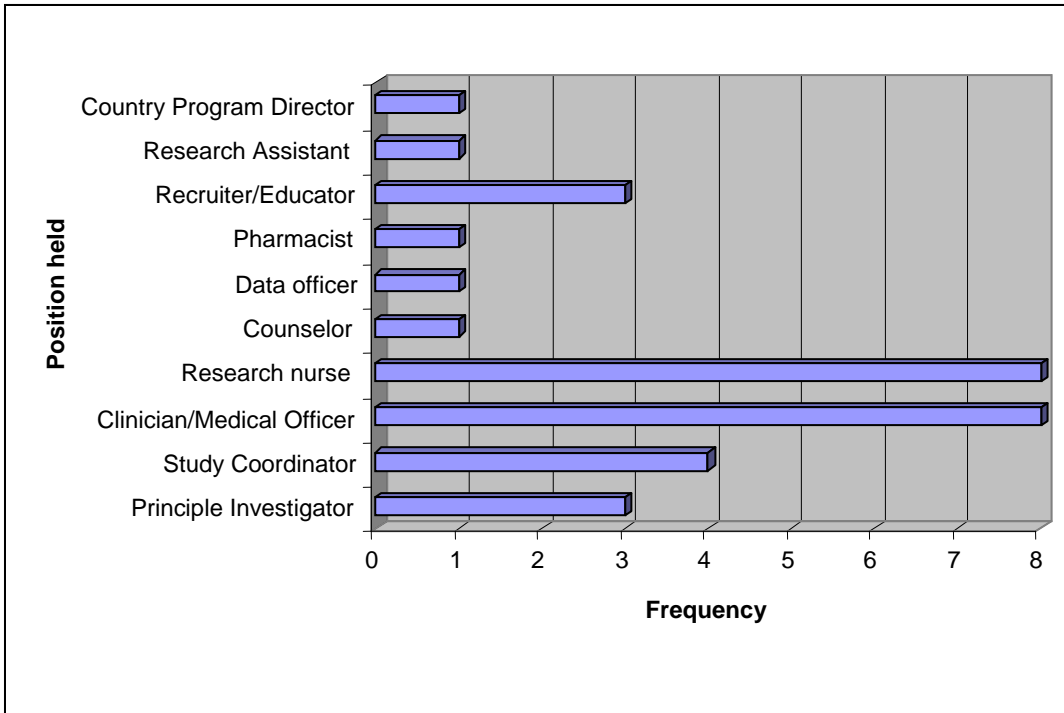


Figure 2. Distribution of sample by position held

Approximately half of the responses (n=16) came from research nurses and clinicians. The least number of respondents were data officers (n=1), pharmacists (n=1) and counsellors (n=1). Three of the responses were from PIs and four were from study coordinators.

3.4.4 Funders/Sponsors

As represented in figure 3 below, the most prominent funder of HVTs in this study was the US Division of AIDS (DAIDS). Approximately 65% (n=20) of the researchers reported DAIDS as one of the funders of the trials.

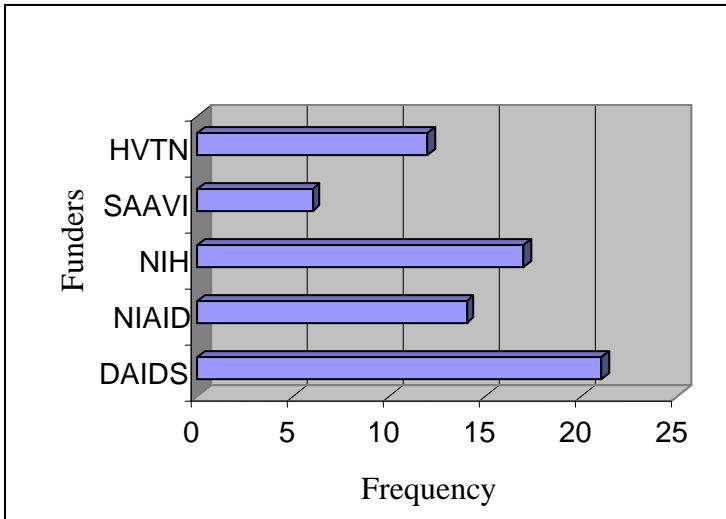


Figure 3: Distribution by Funders

According to responses from researchers, DAIDS funds HVTs in both East and Southern Africa. The second most common funder of HVT sites preparing to conduct and currently conducting HVTs in this study was the US National Institutes of Health (NIH) indicated by with 54.8% (n=17) of the researchers. The results of this study show that HIV Vaccine Trial Network (HVTN) funds HVTs in Southern Africa while the South African AIDS Vaccine Initiative (SAAVI) funds some trial sites in South Africa.

3.4.5 Phase of trials conducted

As shown in figure 4, researchers who participated in this particular study were involved in the conduct of different phases of vaccine trials. Figure 4 shows that fifteen respondents (48.3%) indicated that their trial site was conducting phase II HVTs. Thirteen respondents (41.9%) revealed that both phase I and II HVTs were conducted at their site. Only one respondent was from a trial site only conducting phase I trials. Two participants were based at follow-up sites.

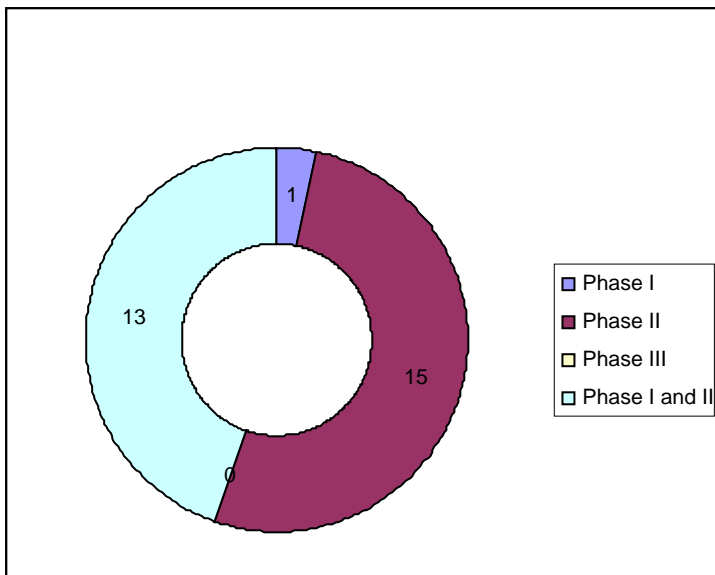


Figure 4. Distribution by trial phase

3.5 Instrument

3.5.1 Content

A constructed questionnaire was the instrument use in data collection (Appendix 5). It consisted of 18 items, a mix of quantitative and qualitative items. The questionnaire was informed by the literature reviewed at the beginning of the study. It consisted of six parts: demographic details, Ethics, Law and Human Rights Dilemmas/problems, resources, infrastructure, needs/gaps and guidelines and law (See Appendix 3).

3.5.2 Validity of the instrument

Validity was not formally assessed. However, the findings of this study reflect what the study intended to investigate. The questionnaire therefore measured what it intended to measure. It had face validity - the items in the instrument represented all facets of the subject of investigation (See Appendix 3) - and was comprehensive enough to collect all the information needed to address the aims and goals of the study. Demographic data helped establish that the instrument was administered to the appropriate population. The sample consisted of researchers in HVTs who are preparing to

conduct or currently conducting HVTs. This is the appropriate population for the study questions being asked.

3.5.3 Reliability of the instrument

To increase the reliability of the data collection instrument, a questionnaire was used instead of an interview and other face-to-face methods of data collection. Questionnaires are more reliable because of their anonymous nature and they also encourage greater honesty (Cohen, Manion, & Morrison, 2007).

Secondly the use of both open and closed-ended items enhanced the reliability of the questionnaire. Using only open-ended questions can lead to laziness and unwillingness to complete questions by respondents while using only close-ended items may result in lack of authenticity in the responses (Cohen et al., 2007). Using both types of items increased the reliability of the instruments.

The questionnaire was reliable in identifying ethics, law and human rights challenges researchers face when conducting HVTs in African countries. Items 7A to 7L of the questionnaire measured these challenges and the reliability calculations yielded a Cronbach's alpha of .919 as depicted in table 1 below in a SPSS output. Table 2 depicts a high item-total statistics of the twelve items.

Table 2 Reliability statistics

Cronbach's Alpha	N of Items			
.919	12			
	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
WorkingCollaborativelyWithParticipants	27.10	39.953	.879	.902
WorkingCollaborativelyWithCommunities	27.07	40.067	.920	.901
SocialValue	27.21	40.741	.762	.908
ScientificValidity	27.07	40.067	.920	.901
SubjectSelection	26.86	46.909	.460	.920
RiskBenefitDetermination	27.00	45.571	.477	.920
IndependentEthicalReview	26.90	45.667	.623	.916
InformedConsent	27.03	40.392	.889	.902
Confidentiality	27.10	40.310	.892	.902
ParticipantHIVInfection	27.38	39.815	.770	.908
ParticipantsPayment	27.10	42.096	.666	.912
HealthCare	28.00	50.214	-.054	.946

3.6 Analysis of Data

To investigate researchers' dilemmas, needs and resources, this study examined three main domains, namely ethics, law, and human rights. Both quantitative and qualitative data analysis methods were used.

Demographic data was analysed using basic descriptive statistics while the rest of the results were analysed using qualitative and quantitative content analysis and Chi-square analysis. Content analysis is the study of recorded human communication and it was chosen because it can be used to analyse both quantitative and qualitative data. "Content analysis is a summarizing, quantitative analysis of messages that relies on the scientific method ... and is not limited as to the type of variables that may be measured or the context in which the message are created or presented" (Neuerdorf, 2002, p.10). When used in a qualitative design content analysis has been defined as a

systematic, replicable technique for compressing many words of text into fewer content categories based on explicit rules of coding (Stemler, 2001). Content analysis enables researchers to deal with large volumes of data much easier (Stemler, 2001). It is a useful technique allowing researchers to discover and describe the focus of individual, group, institutional, or social attention (Weber, 1990). It is for this reason and for its usefulness in examining trends and patterns in documents that content analysis was used as a method of data analysis for this study.

Reliability in content analysis may be discussed in the following terms: stability and reproducibility. Stability refers to intra-rater reliability whereby the same coder gets the same results try after try (Stemler, 2001) or the tendency for coders to consistently re-code the same data in the same way over a period of time. Reproducibility refers to inter-rater reliability whereby coding schemes lead to the same text being coded in the same category by different people (Stemler, 2001). This study used intra-rater reliability because establishing inter-rater reliability often takes longer than intra-rater reliability (Stemler, 2001). Secondly intra-rater reliability encourages the sole coder to critically and deeply familiarise her or himself with the data which enhances reliability of the findings. The study also used SPSS to determine reliability of quantitative items. Using the two methods enhanced the reliability of the study.

Validity, in content analysis, refers to the correspondence of the categories to the conclusions and the generalisability of results to a theory (Stemler, 2001). It is imperative that one defines categories that accurately measure the idea and/or items one is seeking to measure (Stemler, 2001). To achieve validity in this study conclusions were made in relation to the research question, research design, research techniques and instrument of measurement used to establish a coherent and logical flow of this study. The generalisability of conclusions of this study is dependent on how the concept categories were determined, as well as on how reliable these categories are.

Quantitative designs are traditionally concerned with generalising findings and do not provide a deeper understanding of social phenomena, unlike qualitative design (Silverman, 2005). Results of a study are generalisable provided that the sample is representative (Silverman, 2005). It is proposed that the sample of this study was representative of a research team in HVT. The sample consisted of different research teams that make up clinical trials research teams: PIs, research assistants (RAs), recruiters, data officers, pharmacists, counsellors, research nurses and clinicians. Although not randomly selected, this study included researchers from different parts of Africa and this hopefully increased external validity of the results of this study.

3.6.1 Analytic technique of qualitative data

Figure 5 (below) depicts the analysis of the qualitative responses from researchers on ELH dilemmas and the challenges researchers face when conducting HVTs. The first part of the diagram, 'phrases extracted from content', is a list of key words extracted from researchers' responses. The key words were then grouped under a common theme. For example, non-maleficence and co-enrolment were grouped under the theme non-maleficence. Once this was done with all data, common themes were grouped under a common code. For example, the themes non-maleficence, exclusion criteria and reimbursement were grouped under the code ethics. All these themes reflect some of the ethical issues in HVTs as shown in the literature review.

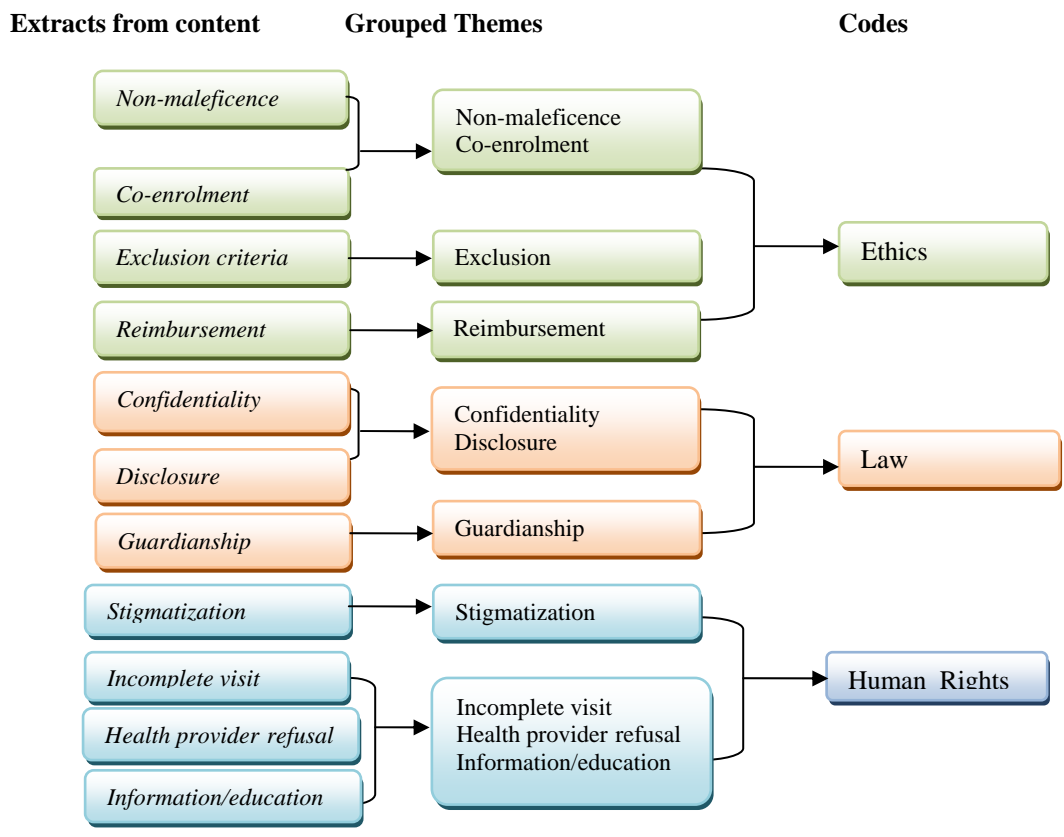


Figure 5: Analysis of Ethics, law and human rights dilemma and challenges

The data was analysed to generate three concepts which resulted in three main codes; ethics, law and human rights. The codes were constructed as illustrated on table 3 below.

Table 3 Analysis of guidelines and legislative frameworks that researchers find useful in conducting HIV vaccine trials

Concept	Definition	Theory	Themes	Code
The first concept that emerged in the data was 'Protection of people'	Researchers are concerned with protecting the welfare of research participants. They face a variety of dilemmas and challenges when trying to achieve this.	Emanuel et al. (2004)	Non-maleficence, subject selection/exclusion criteria, reimbursement It is from these themes that it is established that researchers are concerned with protecting people/participants.	Ethics
The second concept Legal issues	Researchers have concerns about the legal rights and the exercise of these rights by participants	Nation legislatures on the conduct of clinical trials, National guidelines	confidentiality, guardianship	Law
The third is respect for human rights	Researchers have concerns about participants' knowledge and exercise of their human rights.	The Universal Declaration of Human Rights adopted in 1948	rights, stigmatization	Human Rights

The last section of the questionnaire (section F) was used to identify guidelines and ethics resources that researchers prefer to use when conducting HVTs. Figure 6 below is a representation of responses given by researchers. Part A of the graph is guidelines as listed by researchers. These were grouped into three categories: Local boards, National guidelines and International guidelines as shown below.



Figure 6: Guidelines and frameworks listed by researchers

3.7 Ethical Considerations

Ethical considerations are very important in the conduct of all research studies. Before the study is conducted, a proposal or protocol is examined by a REC to determine if the study is ethically appropriate. This particular study was granted ethical clearance by the HDSS Research Ethics Committee of the University of KwaZulu-Natal approval number HSS/0168/08M. The study adhered to the required ethical standards as stipulated below.

3.7.1 Informed consent procedure

One of the crucial aspects of research ethics is the process of informed consent (IC). For this study an IC form (Appendix 2) was attached to each questionnaire emailed to participants. The participants did not sign the informed consent form. Instead, by answering and returning the completed questionnaires, participants consented to participating and this was clearly stated in the consent form. All study participants voluntarily gave consent to participate and they were permitted to withdraw from the study if they wished to do so at any time without penalty. Participants were made aware of

all important concepts and procedures involved in the research including what is expected of them as participants in the study through an IC and a cover letter (Appendix 1) which was also attached to the questionnaire. The cover letter also explained the purpose and rational of the study.

3.7.2 Procedures to ensure confidentiality

Although study participants are usually assured of confidentiality of the information they give, absolute confidentiality cannot be ensured. For example in this study the countries that were sampled are mentioned and there are a limited number of HVT sites in each country. As a result it may be possible to determine which sites were included. It is therefore vital for researchers to put all the necessary procedures in place to maximise confidentiality of information given by respondents and this study achieved this by doing the following.

Questionnaires were emailed to a contact person at each identified HVT site to forward to the research staff. To maximise confidentiality, a common practice is to separate names and other information used to identify participants from the data collected from the study. In the case of this study, participants did not write their names on the questionnaires. Once completed participants returned the questionnaire to the contact person and all completed questionnaires from the site were emailed back by the contact person. Individuals did not return their own completed questionnaires because this might have jeopardised confidentiality. Having the contact person email the questionnaires was a way of ensuring confidentiality because often researchers' email addresses have their names or surnames and therefore make it easy to identify them by their email addresses.

3.7.3 Ensuring a favourable risk-benefit ratio

The risks anticipated in this study were no greater than those ordinarily encountered in daily life making it a low risk study. It was very important to ensure that by participating in this study,

researchers would not in any way experience risk greater than risk they encounter in their daily life while performing their duties.

All research studies have risks, inconveniences or costs, not just economical but also costs in human terms. It is therefore important for the researcher to weigh the costs of the study against the potential benefits. Researchers must always make sure that benefits of the study outweigh the risks or costs of the study and this particular study achieved that. This study did not have direct benefits to the participants but has the potential to benefit researchers working in HVTs in future. The intended benefit of this study is gain of information. This study identified ELH dilemmas faced by researchers. In doing so, we hope that the necessary stakeholders will be informed of the gaps in HIV vaccine researchers' resources and to be able to put programmes in place that will promote more ethical conduct of HVTs by researchers in African countries.

For this particular study, researchers needed approximately 15-20 minutes to complete the questionnaire. In some cases researchers might have taken longer, depending on their comprehension of the questions asked, and the length of their responses. Some researchers might have taken longer to answer the questionnaire because of not having enough time to answer all items at the same time. As a result, some of the inconvenience involved in this study was in the form of time researchers needed to commit to finishing the questionnaire. It is because of this that some sites indicated that they could not complete the questionnaire because of lack of time to do so.

4. Results

4.1 ELH dilemmas and challenges

Quantitative and qualitative items were used to identify ELH dilemmas and challenges researchers face when conducting HVTs in African countries. Items 4 and item 5 of the questionnaire intended to find out what ELH dilemmas and challenges researchers experience at their sites. Item 4, a qualitative open-ended question, required respondents to describe any ELH problem they have experienced in the last years. Item 5 of the questionnaire provided respondents with a list of ELH challenges they might have experienced in the last year when conducting HVTs at their site. This list was informed by the Emanuel et al. (2008) framework, the literature reviewed and personal experience as a researcher. An *'other'* option allowed respondents to add ELH challenges that might have not been on the list provided. These items provided quantitative and qualitative results that help establish ELH challenges researchers have faced in the past year. Ethics, law and human rights challenges are presented separately as follows.

4.1.1 Ethics challenges

Quantitative data as represented by figure 7 showed that researchers conducting HVTs in African countries experience different ethics challenges. These include concern about participants' infection with HIV during trials, determining social values, paying trial participants, working in collaboration with trial participants and working in collaboration with communities.

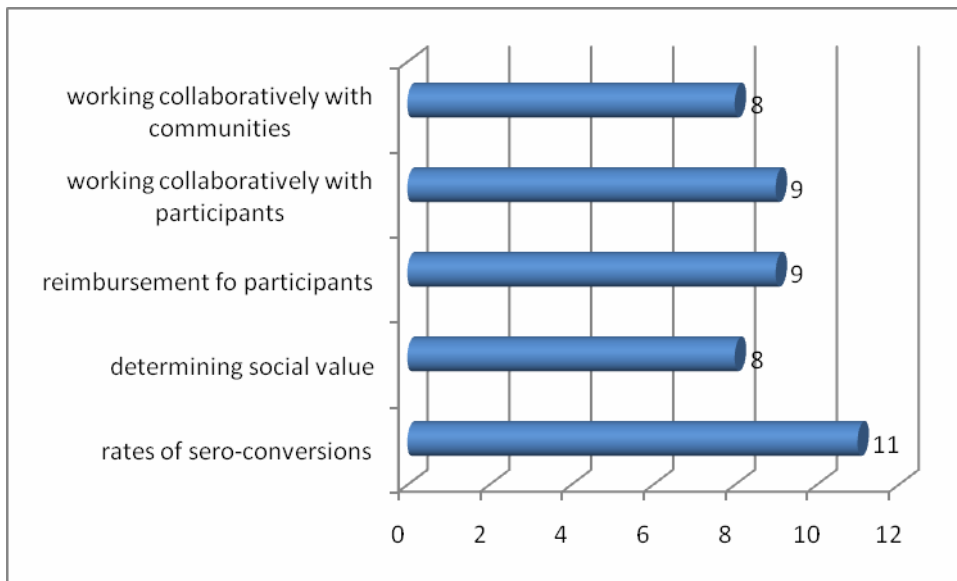


Figure 7. ELH challenges

These ethical challenges are elaborated below.

4.1.1.1 Ongoing respect for enrolled participants

The most frequently reported concern was that the rate of sero-conversions in HVTs. Thirty five percent of researchers (n=11) indicated that participants becoming HIV infected during a trial was experienced as a challenge. This was a challenge in that high rates of sero-conversions have implications for the efficacy of the study drug – it may not be working - and also a challenge in that the research staff was now obliged to secure care for these participants after the infection. A significant association was found between respondents who reported participants’ infection with HIV during trials as a perceived ethical challenge and country in which the trial is conducted. A significant association was found between participants’ infection with HIV during trials as a perceived ethical challenge and country in which the trial is conducted. As depicted in figure 8, researchers from South Africa were significantly more likely to report that HIV infection of participants during trials was an ethics challenge in the last year. This result was significant at ($\chi^2 (3) = 20.990, p < 0.05$).

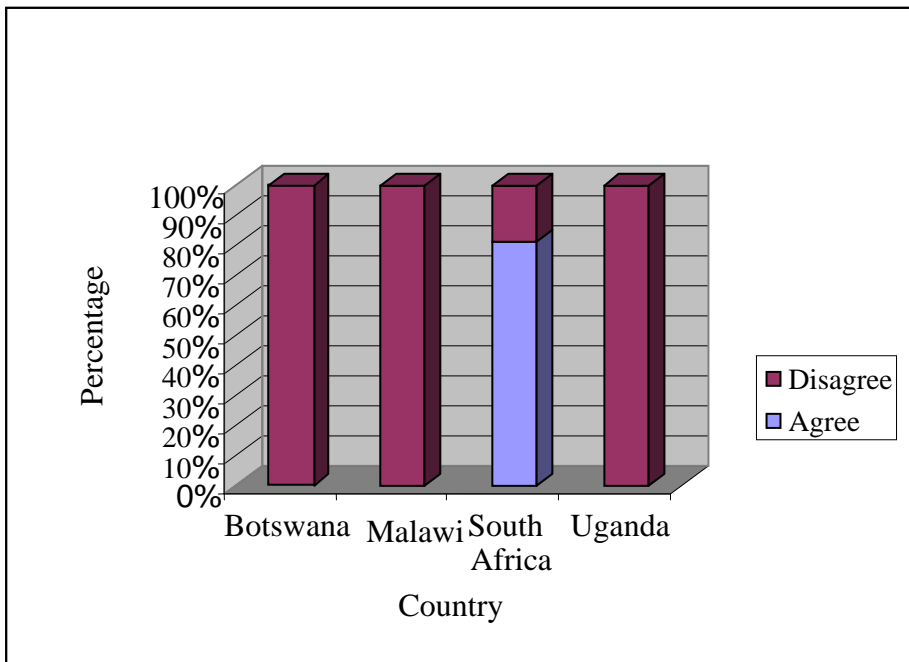


Figure 8. HIV infection of trial participants as a perceived challenge

Paying participants, otherwise referred to as reimbursement, was also a challenge for researchers as shown in figure 9. Approximately 29.03% (n=9) of researchers, all from Southern Africa, indicated that reimbursing trial participants was a challenge.

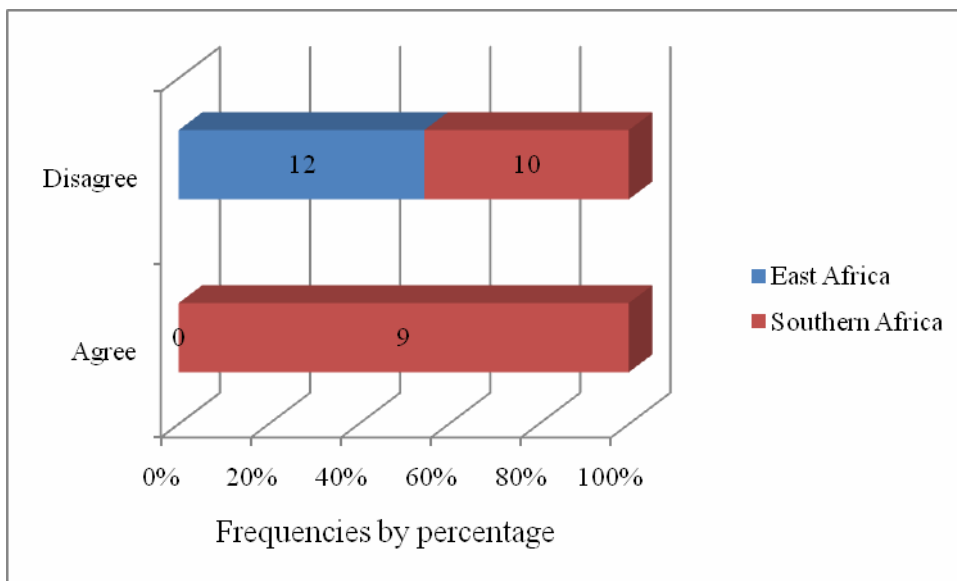


Figure 9. Paying participants as a perceived challenge

Most of the researchers who agreed that paying participants was an ethical challenge that they were experiencing, reported in their qualitative responses that this challenge was associated with the ethical dilemma of co-enrolment of HIV clinical trial participants.

4.1.1.2 Reimbursement

The main qualitative finding regarding researchers' ethics challenges was the concern researchers had about the consequences of reimbursing participants. Just over half of the researchers (n=16) who took part in this study indicated that they believed that many participants were motivated by reimbursement money to take part in HVTs. According to researchers, poor social-economic status in host communities was the main reason why most HVTs participants joined these trials for monetary gain. Some researchers wrote that:

“Poverty; the participants decision to take part may be influenced more by the stipend than the appreciation of the need for research” (East Africa)

“Economic factors – I think many participants choose to join trials for monetary gain” (Southern Africa)

Two ethical challenges emerged as a result of reimbursing trial participants: Participants' lack of comprehension of the informed consent documents and co-enrolment.

4.1.1.2 Social value

Another challenge faced by researchers conducting HVTs in this study was determining social value of research. 25.8% (n=8) of the respondents agreed that determining social value of research was a challenge. A significant association was found between social values as a perceived ethics challenge and country in which trials conducted at ($\chi^2(6) = 44.563, p < 0.05$). As demonstrated in figure 10, researchers from South Africa were significantly more likely than researchers from other sites

sampled in this research to indicate that determining social value was an ethics challenge they have faced in the past year.

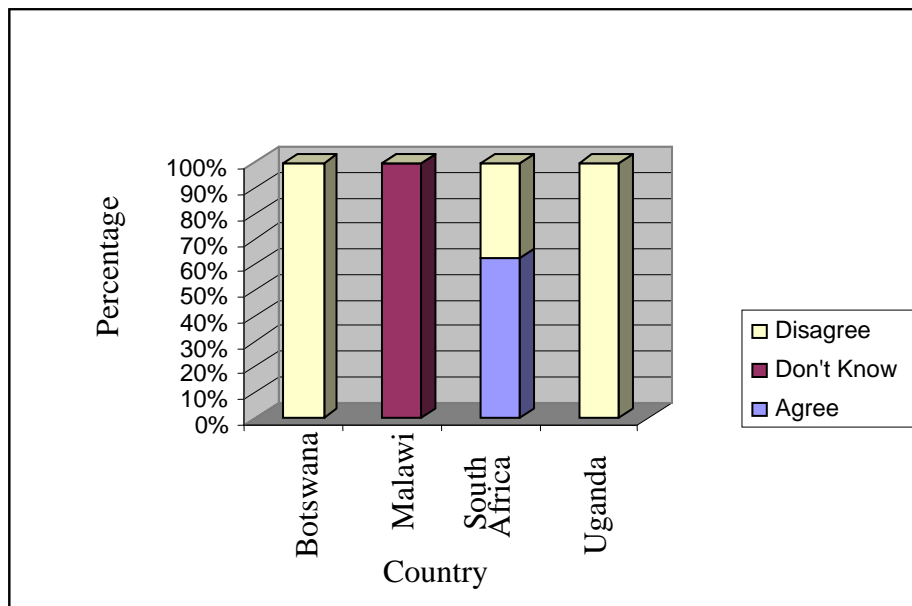


Figure 10. Determining social value as a perceived challenge

4.1.1.3 Collaborative partnership

Figure 11 shows that 29.03% (n=9) of the researchers agreed that working collaboratively with participants has been a challenge in the past year. All of these were researchers from South African HVT sites.

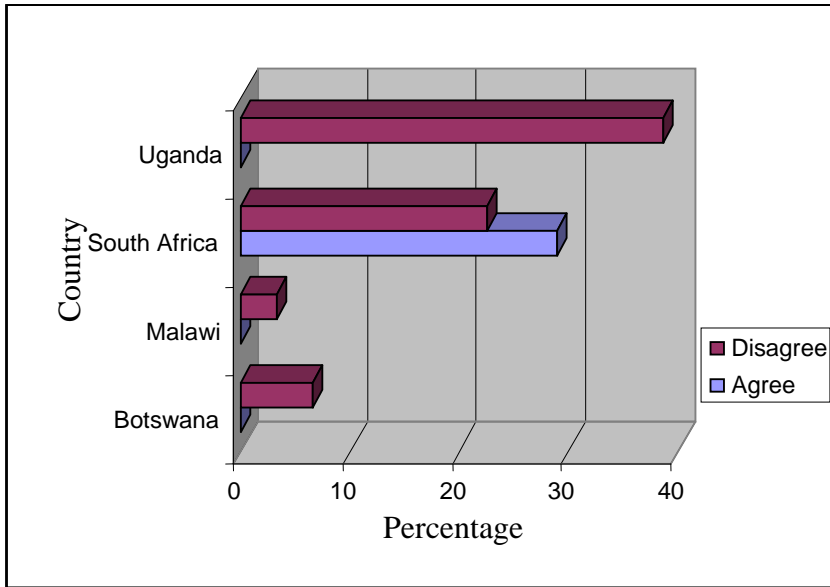


Figure 11. Working collaboratively with participants as a challenge faced by researchers

Half [50%] (n=8) of the researchers from Sites in South Africa reported that working in collaboration with communities has been a challenge as depicted in figure 12 below. This was not indicated by researchers from other countries.

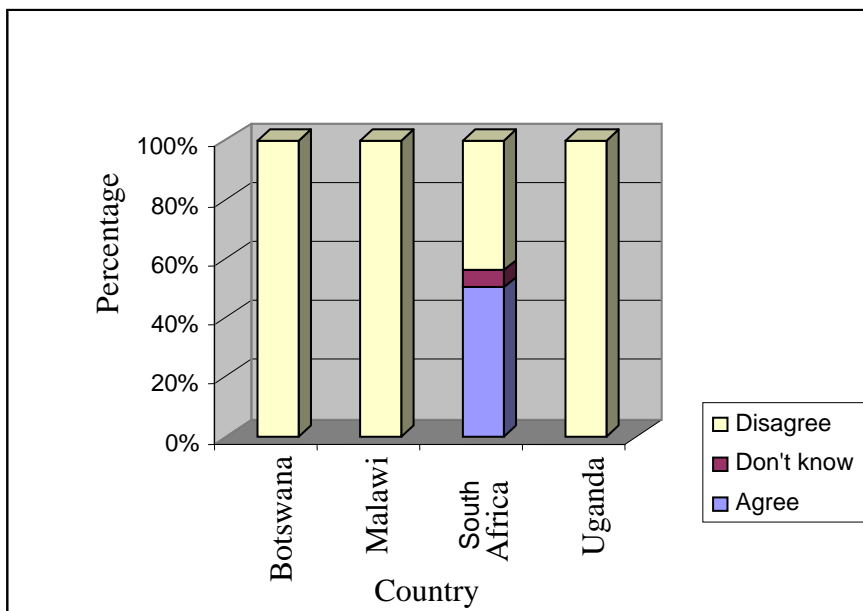


Figure 12. Working collaboratively with communities as a perceived challenge

Other challenges faced by researchers at their site included achieving scientific validity (22.6%), obtaining informed consent (19.4%) and maintaining confidentiality (19.4%). A single respondent, a PI, agreed that selection of participants was a challenge. None of the respondents indicated that independent ethical review of trials was a challenge or a problem.

4.1.1.4 Informed Consent

Firstly, researchers declared that they were concerned that some participants appeared to sign the informed consent form because of their need for money without full comprehension of its contents. To express this concern a study coordinator wrote that:

“Because the communities that we work with have a problem of unemployment, people from these communities may find themselves volunteering for HIV vaccine trials without fully understanding what they are volunteering for, just because the reimbursement looks attractive enough to join a trial. So often one wonders whether informed consent is truly what it is supposed to be or whether participants are not truly informed when they give consent but because of other pressures such as a need to put food on the table for their families they are forced to enrol into these trials”

Another researcher, a clinician, wrote that:

“...it concerns me that some participants join research solely for monetary gain and do not fully comprehend what research is about”.

4.1.1.5 Co-enrolment

Secondly, researchers reported that they faced the challenge of *“Participants enrolling in more than one study at the same time”*. According to some researchers this action is motivated by paying participants in vaccine trials money as reimbursement. The problem of co-enrolment resulted in some sites sharing participants’ information to check for possible participants’ enrolment in more

than one trial. As a result, researchers faced a dilemma of having to share participants' information with other sites. One female researcher, a study coordinator, wrote that:

“Discovering that we have a co-enrolment problem where we had to seek ethics clearance to check our participants' IDs against an existing database from another trial. The ethical problem is the issue of confidentiality but this was not compromised because we only used ID numbers to check and not participants' names”.

Another researcher also reported that *ethical issues around sharing participant identities with neighbouring sites so as to check for co-enrolled participants*” was an ethical dilemma.

Researchers who indicated that they were facing the challenge of co-enrolment at their sites expressed that sharing participants' identities with other trial sites to ensure that potential participants were not enrolled by another site was a dilemma they were experiencing. On the one hand they assured participants that their information will be kept confidential and on the other hand, they were obliged to ensure participants' safety and one way of doing so was making sure participants do not enrol in more than one product testing trial. They obtained permission from the local REC to put structures in place to check for co-enrolment.

Some researchers from two sites in Southern Africa reported that they recently stopped a trial due to safety concerns about the vaccine tested. As a result, researchers from these vaccine trial sites reported that they have experienced a number of ethical dilemmas. Firstly, one researcher wrote that:

“Non maleficence

This key pillar of ethics may have been compromised when it became evident that the vaccine used may actually predispose certain participants to HIV infection.”

This researcher was expressing that finding out that vaccines may predispose certain participants to HIV infection was an ethical challenge she faced. Researchers stated that they were faced with a dilemma when they were required to explain the situation to participants. Not being able to give trial participants clear explanations of the situation at hand was a challenge. To express this dilemma another researcher wrote that:

“Lack of information/ not knowing what could have caused participants to be susceptible to acquiring HIV infection...This is a dilemma: human right, participants deserve to know all the information whether good or bad”,

4.1.2 Law dilemmas and challenges

The main finding in this section was the concern that one of the legal dilemmas they have experienced in the past year was parents not permitting their children or dependents to participate as volunteers in HVTs regardless of them being legally allowed to consent. Researchers from both regions that took part in the study reported that this was a legal dilemma they faced.

Researchers from one of the HVT sites in Southern Africa indicated that:

“Participant was stopped in the study by parent even though he was legally allowed consent”

These researchers reported that sometimes, where adult consenting individuals are already enrolled in a trial, parents demand for them to be terminated as trial participants.

“Parents insisting their children be terminated from the study despite being legally independent”

Researchers from one site in East Africa, on the other hand, identified males’ refusal for their female partners to participate in trials regardless of their legal right to participate, as a challenge.

“Male spouse refusal of female partner’s participation in trial (female depending on spouse’s permission to take part)”

In both cases, refusal by parents and male spouses for their children and female partners respectively, to take in HVTs alters the number of potential study participants and in so doing may subsequently jeopardize the ability of the research team to meet recruitment and retention targets.

There were differences in some of the legal challenges researchers from the two regions experienced when conducting HVTs at their respective sites. The following are results on legal dilemmas and challenges by region.

4.1.2.1 East Africa

When responding to the item ‘Do you have concern about any legal aspects of conducting HIV vaccine trials?’ the majority of researchers in this region reported that they were concerned with the fact that it was not easy for trial participants to take legal action in cases of malpractice. Another finding from researchers in East Africa was lack of cooperation from some health care service providers in providing the necessary service to trial participants.

“Refusal by some health service providers to provide HIV testing to trial participants requesting contraception due to confusion that might come from their HIV test result”

4.1.2.1 Southern Africa

Some researchers in Southern Africa reported that ensuring confidentiality and privacy of participants’ data especially where disclosure of the information is in the best interest of the participant is sometimes a challenge. A study coordinator wrote that:

“Participants’ confidentiality and privacy issues, where the participant/partner is at risk but because you cannot disclose such info to anyone even though it is for the best interest of the participant”

Other legal concerns include the future impact of vaccine candidate given to participants. Often after being terminated from HVT or at the end of HVT participants are reportedly not followed up. As a

result, the future impact of the vaccine on former trial participants is not investigated for possible future impact. Some researchers reported that they have concerns about the permanent physical impact of the study drug on the participants.

“Physiological; permanent impact can take place in participants’ physiological mechanisms”

Although not reported by many researchers, lack of knowledge regarding legal frameworks informing the conduct of trials was one of the law concerns raised. One researcher wrote that:

“... I feel that there is lot researchers don’t know about the legal framework”.

4. 1.3 Human Rights challenges

As shown in figure 13, providing health care service to trial participants was the main quantitative finding regarding human rights dilemmas researchers experience when conducting trials. Sixty-seven point seven percent [67.7%] of researchers from East and Southern Africa agreed that providing health care services to trial participants was a challenge.

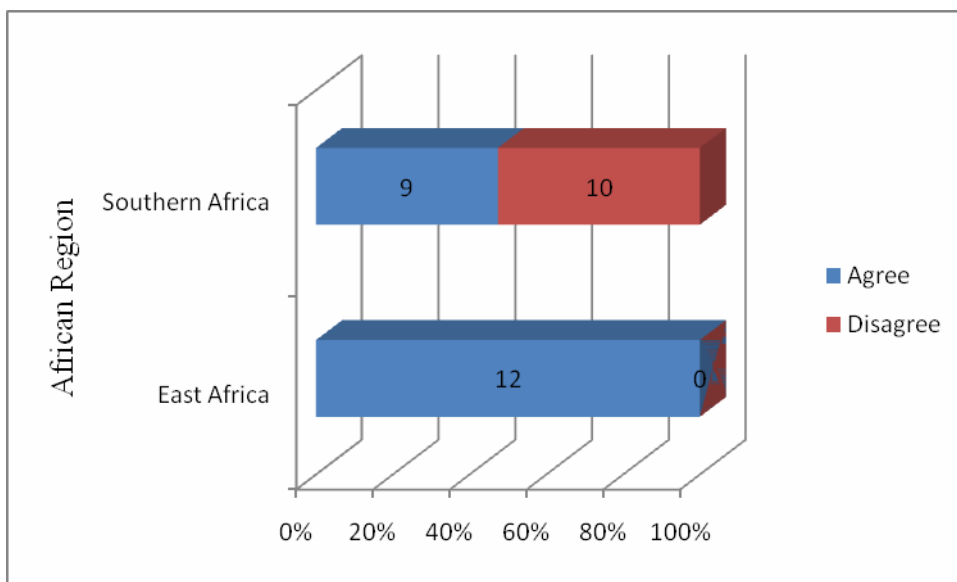


Figure 13. Providing health care service for participants as a perceived challenge

Almost half of respondents from Southern Africa and all researchers from East Africa agreed that providing health care service for participants was a challenge. Researchers also reported that cultural factors, socio-economic factors and lack of knowledge and illiteracy compromise participants' ability to exercise their rights. Figure 14 depicts quantified qualitative findings reflecting researchers' human rights concerns.

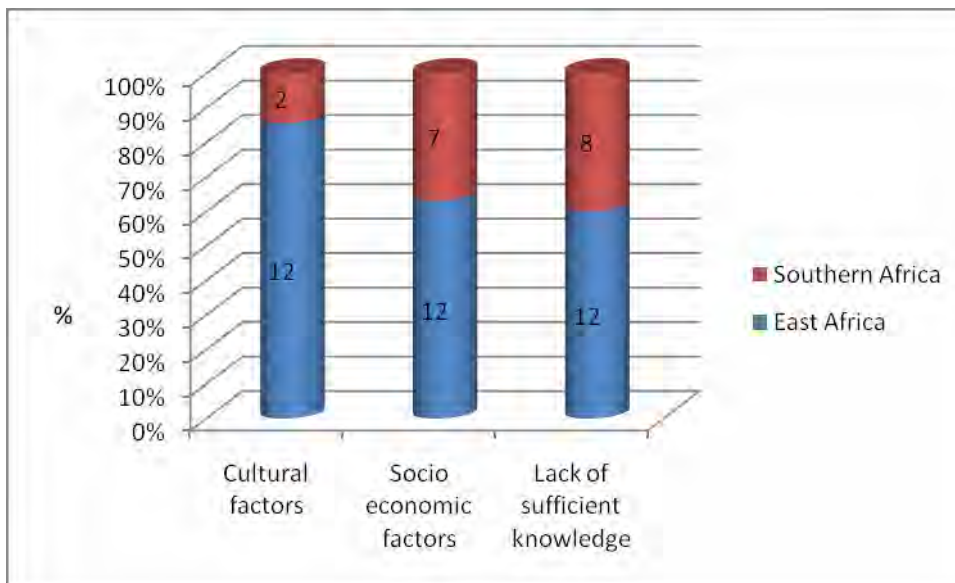


Figure 14. Researchers' Human Rights concerns

The main qualitative finding in this section was that three factors compromised people's ability to exercise their human rights when it come to making a decision to volunteer as a trial participants. These were namely illiteracy and lack of knowledge, socio-economic factors and cultural factors. Researchers from both regions noted that they experienced these factors as compromising people's autonomy.

4.1.3.1 Illiteracy and lack of knowledge

Trial participants

Researchers reported that HVTs often take place in host communities with high rates of illiteracy. As a result, most individuals volunteer to be trial participants without a full comprehension of issues

around human rights, ethics and of the research procedures. When responding to the item ‘Do you have any concerns about the human rights of the communities in which you work?’ researchers indicated that the communities need to be trained on ethical issues. One respondent wrote that:

“...communities have no idea on ethics issue, is need to be trained on it”

Researchers, Ethics committees and other governing bodies

A human rights concern was that not only participants but also researchers and RECs lack the necessary knowledge to ensure appropriate conduct of clinical trials. One researcher wrote that:

“...as I have indicated that Ethics committees and other governing bodies lack clinical trial knowledge and also scientists or Researchers in this field lack ethical knowledge in the context of clinical trials research”

4.1.3.2 Socio-economic factors

Researchers also reported that most participants’ human rights are limited by their need for money due to poor socio-economic status of most target populations. To express this concern, researchers wrote the following:

“The national and local socio-economical context makes the re-imbusement for participation a possible overwhelming incentive for taking part”.

A few researchers reported that as a result of potential participants’ poverty status, some researchers tend to exploit these individuals and communities.

“Yes, some researchers take advantage of the socio-economic problems of the community to lure them into participating without first making sure that the community understands what research or clinical trials is”

4.1.3.3 Cultural factors

Some researchers reported that the participants' rights, especially female participants' rights are compromised by some cultural obligations such as being required to be submissive to men.

Researchers who reported this were from East Africa. Some of the researchers wrote that:

“Female participants’ autonomy and rights may be limited by local cultural perceptions and practices”.

“Yes, Cultural practices that demand that women be submissive to men”

Another human rights concern that researchers reported was exploitation of trial participants.

According to some researchers, some trial participants are exploited by researchers as a result of a variety of contexts of vulnerability such as poverty and being a student. The following were some of the responses from researchers:

“The other concern is conducting clinical trials in areas where there is poor patient management, e.g research only looking at data collection but not making sure that the participants is managed properly if they become sick. I am not saying that they should duplicate what the primary health care is providing but at least help the local HCP by strengthening what they already offer”.

“Being next to a tertiary institution their willingness to participate may be exploited. Often the same people will volunteer every time”.

“Exploitation of rights for the benefit of the researchers and science is always a looming possibility. At the moment, adequate measures seem to be in place to prevent this”.

According to researchers from East and Southern Africa, social harm of trial participants in the form of stigmatisation and discrimination is a human rights challenge they faced at their sites. Researchers reported that some trial participants experienced discrimination as a consequence of participation in trials. This was expressed by a number of researchers including PIs:

“...participants may suffer discrimination or prejudice as a result of participation in the study”

(Southern Africa)

“Stigmatisation of potential participants by them being labelled guinea pigs by their peers and some in community” (East Africa)

In some cases, according to researchers from East Africa:

“Screen –outs were assumed to be HIV positive by other participants although there were other reasons for screen-outs”.

Researchers from both East and Southern Africa said that they were facing another human rights challenge in the form of blood specimen collection. Researchers reported that they were experiencing difficulties and challenges explaining to participants and convincing participants to allow for the necessary blood specimen collection.

“Convincing the participant that the number of blood tubes are required and justified” (East Africa)

Researchers from Southern Africa added that this challenge *“raises the question of whether participants believe that we are reimbursing them for their blood samples rather than their time /transport”*. To express her thoughts, a clinician from Southern Africa gave an example of a scenario that took place at her site recently:

“A participant was scheduled for a visit but did not want to complete the blood draws for the visit but insisted on receiving the full reimbursement for the visit. Our policy is to reimburse a fraction of the full reimbursement if the visit is not completed. The participant was angry and upset because he felt that we were only going to reimburse him in full if he agreed to do the blood draws.”

4.2 Needs and material resources

4.2.1 Identified needs

Researchers from East and Southern Africa listed different perceived gaps and resource needs that needed to be attended to and rectified.

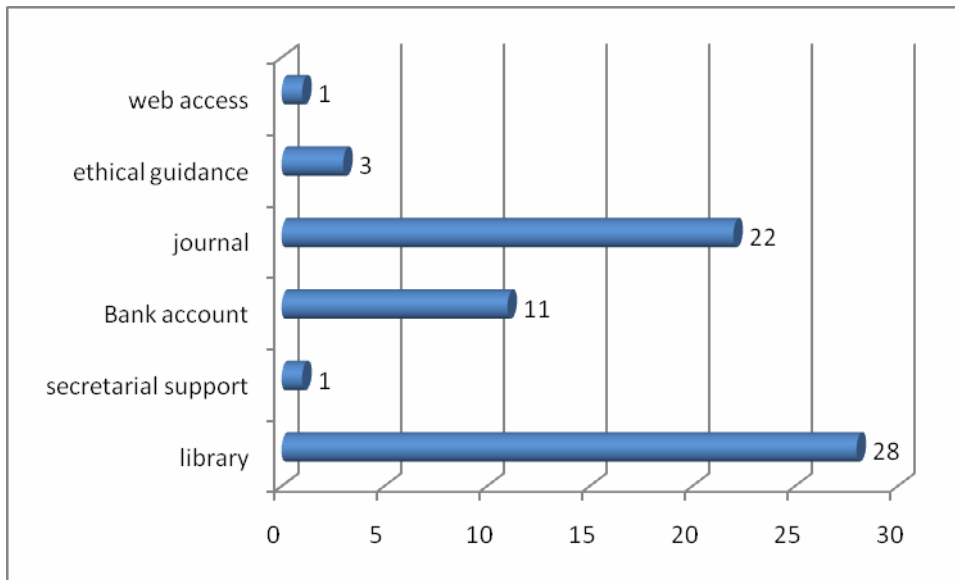


Figure 15. Identified needs

4.2.1.1 East Africa

Researchers mostly reported a need for awareness of participants' autonomy, especially for female participants. These researchers noted that women's rights are sometimes compromised by societal expectations and

“Myths and misconceptions regarding contraception in female participants”.

Secondly, these researchers reported a need to allow for *“HIV test result disclosure in the presence of potential harm to others by participant”*

4.2.1.2 Southern Africa

Overall, researchers in Southern Africa reported a need for the communities to be educated about research, and ethical issues regarding consent. Some of the responses included that:

“Informed consent needs to explain everything (transparency)” and

“Education & evaluation pre enrolment should be emphasized”.

“... communities have no idea on ethics issue is need to be trained on it”.

According to researchers there is a need for the communities to understand and accept research and clinical trials.

4.2.2 Infrastructure

Researchers conducting HVTs in African countries were asked about availability of infrastructure and other related resources at their respective sites. Although respondents’ indicated that they had access to most of the necessary infrastructure and material resources needed for the conduct of HVTs, 90.3% (n=28) did not have a library. Seventy-one percent (n=22) of researchers did not have site journals and 35.5% (n=11) did not have a study bank account.

Table 4 Availability of infrastructure and material resource

Infrastructure	Yes	No
Library	9.7% (n=3)	90.3% (n=28)
Bank Account	64.5% (n=20)	35.5% (n=11)
Site journal	29% (n=9)	71% (n=22)

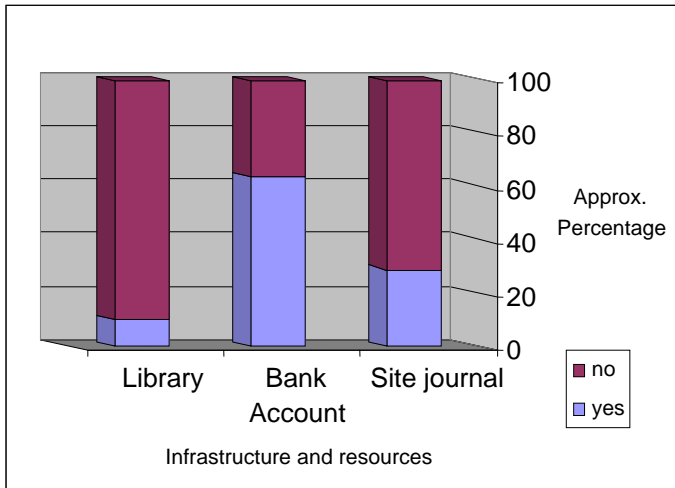


Figure 16. Availability of Infrastructure and resources

All (35.5%) of researchers who indicated that their site did not have a bank account were from South African sites that took part in this study. There were times when researchers from one site gave conflicting answers. For example, in one of the South African sites 22.6% (n=7) of researchers said they had site journals while 77.4% (n=24) said they did not have site journals.

Only three researchers responded to the qualitative item seeking to identify availability of infrastructure at their site. These were their responses:

“Library with latest books and journals”

“Office or computer for the CAB members especially the executive committee”

4.2.3 Material resources used to solve ELH problems at site

Respondents were asked to list and rate material resources they have used at their respective trial sites to solve ELH problems.

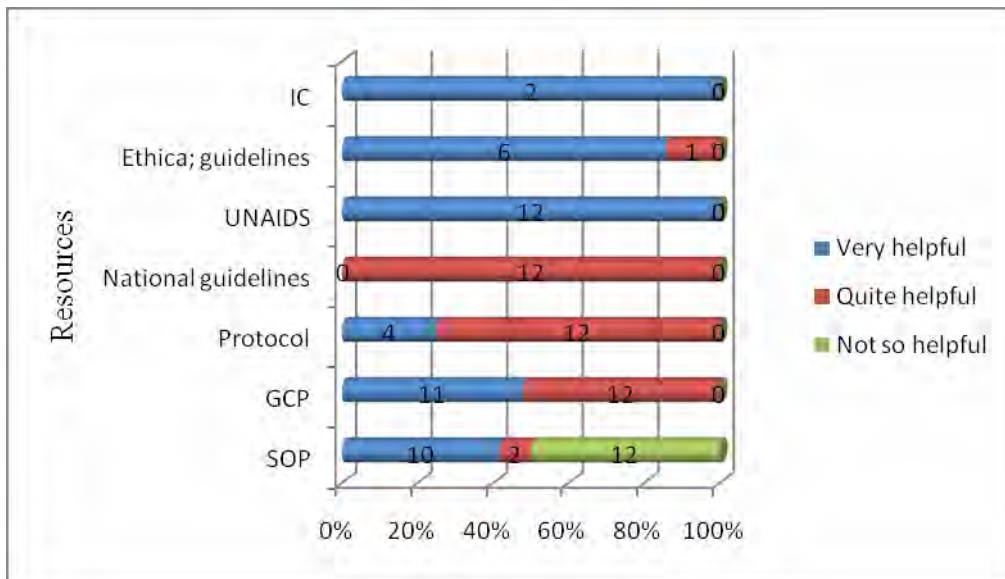
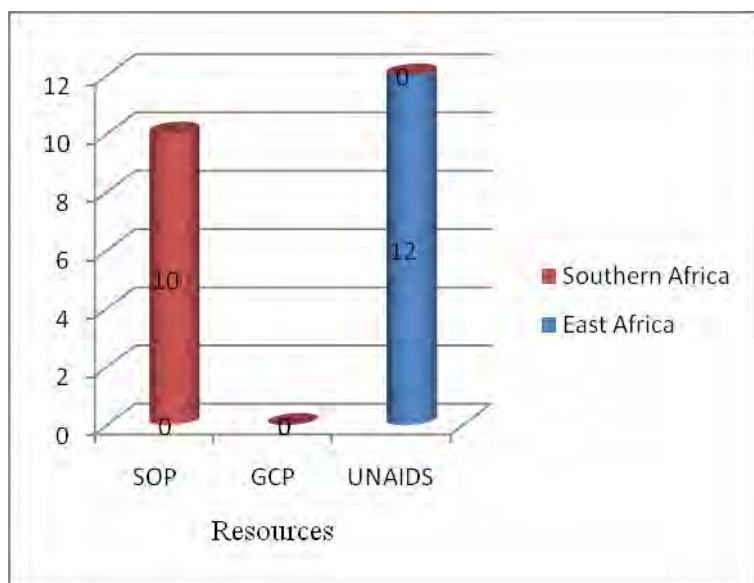


Figure 17. Resources perceived as helpful

Standard operating procedures (SOPs) were listed by most researchers (n=24) followed by Good Clinical Practice (GCP) guidelines with a total of 23 researcher listing them. The study protocol was the third most listed resource perceived as helpful by researchers, with 16 researchers listing it. Researchers rated these resources according to their helpfulness under the options ‘*very helpful*’, ‘*quite helpful*’ and ‘*not so helpful*’. UNAIDS (2000, 2006) guidelines were rated as ‘*very helpful*’ by 12 researchers. GCP guidelines were rated ‘*very helpful*’ by 11 researchers while SOP document was rated ‘*very helpful*’ by 10 researchers.

Three resources namely, national guidelines, – two of the four countries that took part in this study, South Africa and Uganda, have ethical guidelines specifically for the conduct of HVTs - the protocol and GCP guidelines were rated as ‘*quite helpful*’ by 14 researchers each. The SOP document was the most listed but half (n=12) of the researchers who listed it rated it as ‘*not so helpful*’. The SOP was the only listed resource that was rated as ‘*not so useful*’. Other resources that respondents listed were the constitution, CIOMS, HSP and HAVEG articles. These were only listed but not rated by some respondents.

As demonstrated in figure 17 above, there were differences in the way researchers from the two regions listed and rated resources that they perceived as helpful in helping them solve ELH challenges. Figure 18, 19 and 20 illustrate these differences.



Researchers from East Africa reported that UNAIDS guidelines were very helpful when solving ELH problems. None of the researchers from Southern Africa listed UNAIDS guidelines as helpful; instead they listed and rated the SOP as very helpful. These were the only two resources rated by researchers

as very helpful.

Figure 18. Resources perceived very helpful

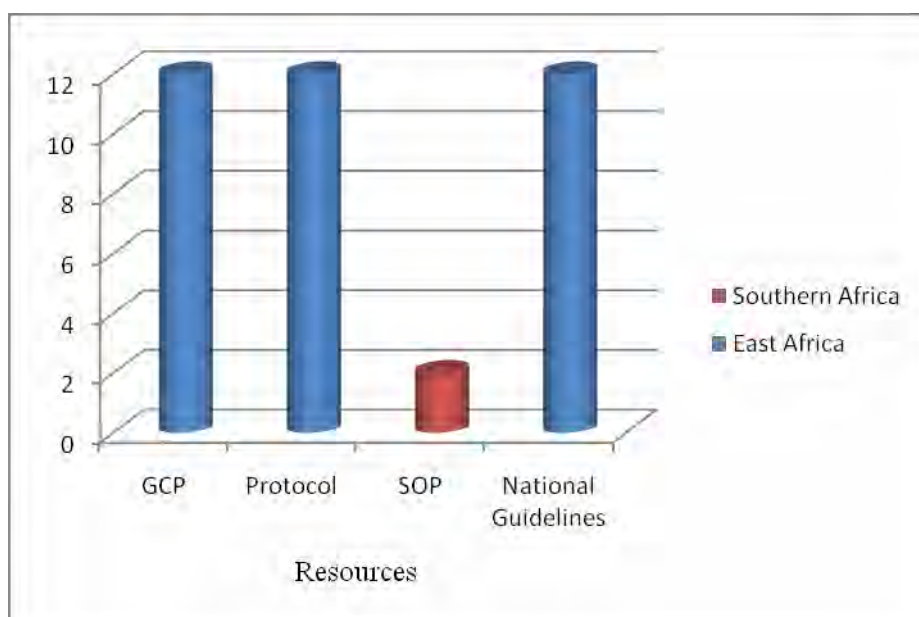


Figure 19. Resources perceived as quite helpful

Researchers from East Africa rated GCP, the protocol and national guidelines as having being quite helpful in solving ELH problems in the last year. A few researchers from Southern Africa rated their study SOPs as quite helpful.

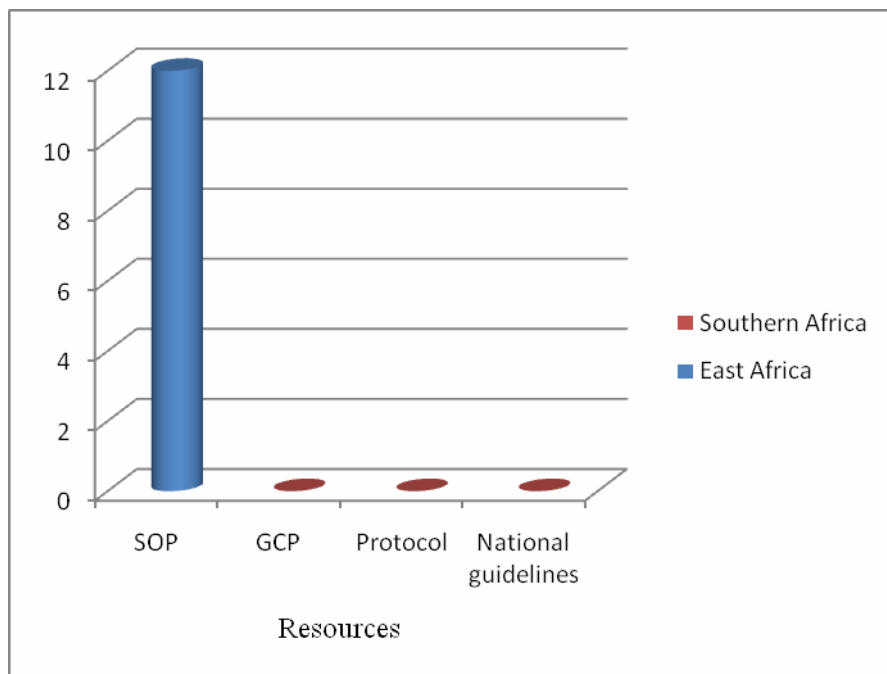


Figure 20. Resources perceived as not so helpful

Only one of the listed resources was rated as not so helpful. This was the SOP and although researchers from Southern Africa rated it as very helpful, researchers from East Africa rated it as not so helpful.

Of all members of the research staff, the medical officer/clinicians and research nurses listed and rated more resources as helpful in solving ELH challenges when compared to other research staff members. There was a slight difference in rating of resources by different research staff. For example, study coordinators only listed and rated GCP guidelines as very helpful. Surprisingly, both study coordinators and PIs did not list study protocols as a very useful resource. It was the clinicians, research nurses and recruiters who listed the study protocol as very useful.

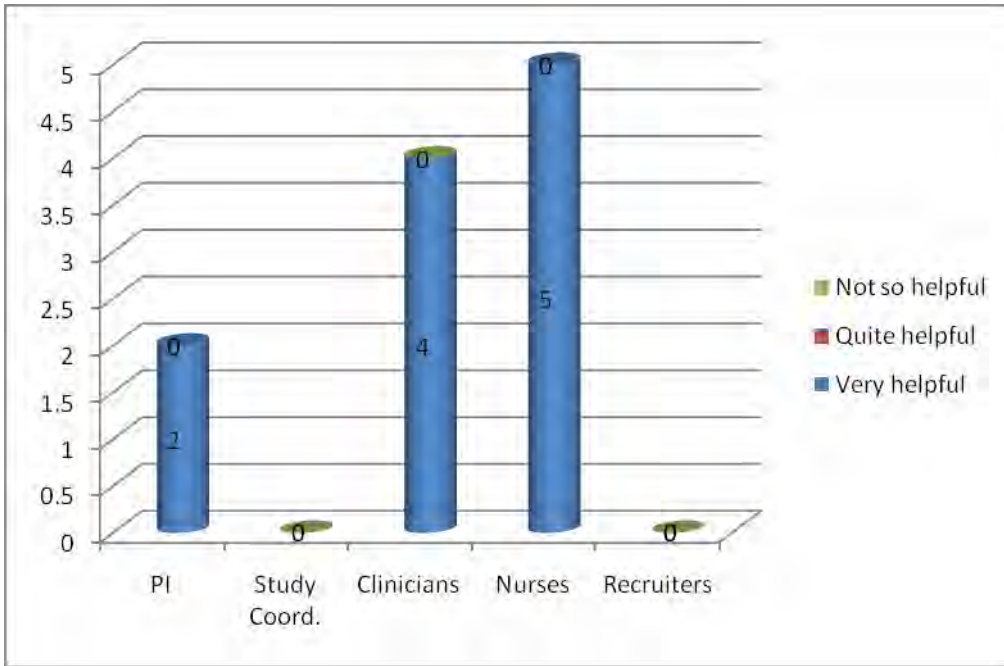


Figure 21. UNAIDS guidelines as perceived by researchers by position held

Clinicians and researcher nurses rated the UNAIDS (2000) and/or UNAIDS (2006) as very helpful in solving ELH problems as shown in figure 21. The only other research staff who rated UNAIDS (2000) and/or UNAIDS (2006) guidelines as very helpful were the PIs.

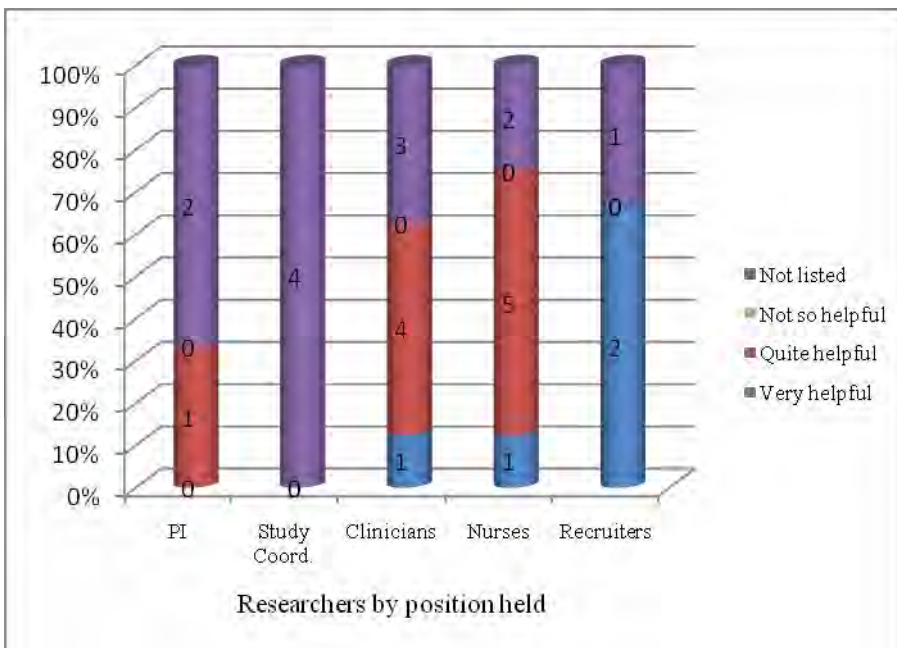


Figure 22. Protocol as perceived by researchers

Recruiters were the research staff who most frequently rated the study protocol as very helpful as shown in figure 22. This was followed by clinicians and nurses who also rated the protocol as very helpful. None of the study coordinators listed the study protocol as helpful. None of the study coordinators listed the study protocol as helpful.

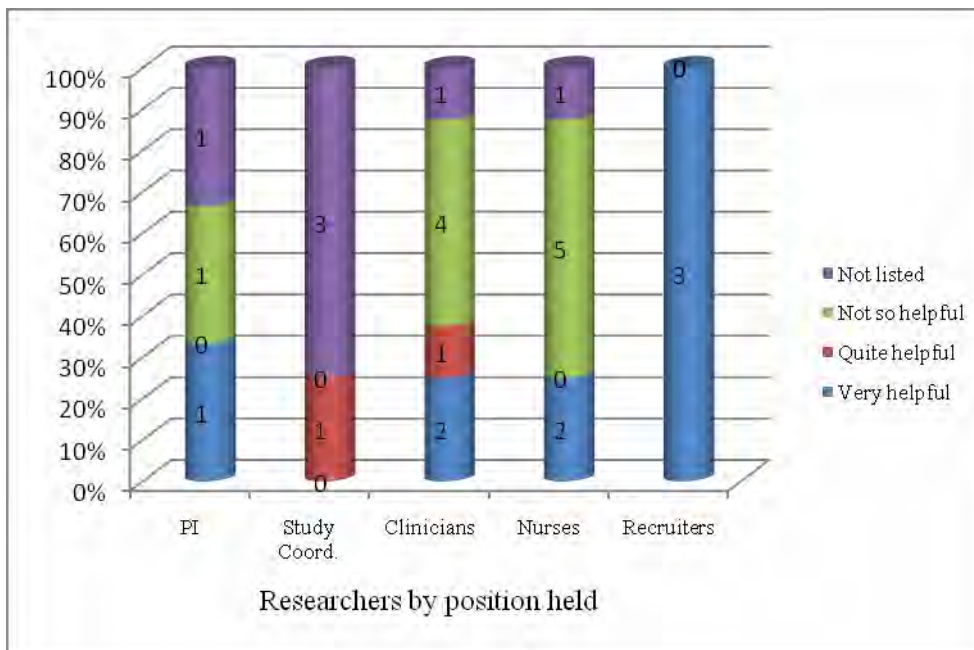


Figure 23. SOP as perceived by researchers by position held

All recruiters who took part in this study rated the SOP as very helpful followed by clinicians and nurses as shown in figure 23. Only one of the study coordinators and PIs rated the SOP as very helpful. Seventy-five percent (75%) of study coordinators did not list the SOP as helpful.

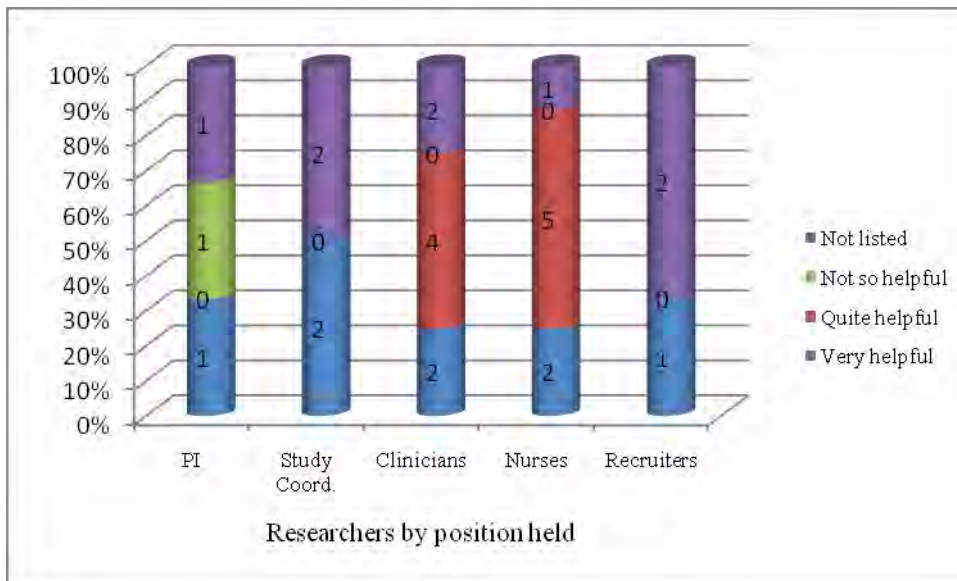


Figure 24. GCP as perceived by researchers

Figure 24 shows that the clinical staff – research nurses and clinicians - were the research staff members to report that GCP guidelines were mostly helpful in solving ELH problems. Twenty-five percent and sixty-two point five percent [25% and 62.5%] of research nurses rated GCP as very helpful and quite helpful respectively. Fifty percent [50%] of the study coordinators rated GCP as very useful but the other half did not list GCP as helpful.

Other resources that were listed included ethical guidelines, national guidelines, South African good clinical practice guidelines, OHRP human subject protection, HAVEG articles, UNAIDS (2006) HIV vaccine guidelines and informed consent documents. Approximately 16% of the researchers did not list any resources as having helped them deal with ELH problems in the last year when conducting HVTs.

4.3 Guidelines and frameworks used to solve ELH dilemmas

A variety of ethical and legal guidelines were listed by researchers as being useful in providing guidance on how to conduct HVTs. These guidelines were a mixture of national and international

guidelines. Researchers from East Africa found national guidelines to be very useful. However it was evident that some researchers still use and find some international guidelines useful in conducting HVTs.

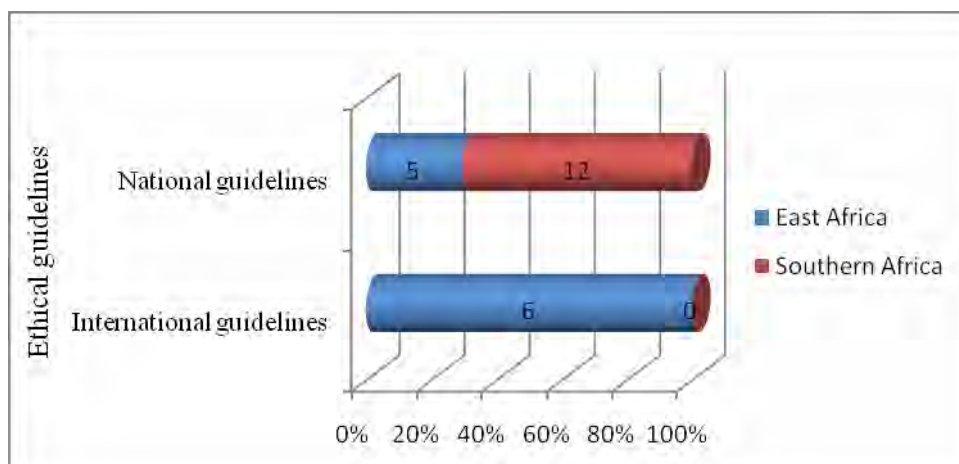


Figure 25. Ethical guidelines perceived as useful

Researchers did not report any guidelines or frameworks that they found problematic but reported that they faced challenges when using ethical guidelines in their countries. The biggest challenge was said to be lack of a reading culture and illiteracy in most host communities. Another challenge expressed by researchers from both regions was the lack of contextual relevance of some guidelines. To express that these guidelines should be localized: Some of the respondents wrote that:

“They are not yet customized to be in the South African context”.

This response shows that there are researchers who are not well informed about existing national guidelines (MRC, 2003) in their respective countries. Contrary to the extract from a respondent above, South Africa does have ethical guidelines specific for the conduct of HVT (MRC, 2003).

4.4 Summary of results (Main findings)

This research study produced several main findings. Firstly, different research sites in Africa face a different ELH challenges. For example, sites in Southern Africa indicated that the high rate of sero-

converters and reimbursement of trial participants were the two most common ethical challenges respondents experienced at their sites. In East Africa, researchers experienced parents not permitting their adult children or adult dependents to participate as volunteers in HVTs, regardless of them being legally allowed to consent, as a legal challenge.

Another main finding of this study is that there has been improvement in availability of infrastructure across HVT sites in Africa. Most participants reported that they have most of the infrastructure necessary for the successful conduct of trials. Nevertheless researchers still indicated the need for site libraries. Most researchers reported that they did not have a library at the HVT site. Researchers did however list the different resources they use to solve ELH challenges. UNAIDS (2006) guidelines and the SOP documents were rated as the most helpful resources that helped researchers solve ELH problems during their past year. Researchers did not report any guidelines or laws governing the conduct of HVTs as problematic. The findings do however show that most researchers find context relevant guidelines as the most appropriate to use in conducting HVTs in Africa. Examples of such guidelines are country specific guidelines – Kenya (NCST, 2005) and South Africa (MRC, 2003) - on the conduct of HVT.

5. Discussion

5.1 ELH challenge

5.1.1 Ethics dilemmas

5.1.1.1 Ongoing respect for enrolled participants

Paying or reimbursing HVT participants, prevention of HIV infection in trial participants and offering treatment to participants who become infected during the trial are three ways of demonstrating ongoing respect for enrolled HVT participants that will be discussed below.

The South African Medicines Control Council (MCC) policy is that trial participants be paid a flat rate of R150 per visit in clinical trials (Koen et al., 2008). Some observers believe that payment to trial participants is wrong in that it may be coercive, while others believe it is acceptable and possibly necessary to enhance recruitment for clinical investigation (Grady, 2005). Both qualitative and quantitative findings of this particular study showed that reimbursement of participants raises ethical concerns at different African HVT sites. The general perception amongst researchers who pointed out that paying trial participants may lead to ethical dilemmas was that participants' motivation to take part in HVT in most cases was the monetary gain from participating in trials. This was due to a variety of reasons including the need for money as a result of high rates of poverty in some host communities and low levels of education or high illiteracy rates.

These findings reiterate a number of ethical concerns that have been expressed regarding reimbursement of research participants (Grady, 2005). Offering payment or reimbursement to trial participants with the intention to enhance recruitment and to enable people to enrol in trials without financial sacrifice – and by providing an enticement or incentive to participate in research - is a common yet controversial practice in research conduct (Grady, 2005). The concern is that this may unduly influence some individuals to participate in the trial (Emanuel, Xolani & Herman, 2005;

Kwagala, Wassenaar & Ecuru, 2010). Draper et al. (2009) concluded that paying research participants can be problematic. This is because vulnerable individuals – for example those from socially or financially deprived background – may be motivated by their financial need to participate in research. In another study Udrea et al. (2009) found that a high percentage of participants – especially patient with low education levels ($p=0.03$, Fisher's ANOVA) – reported that payment was their motivation to choose to participate in a clinical trial.

Paying research participants also raises ethical concerns over potential for trial participants to overlook possible risks of participating in the trial because of being preoccupied by the incentive (Grady, 2005). Trial participants may also be influenced by money received for their participation by not being honest or not disclosing information that may result in their termination from the trial (Koen et al., 2008) and this may have implications about validity of the data collected.

On the contrary, payment or reimbursement of HVT participants may be important to research to the extent that it encourages and facilitates participation (Govender, 2005). Trial participants are usually reimbursed for expenses – for example transport - directly related to participation in the trial (Koen et al., 2008). Part of the reimbursement may also be a show appreciation to participants' contribution to the research undertaken. Therefore reimbursing participants is one way of demonstrating continues respect and appreciation for trial participants.

Furthermore, offering reimbursement may enable individuals who otherwise may not afford to participate in HVT to take part in the research (Grady, 2005). In cases like this one, financial incentives proof to be necessary to overcome financial barriers. In addition offering trial participants money may not only be essential to general recruitment but also helpful in accomplishing the goals of ethnic, racial, gender and social diversity of individuals subjects participating in clinical research

(Grady, 2005). However, there is limited empirical evidence showing or demonstrating that reimbursing trial participants is necessary and/or effective for the recruitment of clinical research participants (Grady, 2005). Nevertheless Kwagala et al. (2010) recommends standardisation of reimbursement across comparable studies with an aim to promote high-quality research, voluntariness, and preventing unfair reimbursement practices in research.

Another way of demonstrating on-going respect for enrolled participants is prevention of HIV infection amongst trial participants. Prevention of HIV infection amongst trial participants was reported as an ethical challenge faced by researchers conducting HVTs in African countries. Researchers reported high rates of participants becoming infected with HIV while in the trials. Researchers in South Africa were more likely to indicate that participants' infection with HIV while in the study is one of the challenges they face. South Africa has the highest population of people living with HIV and an estimated 1500 new infections are reported every day (UNAIDS, 2008). Furthermore, the sites that took part in the study were based in KwaZulu-Natal and Gauteng Provinces of South Africa. KwaZulu-Natal has the highest HIV incidence and prevalence rate in South Africa (Nicolay, 2008) while Gauteng has the fourth highest incidence and prevalence rate (www.doh.gov.za). Therefore rate of people getting infected during trials may be a reflection of the HIV incident rate in these areas of research.

Trial participants often benefit from participating in HVTs in that their health is monitored through the conduct of a variety of test such as tests for HIV, medical and physical examinations. Providing medical and care services to reduce risk of HIV infection amongst trial participants is one way of protecting the wellbeing of research participants (Essack et al., 2010). For example, providing participants who get sick during participation in trials – for example those who acquire sexually transmitted infections - with treatment and the necessary care to ensure that they are fit to continue

participating in the trial. Therefore if a participant becomes infected with the HI virus during participation in a trial, there are implications for treatment continuity of care.

Many studies on HVTs examine the ELH needs, concerns and welfare of trial participants (c.f. Lindegger et al., 2006; Strode, Slack, Grant, & Mushariwa, 2005; Wassenaar & Barsdorf, 2007; Wassenaar & IJsselmuiden, 2007). Slack et al. (2005) investigated provision of HIV treatment to trial participants who become HIV positive during trials. As reported by most researchers in this study, the rate of sero-conversions in HVTs is high – research participants did not indicate how high in percentage the rate of sero-conversion is. As a result, researchers need to provide the necessary treatment and care to trial participants who become HIV positive during HVTs. Researchers have reported that providing the necessary health care to participants is a challenge. Although researchers did not elaborate on why this is a challenge, it is thought that lack of sufficient funding might be one of the reasons for this. Slack et al. (2005) however concluded that sponsors have the obligation to provide treatment for participants who become HIV positive on the grounds of beneficence. Therefore, the more participants seroconvert during the trial, the high the costs of the trial due to costs of treatment and care.

Respect for trial participants should continue after trial closure. For example all necessary information should be communicated to previous participants, especially information about post trial services. A study conducted by Ciaranello et al. (2009) reported that participant reimbursement for participating in trials (74%) was mentioned more often in the complete trial documents than information about post trial services.

5.1.1.2 Social value

In order to justify the use of limited resources and exposure of participants to potential harm, research must demonstrate social value to trial participants, the population they represent, the local community, the host country or the world

(http://nhrec.net/nhrec/code.html#Ethical_Principles_and_Guidelines_for_HREC's_approval_of_research). Demonstrating social value of research requires researchers to first determine what is considered social value. Researchers from this study reported that determining social value is an ethical challenge they faced. Various factors may contribute to this challenge. One of the factors that researchers reported is that most of the ethical and research guidelines are not local but international as a result they lack applicability regarding outlining determinants of social value in research. This was reported mainly by researchers from South Africa. Contrary to these reports, South Africa does have national guidelines that inform HIV and AIDS research (MRC, 2003) thus indicating lack of sufficient information – on the side of researchers – about the current ethical guidelines in their respective countries. In some instances, international guidelines are modified to suit national requirements, for example the South Africa HIV guidelines are adapted from UNAIDS (2000) guidelines and the South African Good Clinical Practice guidelines (Department of Health, 2006) which were adapted from ICH-GCP guidelines (DAID training, 2008). Apart from South Africa, other African countries such as Kenya (“Kenya national guidelines”, 2005) and Uganda (Grant et al., 2005) also have national guidelines for AIDS research.

The literature suggests that researchers might utilize two inter-related strategies to maximise social value of research (Lairumbi et al., 2008). These are collaborative partnerships with policy makers and communities from the beginning of research, and dissemination of research findings to trial participants, policy makers and implementers after the completion of the research (Lairumbi et al., 2008). Researchers should evaluate issues that are considered to lead to improvements in health and

contribute to meaningful knowledge in their different HVT contexts and disseminate such information to all relevant stakeholders during and after the conduct of research (http://nhrec.net/nhrec/code.html#Ethical_Principles_and_Guidelines_for_HREC's_approval_of_research). This is one way researchers can demonstrate what is considered social value of their research and doing so shows ongoing respect to not only trial participants but also host and local communities.

5.1.1.3 Collaborative partnership

Researchers in South Africa reported that they experienced ethical challenges when working collaboratively with participants and communities. All but one researcher who reported this were from sites that have experienced co-enrolments of a few participants who were enrolled in a HVTN vaccine trial undertaken at their site. They uncovered that these few participants were enrolled in their trial were enrolled in another trial at a different research site. These events of co-enrolment have led to uncertainties amongst these particular researchers regarding which individuals to enrol in HVTs. Although study educators and recruiters informed potential participants of the exclusion criteria - being enrolled in another trial, thinking of enrolling in another trial, having being enrolled in another trial in the last twelve months - participants were apparently not honest about their answers. This has led to some researchers believing that participants exploit research in that they do not participate in HVTs to make a contribution to science but for their own monetary gain. As a result it has become difficult for researchers at these sites to work with participants and communities. Co-enrolment is also a risk to participants and a threat to scientific validity of the research.

UNAIDS (2006) guidelines stipulate that partnership with communities should be built to yield research that is responsive and that addresses communities' needs and priorities. Collaborative partnership with trial participants and with communities has been shown to enhance social value of

research (Lairumbi et al., 2008). Researchers who work collaboratively with host communities from the beginning and throughout the conduct of HVT are more likely to better determine what will constitute social value of their research for the communities they are working with. This way, resources may be accordingly distributed to enhance social value of the research. Lairumbi et al. (2008) reported that ineffective partnerships among stakeholders may limit the potential social value of research.

5.1.1.4 Informed Consent

Most trial participants in HVTs in African sites are from poor communities and are illiterate as indicated by researchers from sites in both South Africa and Uganda. As a result of low literacy rates and/or high illiteracy rates in these populations, the comprehension of the IC process amongst potential trial participants is always problematic and difficult to establish. Studies by Lindegger et al. (2006) and Elsayed and Kass (2007) indicate that comprehension of the IC and subsequently obtaining valid consent from potential participants is a challenge. This is in part due to lack of understanding of the research process by potential trial participants because of factors such as illiteracy and language barriers (Elsayed & Kass, 2007). These and other social factors render these populations vulnerable.

Lindegger et al. (2006) sampled 59 participants, of which 53 were potential trial participants, to investigate the level of understanding that HVT participants have when joining vaccine trials. The study focused on how well participants understood IC forms and other information about the trials. The results showed that there was a low level of understanding amongst participants. Lack of comprehension of the IC and other study documents is a challenge that some researchers in this particular study reported. One factor that contributes to this lack of understanding on the part of the participants is the high illiteracy rates – as mentioned above - in most host communities. As a result,

some participants may be enrolled in HVTs across African sites without a full understanding of the trials. For example, in one of the HVTs in Southern Africa, some trial participants did not acknowledge the fact that they might be on the placebo arm. As a result, participants practice unsafe sex with the belief that they are on the active arm and that they tested vaccine prevents HIV infection – putting participants at risk of HV infection.

5.1.1.5 Favourable Risk-benefit ratio

When investigating researchers' ELH dilemmas and challenges, protection of subjects, legal rights and respect for human rights were examined. One of the challenges that researchers faced at their trial sites was protecting trial participants from any harm. Some researchers from some sites in South Africa and Botswana indicated that one of the vaccine trials had to be closed due to findings suggesting that the vaccines may predispose certain participants to HIV infection. Explaining to trial participants why the trial had to be stopped was a challenge. This is an example of unexpected challenges that researchers face when conducting HVTs. In his investigation of different ethical challenges that professional and academic researchers encounter in the health field in both non-clinical and social research, Grinyer (2001) concluded that 'unexpected problems' was a challenge that researchers face.

Explaining to trial participants why the trial had to be stopped was a challenge because sometimes researchers themselves cannot explain side effects and complications caused by study products under investigation hence it becomes very difficult to explain to study participants at the time they need explanation. This lack of sound explanation to participants may lead to loss of trust in research and researchers by participants and the community. This may subsequently lead to individuals refusing to participate in future trials as a result of lack of trust in the process of research.

5.1.2 Legal challenges

The main challenge researchers in East and Southern Africa reported facing when conducting HVTs was reported prevention of individuals of consent age to participate in trials. This could be either parents not permitting their adult offspring taking part in trials or male partners not permitting their female partners taking part in HVTs. A preliminary study conducted in Zimbabwe investigated the possible impact of relationships on decision-making process and autonomy of women (Nyika, Wassenaar and Mamotte, 2009). The findings of this study showed that 87.6% of women sampled were prepared to talk to their husbands before participating in health research (Nyika et al., 2009). Only 6.2% of the women reported that they will keep participation secret from their husbands. The study also found out that educational level, age, employment status and marital status of participants were significantly associated with autonomous decision-making process. The findings of the Nyika et al. (2009) study and those of this particular research on researchers' ELH challenges show that compromised autonomous decision-making may lead to a limited exercise of women's legal rights – such as the choice to participate in HVT if one is of legal consent age.

Preventing women from participating in HVT may also jeopardise chances of finding women initiated prevention measures. Wassenaar and Barsdorf (2007) pointed out that women's participation in HVTs is important to contribute finding women initiated prevention measures. In this study, researchers reported that some women were reported to be talked against participating in HVTs by their parents, male partners and other relatives. This is an example of how some women lack autonomy when making decisions about participating in HVTs. Consequently, in some research sites researchers face the challenge of not meeting their recruitment and retention targets.

Recruitment is an ethically sound objective for research that is scientifically valid – therefore failing to meet recruitment targets may hinder scientific validity and subsequently ethically sound research (Emanuel et al., 2004). Study recruitment and retention target numbers are determined scientifically

to enhance production of valid results statistically. Failing to meet these numbers may mean that results of the study/research may be invalid. Secondly, one of the obligations of researchers is to ensure participants' autonomy and exercise of their free will (Emanuel et al., 2005). Failure to do so is unethical. It may also be a reflection of failure of governments to ensure education to their people as far as comprehension of national consent age and what it means or the dominance of local culture over Western laws and frameworks.

The Universal Declaration of Human Rights (UN, 1948) stipulates that everyone has the right to health. Some governments have adopted this into their human right charter to indicate that they have the obligation to ensure education and health services, amongst other things, to their people (<http://www.ditshwanelo.org.bw/botswana.html>). Although individuals might be enrolled in HVTs, health service providers still have the obligation to support participants' health care. Therefore where necessary, participants should be able to access their local health care providers. Unfortunately this is not always the case as researchers from East Africa reported that some health care providers refuse to provide services such as HIV testing and contraception to HVTs participants. Some health care providers might refuse to provide service to HVTs participants to avoid involvement with such individuals in case these participants experience adverse events that may require them to be part of explaining the cause. Refusing to provide such service, means health care providers are not part of the research because they are not accountable for any adverse events or other forms of social harm directed at trial participants.

Some researchers reported that trial participants find it difficult to take legal action in case of trial related injury against them. This according to these researchers is a legal dilemma that needs to be looked at. This dilemma needs to be further investigated especially since there are factors, such as desperation for money and fear of punitive actions which can limit individuals' exercise of their legal

rights. Researchers reported that poverty of most trial participants in African HVT sites renders these individuals vulnerable and therefore powerless as far as challenging the research or defending themselves from possible malpractice and future impact of the study drug. Some researchers pointed out that at times participants are not thoroughly followed up after closure of the trial. If they experience drug effects of the experimental vaccine later on in life, the research staff of the trial in question is not available to offer assistance.

5.1.2 .1 Disclosure

One of the factors driving the spread of HIV in Africa is failure to disclose HIV infection by infected individuals (Gorbach, et al., 2004; Ramjee et. al., 2010). In all HVTs, participants are regularly tested for HIV infection. Where a participant is seen to have sero-converted, they are encouraged to disclose their status to those close to them, especially their sexual partner (WHO, 2004). This information is given to these individuals for them to ensure they use condoms all the time to prevent infecting others and for their sexual partners to also test to find out their own status. Although some participants disclose their status to the important others in their lives, many individuals decide not to disclose their status. In doing so, these individuals risk re-infection and spreading the virus to their sexual partners and all those who are in their sexual network. Researchers reported that convincing trial participants to disclose their HIV status and bring their sexual partners for VCT was a challenge.

Researchers face the legal dilemma of feeling obligated to make those at risk of HIV infection aware of their risk and on the other hand having to ensure confidentiality of their participants' information. Often researchers do all they can to encourage infected individuals to disclose their status to those at risk of infection but this is never guaranteed. This uncertainty remains a dilemma for researchers as they conduct HTVs and work on HIV prevention.

5.1.3 Human rights challenges

Providing health care services to trial participants was perceived as a human rights challenge by some researchers from East and Southern Africa. As a result of limited funding in HIV/AIDS research in Africa (IJsselmuiden, 2007) researchers are sometimes not able to provide all the necessary health care services to participants. This becomes a human rights dilemma in that trial participants are volunteers whose participation in HVT contributes towards finding a preventive vaccine for HIV/AIDS. However, provision of treatment for participants who become infected with the HI virus during HVTs is a source of many debates (Belsky & Richardson, 2004; Slack et al., 2004).

On the one hand, some researchers believe that they should provide ancillary care needed by trial participants while some believe that the purpose of HVTs is to generate information and find a successful HIV vaccine not care for patients (Belsky & Richardson, 2004). Slack et al. (2004) present three arguments made in regard to provision of HIV treatment for enrolled trial participants. Researchers and funders may provide treatment to trial participants as compensation for trial-related-injury, as an expression of justice and/or as an expression of beneficence.

It is therefore crucial for researchers to have on-going communication with their participants (Emanuel et al., 2008). Trial participants must be told about everything that concerns the trial at the screening process. As part of the study's risk-benefit assessment, participants must be made aware of all risks and potential benefits of taking part in the study (Emanuel et al., 2005) including if the study has limited health care resources. This must take place before the individual enrolls in the study. However, this information is not usually given to participants. Firstly because researchers may not feel trial participants need to know about issues concerning funding and availability of resources.

Secondly, researchers are sometimes pressured to meet enrolment and retention targets (Gul & Ali, 2010). It is therefore important to researchers that they do their best to enrol as many people as needed. Telling participants about limited resources and how this may affect their participation in the trial may act as a counter process in that participants who feel that their health might be jeopardized if they enrolled in a trial are less likely to enrol in such trials. However with so many people in Africa living in poverty, some individuals may still enrol with the knowledge that they will get reimbursed for participation (Kwagala et al., 2010). This result in another human rights dilemma in that potential trial participants may not voluntarily take part in trial but may be unduly influenced (Emanuel et al., 2005) by the monetary gain that comes with participating in health research. As discussed above, reimbursement money has been seen to be a motivation for many trial participants from poverty stricken communities. More than half of the researchers reported that according to them socio-economic factors together with illiteracy and cultural factors in some communities limits the exercise of human rights by trial participants.

Participants' illiteracy remains a challenge for some researchers. As a result of illiteracy some participants find it hard to comprehend the IC and other aspects of the study (Lindegger et al., 2006). In some trial sites, all study materials are translated into the home language and thorough explanation is provided for participants who battle to understand. Sometimes the process includes the participants, the staff explaining to the participants and a witness (DAIDS training, 2008). A witness serves to confirm that all was done to ensure that the participant understood everything about the study (DAIDS training, 2008). Participants who enrol in trials without a full understanding of the trial, its purpose and all that concerns the trial, are less likely to express their dissatisfaction and to take legal action where they feel their rights have been violated or their health compromised.

Cultural factors also sometimes limit participants' exercise of their human rights. Women are especially affected by cultural beliefs and practices. Women in most cultures around the world are submissive to their male partners and often act in ways that do not necessarily please them but please their partners (Nyika et al., 2009). In most African societies women often need to consult their husbands (Nyika et al., 2009), fathers and other significant males in their lives to participate in a variety of activities including participating in health research. Therefore they do not decide on matters that concern them but have the men in their lives to do so for them. This limits women's exercise of their free will and rights (Molyneux et al., 2005). As reported by all researchers from East Africa, women are sometimes prevented by their male partners to take part in trial(s). As the most affected gender, more and more women are starting to realise the importance of their participation in HVTs (Wassenaar & Barsdorf, 2007). Any factor that prevents them from doing so does not only limit their exercise of human rights but also hinders efforts towards finding an HIV/AIDS preventive vaccine.

5.2 Needs and resources

There is significant reported improvement in the availability of infrastructure for the conduct of HVTs. This may be because Africa has received much funding for HIV/AIDS research since the beginning of the conduct of HVTs in Africa (UNAIDS, 2003). Although there is still more to do as far as providing all needed infrastructure, most African vaccine trial sites that took part in this study reported having most of the infrastructure needed for the conduct of HVTs. The main infrastructure missing, according to researchers in African countries were libraries and journals at sites.

Researchers did not report any reasons for lack of some infrastructure at their sites.

5.3 Guidelines and frameworks

There is an increasing preference for the use of context applicable guidelines among researchers working with human participants (Fadare & Porteri, 2010). Although there are still researchers who prefer international guidelines, most researchers reported that they find national guidelines helpful. As more and more HIV/AIDS research takes place in Africa, it is becoming evident that some international ethical guidelines and frameworks are not applicable to African settings. For example, some international guidelines are said to not accommodate and address cultural factors that may influence the conduct of research (Fadare & Porteri, 2010). It is crucial for guidelines to be inclusive of cultural knowledge in order to establish a mutual understanding between the research team and the host community (Tindana, et al., 2007). Failing to do so may lead to some communities becoming resistant to the research because they perceive it to be countering their cultural practices and norms. Therefore researchers need to be guided by guidelines that are context relevant – such as the MRC’s (2003) guidelines on ethics for medical research: HIV preventive vaccine research and UNAIDS (2007) GPP guidelines.

Researchers from Uganda all reported that they prefer their national guidelines (Grant et al., 2005) on the conduct of trials. The success of Uganda in the fight against AIDS may be contributed to by such initiatives, implementing national guidelines. There is need for other African countries to implement their own national guidelines to the conduct of trials. Only Kenya (“Kenya national guidelines”, 2005), South Africa (MRC, 2003) and Uganda (Grant et al., 2005) appear to have done so to date.

5.4.1 Theoretical frameworks

5.4.1.1 Ethics

The Emanuel et al. (2004; 2008) framework was used to investigate ethical challenges researchers face on site. The framework was helpful in informing part of the questionnaire that was used to collect data. The framework was also successful in identifying some of the challenges that researchers face when conducting HVTs in African countries. The framework helped identify maintaining ongoing respect for enrolled participants, to working collaboratively with participants, working with communities and determining social value as ethical challenges. However the Emanuel et al. (2004) framework did not address some ethical challenges that researchers face. Below are some of the ethical requirements that the framework does not cover.

The last ethical requirement in the Emanuel et al. (2004) framework is respect for enrolled participants. This requirement states that trial participants must be ensured of confidentiality of their information and that current and former participants must be allowed access to successful treatment and any new information that is generated from a study they were part of. This ethical requirement can be enhanced by adding the need for continuous regular feedback to current and former trial participants. By only stating that participants are allowed access to information, the framework does not highlight giving continuous regular feedback to current and former trial participants as one of the responsibilities of researchers. Often researchers mention that one of the benefits of participating in trials and research is gaining information. However, comprehensive feedback is seldom given to research participants. It is for this reason that providing feedback to participants must be highlighted as an essential part of any research process by frameworks on ethical requirements.

Some of the researchers who took part in this study mentioned that they experienced co-enrolments at their site. As a result of co-enrolments at these sites, some participants, those who were enrolled in

more than one study, were terminated from the trials. Co-enrolment at these sites was an unanticipated problem. As reported by one of the study coordinators who took part in this study, systems such as sharing participants' identities with other research sites were introduced after the events of co-enrolment. The Emanuel et al. (2004) framework does not cover handling unanticipated problems as one of the ethical requirements when conducting HVTs. As a result it cannot be used by researchers in solving unanticipated problems in HVTs. A framework that covers handling of unanticipated problems in HVTs as an ethical requirement is needed in that HVT environment is often unpredictable.

Researchers are faced with a variety of unanticipated challenges continuously. For example due to the events of co-enrolments in some HVTs in African countries, co-enrolled participants were terminated from the study. These participants were already using the study product but once terminated they were not followed up. As a result the future impact of the study product on these individuals will never be known because they were not followed up. Ethical frameworks must cover ethical issues such as this to ensure continuity of care of trial participants even after the end of their participation in the trials.

Moreover the Emanuel et al. (2004) framework elaborates on working collaboratively with communities as an ethical requirement in clinical trials. The word community is usually used to refer to a rural oriented society. Therefore the Emanuel et al. (2004) framework does not elaborate on ethical requirements of clinical trials taking place in a variety of settings, for example urban settings. As a result this framework might be seen to not be applicable in all settings.

5.4.1.2 Law

Laws of African countries that took part in this study were used as a framework to investigate laws challenges that researchers face when conducting HVTs. Using the different legal frameworks was useful in identifying how far African countries that took part in the study are in establishing policies and laws that guide the conduct of HVTs. The establishment of laws concerning the conduct of HVT help improve legal issues concerning the conduct of HVTs. By referring to these laws, researchers are able to identify legal issues that are not addressed by current laws concerning the conduct of HVT. For example, some laws relating to the conduct of HVTs in Africa do not cover issues around consent age. In such cases it may be useful to use other relevant laws or guidelines such as UNAIDS (2007) paper on enrolment of adolescents in clinical trials and dealing with issues surrounding consent age. Although countries have consent ages, some African societies still do not follow this when it comes to decision making on whether to join HVTs or not. Researchers from both Southern and Eastern Africa reported that there are participant of consent age who are refused to take part in HVTs by either their parents or male partners. Therefore using a variety of available national and international laws as guidelines to inform the investigation of legal issues that researchers face when conducting trials in Africa was helpful in identifying gaps in law concerning the conduct of HVTs.

On the contrary, using different laws that direct the conduct of HVTs in Africa countries was difficult. It was not possible to compare legal issues regarding the conduct of HVTs in African countries that took part in this study using a single framework. Therefore it is not easy to assess the progress of countries in relation to other countries in this regard (Grant et. al., 2005).

5.4.1.3 Human rights

The Universal Declaration of Human Rights (UN, 1948) was used as a Human Rights framework. Through this framework it was established that African countries that took part in this study

experience similar human rights dilemmas and have similar human rights concerns when conducting HVTs. Using the declaration of Human Rights was useful in confirming that human rights are universal hence researchers from different parts of Africa had almost similar Human Rights concerns.

6. Limitations of the study

When conducting a study, the researcher has to always expect limitations or constraints. In this particular study the biggest limitation was inability to access some HVT research sites. Some sites that were identified via internet searches could not be researched mostly because the phone numbers given on the websites were incorrect. Various alternative attempts, like emailing the sites, also failed. As a result not all countries that were conducting HVTs at the time of data collection were sampled for this study. At the time of data collection, a total of eight countries were identified – in different clinical trials websites – as conducting and/or preparing to conduct HVTs. However, the HVT sites that took part in this study were from only four countries. Furthermore, two of the six research sites that participant(s) were follow-up sites.

Another limitation of this study was a small sample size which was a result of the following outlined reasons:

1. At some sites language was a barrier. In some French speaking African countries, it was difficult to communicate with reception staff. As a result sometimes the correct people could not be reached after numerous attempts.
2. Limited funds for this study meant the researcher had to choose the most inexpensive means of data collection. In this case email survey was used. Email surveys have very low response rates, evident in this study. A different method like face to face interviews or presence will have yielded better sample size. This is because the researcher would have made

3. Researchers' apparent lack of interest in the study was another limitation. Being a study on researchers' need, it was expected that researchers would find this as an opportunity to express their ELH challenges and needs. Unfortunately this was not so. After continuous follow ups approximately half of the researchers did not return completed questionnaires. Some of the reasons for this were that they are too busy at their site. In some instances contact persons promised to make their respective PIs aware of the study but after numerous attempts for feedback, they still had not done so. Some researchers were sent the questionnaire but never returned it after several follow ups.

As a result of the above-mentioned limitations regarding a small sample size, researchers from other part of Africa - for example Westerns and Central Africa - were not represented. This means that the results of this study need to be interpreted with caution when applied to regions of Africa which did not take part in this study. Researchers from these unrepresented regions might have different ELH challenges which – this study may not have identified - may also need to be investigated.

7. Conclusions and recommendations

7.1 New knowledge

This study hopefully contributed to new knowledge through several new findings. The study identified ethical issues that researchers face when conducting HVT that have not been documented before. An example of such knowledge is the events of co-enrolment. Some HVT sites are experiencing an increasing number of participants who enrol in more than one HVT at the same time. Need for money due to high poverty rates in most host communities was said to be the

motivation for co-enrolment. Co-enrolled participants gain from this action by collecting reimbursement money at different sites and use the money for their livelihoods. This finding has highlighted the need to investigate poverty as a barrier to the exercise of human rights as co-enrolment is becoming a serious problem in African countries because of financial desperation among trial participants (Kwagala et al., 2010).

This study also indicates that there is need to educate and update the research staff about relevant and available ethical and legal frameworks that inform the conduct of HVTs in their respective countries. Researchers expressed the need for locally relevant ethical guidelines. Researchers reported that the main disadvantage of most ethical guidelines used in HVTs is that they are not applicable to some setting especially African settings. Researchers who expressed this concern were from countries that did have national guidelines thus they were unaware of these ethics guidelines.

7.2 Conclusions

Researchers in HVTs in African countries reported that they experience ethics, law and human rights challenges when conducting HVTs at their sites. The main ethical challenge that researchers face when conducting HVTs arises from the high number of enrolled participants who become HIV positive during the trial. No specific percentage was given to demonstrate the extent of sero-conversion at these sites. Other ethical challenges that researchers faced include determining social value of the research, paying participants, working collaboratively with participants and communities and explaining trial closure to participants. When asked about legal challenges that they face at their sites, researchers reported that prevention of individuals who want to participate in HVTs by their parents and/or male partners was a dilemma they face. Researchers reported that at times they terminate participants who meet study inclusion criteria due to demands to do so from their parents and/or male partners. Researchers also reported the lack of support from health care service

providers when it comes to caring for trial participants. Other legal challenges reported by researchers include issues around privacy and confidentiality of participants' information, and future impact of the study drug on the health of the participant after the end of the trial.

The main human rights concern was the understanding of consent age in African countries by communities. It was established that despite the respective consent age of countries, most communities are still driven by cultural or societal norms and beliefs when it comes to deciding who takes part in HVTs. Parents and male partners often decide for their children and female partners to take part or not to take part in HVTs. The results of this study show that most African HVT sites have most of the infrastructure needed for the conduct of HVTs. Most researchers however reported that they do not have a library at their sites.

7.3 Recommendations

To improve the conduct of HVTs in African countries the following are recommended:

- a. Creation of a network between HVT sites in Africa where researchers can interact and share their challenges, problem solving skills and new strategies to improve the conduct of clinical trials in Africa. This would prevent incidents such as co-enrolments because sites would be aware of which participants are enrolled where. This should be validated by the AAVP.
- b. It would also be useful for researchers to have regular workshops where they come together and share information on the conduct of trials.
- c. Encourage refresher training of research staff on different guidelines that inform the conduct of HVTs such as UNAIDS (2007) guidelines on community involvement of host communities at the all levels of trials, from planning, to implementation, to follow ups. Most researchers who took part in this study were often unaware of some relevant available guidelines that inform the conduct of HVTs.

- d. It is crucial that HVT websites have the correct contact details to allow easy access to these sites. In addition, websites must be updated regularly. This would not only be useful to other researchers but would also be useful to all who need to access the site and information from the site.
- e. There is need for libraries and site journals within HVT sites. This would improve the culture of reading amongst those who visit the site and trial participants, and this would also encourage researchers to remain abreast of new developments in the field.
- f. There is need to educate host communities about human rights. This study reflected that a lot of individuals are not aware of their human rights. An example of this is individuals who are not permitted to participate in HVTs, regardless of being of consent age, by the significant others in their lives.
- g. There is need for health care providers, department of health and HVT research staff to work collaboratively to provide care and treatment to participants who place themselves at risk by participating in HVTs.

7.3.1 Recommendations for further research

- a. Research the HIV incidence rates in HVTs in Africa and how this informs provision of ongoing care and respect for trial participants.
- b. Investigate the extent of co-enrolment in African HVT sites. Explore motivation for and implications on participants' health (Gajic et al., 2004).
- c. Evaluate the extent to which money influences recruitment or their willingness to participate in HVTs.

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9. Appendices



Appendix 1 - Cover letter

Ethics, law and human rights dilemmas, needs and resources of researchers in HVT in Africa

Cover letter

Dear Colleague

My name is Tshegofatso Precious Phalane. I am a Masters student in Research Psychology at the University of KwaZulu-Natal, South Africa. I am conducting a survey on the ethics, law and human rights dilemmas, needs and resources experienced by researchers and trial site staff. The study being conducted on behalf of the WHO/UNAIDS African AIDS Vaccine Programmes Ethics, Law and Human Rights Collaborating Centre (AAVP ELH). AAVP ELH works to both assess and strengthen the ethical-legal framework and facilitate the ethical conduct of HIV vaccine trials in selected African countries proximal to running trials.

The purpose of this study is to investigate the ethical, legal and human rights dilemmas and needs, of researchers and the availability of the necessary material resources and infrastructure for the ethical conduct of successful HIV vaccine trials in African countries. This study will also evaluate the appropriateness and relevance of legal frameworks and ethical guidelines adopted at trial sites. This study has received ethical approval from the University of KwaZulu-Natal Human & Social Science Ethics Committee. The results of this study will be developed into a technical report for AAVP ELH, a Masters thesis and a hopefully a peer-reviewed publication.

I would like to invite you to complete the attached questionnaire. The questionnaire should take approximately 20 minutes to complete. Your answer sheet will be unlinked on receipt and your email will be deleted. This report will be made publicly available, however no personally identifiable details will be released and only aggregated information will be reported. Regional differences may be highlighted, but no individual product or trial site will be named. Identifiable responses from individual researchers or sites will not be publicized or released to any party other than a selective committee of the AAVP sponsors (WHO/UNAIDS HIV Vaccine Initiative), in order to assist with the potential development of programmes and/or materials to respond to the ELH needs and concerns of researchers in HIV vaccine trials in Africa. Such information will be treated with the strictest confidentiality and will be used only to identify ELH needs and concerns of researchers.

Individual feedback on the results of the research will be given to each site. A potential benefit of this study is the development of capacity building programmes and materials that reflect the ELH dilemmas, needs, guidelines and resources of researchers in HIV vaccine trials.

You are free to decline to participate in this study, or to withdraw your information, at any time.

Should you have any queries regarding this research, please contact the chairperson of AAVP ELH, Prof Douglas Wassenaar: Tel: +27 33 260 6165; Fax: +2733 260 6065; Email: Aavp1@ukzn.ac.za

I would be most grateful if you could complete the attached questionnaire and return it to me, Ms Tshegofatso Phalane via email: phalane@ukzn.ac.za before

Your participation is much appreciated. If you have any queries please do not hesitate to contact me on + 27 31 260 1970 or by email phalane@ukzn.ac.za .

Yours Sincerely

Tshegofatso Precious Phalane

Appendix 2 – Informed consent



Ethics, law and human rights dilemmas, needs and resources of researchers in HVT in Africa

Informed consent

Dear Colleague,

My name is Tshegofatso Precious Phalane from the University of KwaZulu Natal in South Africa. I would like to ask you to consider completing a questionnaire for the Ethics, Law, and Human Rights Group of the WHO-UNAIDS African AIDS Vaccine Program (AAVP). I am also doing this research towards my Masters degree in research psychology.

AAVP is a WHO/UNAIDS funded initiative dedicated to developing the capacity of African countries to work in a context of equal collaboration with sponsors and investigators regarding their participation in HIV vaccine research. Within the AAVP is the Ethics, Law and Human Rights Working Group (ELH). The ELH is situated at the School of Psychology, University of KwaZulu Natal, Pietermaritzburg. The ELH chair is Prof Doug Wassenaar, the Coordinator is Ms Nicola Barsdorf, and ELH Executive members are Ms Cathy Slack (HAVEG), Adv Ann Strode (School of Law, UKZN) and Dr Pamela Andanda (School of Law, University of the Witwatersrand)..

The ELH works to both assess and strengthen the ethical-legal framework and facilitate the ethical conduct of HIV vaccine trials in selected African countries proximal to running trials. I am conducting research for the ELH regarding the ethical, legal and human rights needs and concerns of researchers in HIV vaccine trials in African countries preparing for or currently conducting HIV vaccine trials. The purpose of this study is to investigate not only ethical, legal and human rights needs, but also the availability of the necessary material resources and infrastructure for the ethical conduct of successful HIV vaccine trials in African countries.

The results of this study will be:

1. Developed into a thesis in partial fulfillment for Masters of Arts (Research Psychology).
2. Developed into a technical report for UNAIDS AAVP.
3. Developed into a manuscript for publication.

No personally identifiable details will be released and only aggregated information will be reported. Regional differences may be highlighted, but no individual product or trial site will be named.

You have been chosen as a potential participant because you meet the inclusion criteria for the category 'researcher' in HIV vaccine trials. The study will sample researchers all over Africa, wherever there is preparation for, or HIV vaccine trials currently being conducted. After combining all responses, we hope to learn more about the ethical, legal and human rights needs and concerns of researchers in HIV vaccine trials in African countries which will help us make useful recommendations to remedy any gaps to the relevant authorities and organizations through UNAIDS and AAVP.

Please understand that your participation is voluntary and you are not obliged to take part in this study. The choice of whether to participate or not is yours alone. However I will really appreciate it if you shared your thoughts with me. If you choose not to take part in answering these questions, you will not be affected in anyway whatsoever. If you agree to participate you may stop at anytime and discontinue or withdraw your participation and there will be no penalties and you will not be prejudiced in any way.

I will not be recording your name anywhere in the questionnaire and no one will be able to link you to the answers you give. All individual information will remain confidential. The questionnaire will last about 20 minutes (tested through a pilot). I kindly request that you are as open and honest as possible when answering these questions and remember that there is no right or wrong answer.

Once the study is complete, findings will be sent to you via email to inform you of the main findings.

The study has been approved by the faculty Research Ethics Committee of the University of KwaZulu-Natal, approval number HSS/0168/08M

If you have a complaint about any aspect of this study you may contact Tshegofatso Phalane at UKZN by email phalane@ukzn.ac.za or my supervisor, Prof Doug Wassenaar at Wassenaar@ukzn.ac.za. Complaints to the Research Ethics Committee may be addressed to Ms P Ximba ximbap@ukzn.ac.za

NB the above section is for you to keep but kindly return the questionnaire once completed.

By completing this questionnaire I acknowledge that the purpose of this study is clear to me and that I am participating freely and voluntarily. I understand that I may withdraw from this study at any time and that none of my personal details will be recorded or released in an identifiable way.

I understand that feedback will be sent to me via email on the results of the completed research.

No signed consent will thus be required.

**AFRICAN AIDS VACCINE PROGRAMME
ETHICS, LAW AND HUMAN RIGHTS COLLABORATING CENTRE**

School of Psychology, University of KwaZulu-Natal
Postal Address: P/Bag X01, Scottsville, 3209 Tel: +27 33 260 6165 Fax: +27 33 260 6065 Email: aavp1@ukzn.ac.za
Website address: http://www.who.int/vaccine_research/diseases/hiv/aavp/en/

Appendix 3 – Questionnaire



ETHICS, LAW, AND HUMAN RIGHTS DILEMMAS, NEEDS AND RESOURCES OF RESEARCHERS' IN HIV VACCINE TRIALS IN AFRICA

Questionnaire

Please return this questionnaire via email to phalane@ukzn.ac.za

or fax to +2733 260 6065 before 30 June 2008

A Demographic information

Position (eg. Medical officer):	
Highest Qualification:	
Site:	
Country:	

1. Are you currently preparing for a HIV vaccine trial? (Tick which applies)

 YES

 NO

2. Are you currently conducting a HIV vaccine trial? (Tick which applies)

 YES

 NO

2a If yes, When did you start the current HIV vaccine trials?

DD	MM	YY

2b The HIV vaccine trial I am currently working on is a Phase _____ trial

3. Who is sponsoring the HIV vaccine trial you are involved in? (Answer in space below)

B Ethics, Law and Human Rights Dilemmas/problems

4. Describe any ethics, law and/or human rights problems you have experienced in the last year (Answer in space below)

--

5. Which of the following are challenges you have experienced in conducting HIV vaccine trials at your site?

Please tick the appropriate answer (1=agrees; 2=don't know (DK); 3=disagree):				
The following issues are ELH challenges				
5a	Working collaboratively with trial participants	(1) Agree	(2) DK	(3) Disagree
5b	Working collaboratively with host communities	(1) Agree	(2) DK	(3) Disagree
5c	Social value of trials	(1) Agree	(2) DK	(3) Disagree
5d	Scientific validity of the trials	(1) Agree	(2) DK	(3) Disagree
5e	Subject selection	(1) Agree	(2) DK	(3) Disagree
5f	Making risk-benefit determinations	(1) Agree	(2) DK	(3) Disagree
5g	Independent ethical review of trials	(1) Agree	(2) DK	(3) Disagree
5h	Obtaining informed consent from trial participants	(1) Agree	(2) DK	(3) Disagree
5i	Maintaining confidentiality	(1) Agree	(2) DK	(3) Disagree
5j	Participants' infection with HIV during trials	(1) Agree	(2) DK	(3) Disagree
5k	Payment of participants	(1) Agree	(2) DK	(3) Disagree
5l	Providing health care services for participants	(1) Agree	(2) DK	(3) Disagree
5m	Other (specify)	(1) Agree	(2) DK	(3) Disagree

C Resources

6. In the last year, which material resources (for example, ethical guidelines, Standard Operating Procedures, Good Clinical Practice guidelines) have you used to solve ELH problems at your site?

a. Name them	b. Rate them		
	1. Very helpful	2. Quite	3. Not so
6a.			
6b.			
6c.			
6d.			
6e.			

6f.			
6g.			
6h.			
Other (specify)			

D Infrastructure

7. Is the following infrastructure available at your site? (Tick which applies)

Please mark the appropriate answer (1=yes: 2=no)					
a. Working space	(1) Yes	(2) No	j. clinical supplies	(1) Yes	(2) No
b. Computer equipment	(1) Yes	(2) No	k. Stationery	(1) Yes	(2) No
c. Printer	(1) Yes	(2) No	l. Secretarial support	(1) Yes	(2) No
d. Telephones	(1) Yes	(2) No	m. Bank account	(1) Yes	(2) No
e. Facsimile	(1) Yes	(2) No	n. Electricity	(1) Yes	(2) No
f. Email	(1) Yes	(2) No	o. Clean water	(1) Yes	(2) No
g. Internet access	(1) Yes	(2) No	p. Journals	(1) Yes	(2) No
h. Copier	(1) Yes	(2) No	q. Ethics Guidance	(1) Yes	(2) No
i. Library	(1) Yes	(2) No	r. Web access	(1) Yes	(2) No
Other (specify)					

8. Is there any infrastructure that you require to perform your job that is not available on site?

E Needs/Gaps

9. Please list and rate any ethics, law and/or human rights needs, which you may have that are not addressed at present.

a. Name them	b. Rate them		
	1. Very important	2. Quite important	3. Not so important
9a.			
9b.			
9c.			
9d.			
9e.			
9d.			
9g.			
9h.			
Other (specify)			

F Guidelines/Law

10. Do you have concerns that the broader national or local social or political context in which you work limit the human rights of your research participants? (Please explain your answer below)

11. Do you have any concerns about the human rights of the communities in which you work? (Please explain your answer below)

12. Do you have any concerns about the human rights of trial participants? (Please explain your answer below)

13. Are there any local cultural factors, which, in your view, may impact on the human rights of the communities in which you work? (Please explain your answer below)

14. Are you aware of any relevant national or regional laws, which protect the rights of participants in HIV vaccine trials? (Please explain your answer below).

15. Do you have concern about any legal aspects of conducting HIV vaccine trials? (Please explain your answer below).

16. Do you have concern about any ethical aspects of conducting HIV vaccine trials? (Please explain your answer below).

--

17. Are there any guideline/laws that you find problematic at your site? List and rate them accordingly.

a. Name them	b. Rate them				
	1. Very restrictin	2. Quite restrictin	3. Not restricting	4. Quite flexible	5. Too flexible
a.					
b.					
c.					
d.					
e.					
f.					
g.					
h.					
Other (specify)					

18. What are challenges to the use of ethical guidelines in your country? (Answer in the space below)

--

THANK YOU FOR YOUR TIME

Please return this questionnaire via email to phalane@ukzn.ac.za

or fax to +2733 260 6065 before 30 June 2008

AFRICAN AIDS VACCINE PROGRAMME
 ETHICS, LAW AND HUMAN RIGHTS COLLABORATING CENTRE
 School of Psychology, University of KwaZulu-Natal
 Postal Address: P/Bag X01, Scottsville, 3209 Tel: +27 33 260 6165 Fax: +27 33 260 6065 Email:
 aavp1@ukzn.ac.za
 Website address:http://www.who.int/vaccine_research/diseases/hiv/aavp/en/

Appendix 4- letter to contact person

Dear Colleague

ETHICS, LAW AND HUMAN RIGHTS DILEMMAS, NEEDS, AND RESOURCES OF RESEARCHERS' IN HIV VACCINE TRIALS IN AFRICA

My name is Tshegofatso Precious Phalane. I am a Masters student in Research Psychology at the University of KwaZulu-Natal, South Africa. I am conducting a survey on the ethics, law and human rights dilemmas, needs and resources experienced by researchers and trial site staff. The study being conducted on behalf of the WHO/UNAIDS African AIDS Vaccine Programmes Ethics, Law and Human Rights Collaborating Centre (AAVP ELH). AAVP ELH works to both assess and strengthen the ethical-legal framework and facilitate the ethical conduct of HIV vaccine trials in selected African countries proximal to running trials.

The purpose of this study is to investigate the ethical, legal and human rights dilemmas and needs, of researchers and the availability of the necessary material resources and infrastructure for the ethical conduct of successful HIV vaccine trials in African countries. This study will also evaluate the appropriateness and relevance of legal frameworks and ethical guidelines adopted at trial sites. This study has received ethical approval from the University of KwaZulu-Natal Human & Social Science Ethics Committee. The results of this study will be developed into a technical report for AAVP ELH, a masters thesis and a hopefully a peer-reviewed publication

The first step in the sampling process involved identifying ongoing and soon to start HIV vaccine trial sites in African countries. The second step is identifying principal investigator (PI), site directors or any right person to talk to regarding participation of your staff in this study. Please kindly let me know if your site staff will be willing to participate in this study. Please send these details to phalane@ukzn.ac.za . A quick reply will be highly appreciated.

Should you have any questions regarding this research, please contact the chairperson of AAVP ELH, Prof Douglas Wassenaar: Tel: +27 33 260 6165; Fax: +2733 260 6065; Email: Aavp1@ukzn.ac.za

Yours Sincerely



Tshegofatso Precious Phalane

Appendix 5 – letter asking for permission

Dear Colleague

ETHICS, LAW AND HUMAN RIGHTS DILEMMAS, NEEDS, AND RESOURCES OF RESEARCHERS' IN HIV VACCINE TRIALS IN AFRICA

My name is Tshegofatso Precious Phalane. I am a Masters student in Research Psychology at the University of KwaZulu-Natal, South Africa. I am conducting a survey on the ethics, law and human rights dilemmas, needs and resources experienced by researchers and trial site staff. The study being conducted on behalf of the WHO/UNAIDS African AIDS Vaccine Programmes Ethics, Law and Human Rights Collaborating Centre (AAVP ELH). AAVP ELH works to both assess and strengthen the ethical-legal framework and facilitate the ethical conduct of HIV vaccine trials in selected African countries proximal to running trials.

The purpose of this study is to investigate the ethical, legal and human rights dilemmas and needs, of researchers and the availability of the necessary material resources and infrastructure for the ethical conduct of successful HIV vaccine trials in African countries. This study will also evaluate the appropriateness and relevance of legal frameworks and ethical guidelines adopted at trial sites. This study has received ethical approval from the University of KwaZulu-Natal Human & Social Science Ethics Committee. The results of this study will be developed into a technical report for AAVP ELH, a Masters thesis and a peer-reviewed publication.

I would like to invite your trial site(s)/research team(s) to participate in this study. If you agree to participate, I would like to request permission to send all your trial site staff an email questionnaire. A decision on the best way to distribute the email questionnaire to your staff will be reached in collaboration with yourself.

Individual's decision not to participate will be respected. The questionnaire should take approximately 20 minutes to complete. I have attached a copy of the questionnaire for your information. The answer sheet will be unlinked on receipt and the return email will be deleted. This report will be made publicly available, however no personally identifiable details will be released and only aggregated information will be reported. Regional differences may be highlighted, but no individual product or trial site will be named. Identifiable responses from individual researchers or sites will not be publicized or released to any party other than a selective committee of the AAVP sponsors (WHO/UNAIDS HIV Vaccine Initiative), in order to assist with the potential development of programmes and/or materials to respond to the ethics, law and human rights needs and concerns of researchers in HIV vaccine trials in Africa. Such information will be treated with the strictest confidentiality and will be used only to identify ethics, law and human rights needs and concerns of researchers.

Individual feedback on the results of the research will be given to each site. A potential benefit of this study is the development of capacity building programmes and materials that reflect the ethics, law and human rights dilemmas, needs, guidelines and resources of researchers in HIV vaccine trials.

Your participation is much appreciated. I would be most grateful if you could inform me of your sites willingness to participate by means of return email to me, Ms Tshegofatso Phalane phalane@ukzn.ac.za.

Should you have any queries regarding this research, please contact the chairperson of AAVP ELH, Prof Douglas Wassenaar: Tel: +27 33 260 6165; Fax: +27 33 260 6065; Email: Aavp1@ukzn.ac.za

Yours Sincerely





Tshegofatso Precious Phalane

Appendix 6 – Identified HVT sites

HVT sites					
Country	Study	Site	Name of PI	email address	Telephone Number
Malawi			Newton Kumwenda	nkumwenda@jhu.medcol.mw	
	HVTN 050		Scott Hammer		
Kenya	RV 172		Merlin Robb	mrobb@hivresearch.org	301-251-8302
	IAVI V001		Etienne Karita	ekarita@psfiavi.rw	250 503 233
Tanzania	RV 172		Merlin Robb	mrobb@hivresearch.org	301-251-8302
Uganda	IAVI V002		Pontiano Kaleebu	Pontiano.kaleebu@wrp-kch.org	
			Susan Allen	sallen5@emory.edu	
Rwanda	IAVI V001		Etienne Karita	ekarita@psfiavi.rw	250 503 233
Zambia	IAVI A002		Anwar Hoosen	hoosen@medunsa.ac.za	27-12-521-5667
	HPTN 027		Laura Guay		
			Francis mmiro		
South Africa		Desmond Tutu HIV Centre	Linda-Gail Bekker	linda-gail.bekker@hiv-research.org.za	27-21-650-6959
		Medunsa HIV Research Unit	Maphoshane Nchabeleng	nchabe@medunsa.ac.za	27-21-521-4110
		CAPRISA, Ethekewini Clinic	Koleka Mlisana	mlisanak@ukzn.ac.za	27-31-260-4562/1921
	HVTN 050		Scott Hammer		
	IAVI A002		Eftyhia Vardas		
			Linda-Gail Bekker	linda-gail.bekker@hiv-research.org.za	27-21-650-6959
Botswana		Botswana-Havard Partnership for HIV research	Myron Essex	messex@hsphmail.harvard.edu	1-617 432 2334
Zimbabwe	HPTN 035		Zvavahera Michael Chirenje	chirenje@uz.ucsf.co.zw	

Appendix 8 – Telephone log: Omitted to protect confidentiality.

	<i>An investigation of ethics, law, and human rights (ELH) dilemma, needs and resources of researchers in HIV vaccine trials in Africa</i>						
Telephone Log							
Date	Time	Person Contacted	Name of trial site	Number dialled	Country	Duration of call	Outcome of call