Ethics, Law and Human Rights Collaborating Centre of the African AIDS Vaccine Programme (AAVP ELH)

University of KwaZulu-Natal, Private Bag X01, Scottsville, Pietermaritzburg, 3209, South Africa

Ph + 27 33 260 6165 Fax + 27 33 260 6065 E-mail: mamotten@ukzn.ac.za or aavp1@ukzn.ac.za

A survey of HIV vaccine trial investigators' awareness and implementation of locally applicable ethical-legal frameworks and statutes

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Jennifer Koen, Farhana Zuberi & Zaynab Essack

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1. EXECUTIVE SUMMARY:

UNAIDS (2007) recommends that biomedical HIV prevention research should not be conducted "when a survey of protective local laws and regulations applicable at the trial site has not been conducted" (p.13), in order to ensure that researchers are able to comply with the locally applicable ethical-legal framework, and to identify potential insurmountable legal barriers to the conduct of the study. This suggests that investigators planning to conduct HIV prevention research should be aware of the locally applicable ethical-legal framework for research. A study of Research Ethics Committees (RECs) in Africa highlighted a lack of knowledge of ethical-legal frameworks as a key challenge in the ethical oversight of research (Milford, Wassenaar and Slack, 2006). Given that many members of RECs are themselves investigators; this suggests that there may also be a lack of awareness of these frameworks among researchers in host countries. In order to design appropriately targeted ethical-legal training for investigators in host countries, including foreign researchers conducting trials in these countries, it was deemed necessary to assess how aware researchers are of the existing ethical-legal frameworks and their reported compliance with them.

This study surveyed (via an email questionnaire) investigators conducting HIV prevention research in four countries in Africa (South Africa, Kenya, Zambia, Malawi) for their awareness and reported implementation of the locally applicable ethical-legal framework, and their recommendations regarding what ethical-legal training for researchers working in the country in which they were working, would be most beneficial. In a few instances telephone interviews, using the survey questionnaire as a guide, were conducted with key informants (n=3).

Across the four countries, of the initial 21 investigators who expressed interest in participating in the study, 12 eventually responded to the survey. Respondents were primarily investigators who were working in South Africa; however, the final sample included representatives working in each of the countries targeted.

Responses indicated that while most respondents were aware of the broad ethical-legal provisions which are outlined in GCP requirements, many did not know the specifics of where in the locally applicable ethical-legal framework they could be found. This raised the question of whether or not investigators should be required to have this specific knowledge regarding the ethical-legal frameworks and provisions. Several respondents suggested that, provided GCP is followed, this detail constituted unnecessary knowledge for investigators. Most respondents acknowledged that broad GCP training had value for providing investigators with an overview of approaches to the ethical-legal conduct of research. However, many also suggested that pragmatic and issue-focused, ethical-legal training would be far more useful for

investigators conducting research in each of these countries. Such training should be responsive to the practical challenges that investigators face and should provide ethical-legal direction for dealing with issues such as the regulatory review process; research with vulnerable groups; blood and tissue specimen storage and future use; the prevention of stigma and discrimination; the payment of research participants; dealing with trial-related harms and compensation for trial related injury; mandatory reporting and disclosure obligations; and sponsor/investigator post-trial responsibilities to participants.

Ethical-legal training by the HIV/AIDS Vaccines Ethics Group (HAVEG) on HIV prevention research with minors in South Africa, was identified as a model for approaching other identified issues. It is recommended that this approach be considered a best practice for ethical-legal training and that such training be expanded and supported.

2. BACKGROUND AND INTRODUCTION:

Given the burden of HIV infection in Africa, there is a concern that the urgency and importance of the goals of HIV preventive (in this case vaccine) research may overshadow the need to protect the well-being and human rights of trial participants (Grant et al., 2005).

Promoting and protecting the human rights of trial participants is important for a number of reasons including the following:

- Medical research is not only about science and the advancement of scientific knowledge, but it is also about human development. For this reason, protecting the rights of human beings is just as important as advancing science;
- Protecting and promoting the rights of trial participants may help to promote good science, since it encourages trial participants to participate in, and remain in, clinical trials; and
- Ethical and lawful research can promote public confidence in the research and its findings (Grant et al., 2005).

Given the increasing volume of research being conducted in Africa (Glickman et al., 2009), it is imperative that African countries develop strong substantive and procedural ethical-legal safeguards to protect research participants (Strode, Slack, Mushariwa, 2005; Grant, Lewis & Strode, 2005). The ethical-legal framework operating in a country helps to balance the goals of science with the rights and welfare of human beings, by providing for structures and processes to oversee, regulate and monitor research on human participants according to accepted norms and standards (Grant et al., 2005). Strode, Slack and Mushariwa (2005) propose that an effective ethical-legal system for research should contain five essential components, namely,

(i) scientific, ethical and policy-making structures to regulate research, that is, approve new medical products, set national ethical standards, and develop research policy;
(ii) research ethics committees (RECs) responsible for the competent ethical review of research;
(iii) national ethical guidelines and standards to guide ethical review;
(iv) laws to protect trial participants; and
(v) mechanisms to monitor and enforce legal rights and ethical standards.

These are discussed in more detail in the section that follows.

2.1 Components of the ethical-legal framework for research

(i) *Scientific, ethical and policy-making structures to regulate research*

The existence of structures and national regulatory bodies to approve new medical products, set national ethical standards and ensure the ethical conduct of research, and to develop research policies and set a locally relevant research agenda, are essential to an effective ethical-legal system for research (Strode et al., 2005).

(ii) *Competent bodies for the ethical review of research*

In an effective ethical-legal system for research, proposed research should be ethically reviewed by appropriate ethical review bodies (RECs) (Strode et al., 2005). Furthermore, these bodies should be "representative, resourced, capacitated, required by law to use national ethical guidelines and accountable to other structures" (Strode et al., 2005, p. 599). RECs are also meant to conduct ongoing monitoring and evaluation of all trials from an ethics and human rights perspective (SAAVI, 2008).

(iii) *National ethical guidelines and standards to guide ethical review*

National ethical guidelines on research (and HIV vaccine research and development specifically) should exist, and RECs should be legally obliged to follow these guidelines (Strode et al., 2005).

(iv) *Laws to protect trial participants*

There should be specific legislation in place to protect trial participants. This legislation should include, *inter alia*, specific provisions regarding: the conduct of research on vulnerable groups (such as children); informed consent; privacy and confidentiality regarding research participation and/or diagnosis and treatment; addressing trial-related harm; compensation for trial-related injuries; and protection from HIV/AIDS-related stigma and discrimination (Strode et al., 2005).

(v) *Mechanisms to monitor and enforce legal rights and ethical standards*

There should be mechanisms in place to monitor and enforce the legal rights of participants and ethical obligations contained in guidelines (Strode et al., 2005). Otherwise, the trial participants are left with little recourse should their rights be violated or the ethical obligations not upheld.

2.2 Rationale

For ethical-legal frameworks to adequately protect research participants, the frameworks must exist at country level and the researchers conducting trials must be aware of and comply with the regulations (Grant et al., 2005). Milford, Wassenaar and Slack (2006) highlight the lack of knowledge of national ethical-legal frameworks as a key challenge to research ethics

committees (RECs) in Africa. Given that some members of RECs are themselves investigators (Milford et al., 2006), this suggests that there may also be a lack of awareness of these frameworks among researchers in host countries. In order to design appropriately targeted ethical-legal training for investigators in host countries, including foreign researchers conducting trials in these countries, it is necessary to assess how aware researchers are of the existing ethical-legal frameworks and their reported compliance with them.

Thus the principal objective of this study was to survey the extent to which HIV vaccine trial investigators were aware of and comply with national ethical guidelines and laws. The countries examined are South Africa, Kenya, Malawi and Zambia. This research was originally conceptualized as an email survey to be sent to HIV vaccine trial investigators in countries whose ethical-legal frameworks governing research were perceived as strong (i.e. South Africa and Kenya), and those whose frameworks were perceived as weaker, (i.e. Zambia and Malawi). The ethical-legal framework for each country is briefly described in the section that follows.

2.3 The Ethical-legal framework for research in South Africa

To date eight preventive HIV vaccine trials have been conducted in South Africa. This has included one trial of a therapeutic HIV vaccine (see SAAVI: www.saavi.org.za).

South Africa has a highly developed ethical-legal framework to regulate trials.

(i) Scientific, ethical and policy-making structures to regulate research

South Africa's research is primarily regulated through the National Health Act (NHA). All clinic trials to be conducted in South Africa will be required to register with the Department of Health and will be issued a study number by the DOH through the National Health Research Ethics Committee (Department of Health, 2008).

In addition, the Medicines Control Council (MCC), a statutory body, must review all clinical trials of both non-registered medicinal substances and new indications of registered medicinal substances. The MCC is mandated with the registration of any medicines intended for human or animal use, and must therefore approve any research which will contribute to the development of a product for registration. The MCC cannot approve research protocols unless these have been reviewed according to accepted ethical standards and have been determined to meet these, and therefore has a procedural obligation to ensure that protocols have been competently reviewed by an independent REC (cf. Strode et al., 2005). In the case of an ongoing trial where there are serious breaches of Good Clinical Practice, the MCC can close a trial down (Department of Health, 2008). RECs are also legally empowered to stop a study or

trial.

The National Health Research Ethics Council (NHREC) is responsible for setting ethical norms and standards for research and for the oversight and accreditation of RECs, which review health-related research protocols. It will have the overall responsibility to promote, ensure and monitor compliance of relevant legislation, regulations and guidelines by approved ethics committees (Department of Health 2008). The NHREC does not conduct reviews of trials or issue ethics approvals. It reports directly to the Minister of Health.

(ii) *Ethical review of research*

Both local and international ethical guidelines include provisions requiring the ethical review of research by competent and accountable independent RECs. Prior to the National Health Act (NHA) the only way of ensuring this was the MCC's capacity to refuse to approve research which it felt had not been adequately reviewed. However, with the National Health Act, RECs must be accredited with the NHREC, meeting certain standards and capacity requirements. The MCC will not approve research which has not been approved by an accredited REC (cf. Strode et al., 2005).

(iii) *National ethical guidelines and standards to guide ethical review*

In South Africa there are various ethical guidelines in existence, including:

Medical Research Council (2002). *Guidelines on ethics for medical research: General Principles*. Available from: http://www.sahealthinfo.org/ethics/book1.htm

Medical Research Council (2003). *Guidelines on ethics for medical research: HIV preventive vaccine research.* Available from: http://www.sahealthinfo.org/ethics/book5.htm

Department of Health (2004). *Ethics in health research: Principles, Structures and processes*. Pretoria: Department of Health
Available from: http://www.doh.gov.za/docs/factsheets/guidelines/ethnics/index.html

Department of Health. (2006). *Guidelines for good practice in the conduct of clinical trials with human participants in South Africa.* Retrieved March 5, 2008, from http://www.doh.gov.za/docs/index.html

A point worth noting is that although these documents are not legally binding, the standards for research outlined in these documents are likely to be upheld in a court of law, and these guidelines therefore form part of the ethical-legal framework for research (cf. Strode et al., 2005).

(iv) *Laws to Protect Trial Participants*

In South Africa, provisions for the protection of trial participants exist in various pieces of legislation, which may not necessarily be specific to research (Barrett Grant & Strode, 2001; Strode et al., 2005).

The *Constitution of the Republic of South Africa* makes provision for the right to bodily and psychological integrity, and for the right to participate in research provided informed consent has been obtained. The right to be protected against social harms such as stigma and discrimination (based on HIV-status) is embodied in the *Constitution* and the *Employment Equity Act*, and the Promotion of *Equality and Prevention of Unfair Discrimination Act* also makes provision for protection from unfair discrimination. The *Constitution* provides for the right to privacy and confidentiality (Barrett Grant & Strode, 2001). The *National Health Act* (section 71) attempts to clarify protections for trial participants and sets some of the conditions for research with human participants.

(v) *Mechanisms to monitor and enforce legal rights and ethical standards*

The MCC has the authority to halt any trial that it has approved in the event of a serious breach of good clinical practice (Harvard School of Public Health, 2008). While an accredited local REC can also halt a study in the event of a serious breach of ethics or good clinical practice, the capacity of RECs to provide continued monitoring of studies is often limited (Strode et al. 2005). The Human Rights Commission can also provide assistance and there are several legal NGOs that provide assistance on issues related to human rights violations.

2.4 The Ethical-legal framework for research in Kenya

To date, six HIV vaccine trials have taken place in Kenya (see www.iavi.org)

[Note: Much of the information in this section is taken from the country report for the 2005 AAVP-ELH legal audit and draft country report for a 2009 AAVP-ELH legal audit]

(i) *Scientific, ethical and policy-making structures to regulate research*

In Kenya, the Science and Technology Act established the National Council for Science and Technology (NCST), a body responsible for, *inter alia*, the co-ordination of all research work in Kenya; for determining priorities for science and technological activities in Kenya; and to advise the government on research-related matters (section 4) (Grant et al., 2005; Grant et al., 2009). The NCST has established the Medical Sciences Advisory Research Committee. This committee is responsible for:

- advising appropriate ministers on the strategies and resources needed to conduct research which meets national priorities;

- encouraging action on research results in the public sector;
- being aware of all ongoing research projects and programmes in the country, and of programmes run internationally, that might be of relevance to Kenya;
- monitoring and enhancing research capacity in Kenya;
- fostering partnerships with international organisations;
- and overseeing the dissemination and publication of research results (section 9) (Grant et al., 2005; Grant et al., 2009).

The Pharmacy and Poisons Board is the drug regulatory authority established under the Pharmacy and Poisons Act. The Board is responsible for the regulatory approval and review of drugs (including vaccines) which are to be used in Kenya and as such it plays a significant role in the approval of clinical trials (Grant et al., 2005; Grant et al., 2009).

The National AIDS Control Council (NACC) is responsible for the co-ordination and oversight of HIV/AIDS prevention and control activities in Kenya. "Whilst the NACC does not specifically play a regulatory role in the ethical-legal framework it is involved in coordinating HIV/AIDS activities and accordingly can play a role in ensuring research is coordinated" (Grant et al., 2005, p.73).

The Kenya HIV/AIDS Vaccine Advisory Sub-Committee (VSC), a multi-sectoral committee including international representatives, is based within the Ministry of Health (MOH) and is mandated to advise and assist the MOH in formulating a national framework for HIV/AIDS vaccine research and development in Kenya. To this end, the subcommittee developed the *National Guidelines for Research and Development of HIV/AIDS Vaccines* in 2005. These guidelines spell out a number of policy issues affecting vaccine research; the roles of government, regional and sub-regional intergovernmental organizations, the African AIDS Vaccine programme, WHO, UNAIDS, vaccine manufacturers, funding organizations, investigators and collaborating institutions. This body is responsible for the initial review of all HIV vaccine protocols (Grant et al., 2005; *Kenya National Guidelines for Research and Development of HIV/AIDS Vaccines*, 2005).

(ii) *Competent bodies for the ethical review of research*

In Kenya, research proposals typically undergo several rounds of ethical review, including review by the host institution and by the NCST. Most research involving human subjects must be approved by the NCST (Harvard School of Public Health, 2008).

The Ethical Review Committee (ERC) of the Kenya Medical Research Institute (KEMRI) is accredited by NCST as a National Ethical Review Committee, and is required to examine all research proposals which involve human participants. The KEMRI ERC sets standards that local

ethics committees must abide by when reviewing proposals. The KEMRI ERC is a multi-sectoral and multidisciplinary committee and most of its members are from outside of KEMRI, which enables the ERC to maintain its independence and to avoid any institutional influence.

For HIV/AIDS vaccine research, the Kenya National Guidelines for Research and Development of HIV/AIDS Vaccines requires investigators to submit a concept paper to the Kenya HIV/AIDS Vaccine Sub-Committee, for review of pre-clinical safety and immunogenicity data, as well as for review of relevance of the trial to the country. The Sub-Committee response is sent to Pharmacy and Poisons Board and the NCST for review, comment/amendment or rejection. Only after approval by both bodies can the research begin (Grant et al., 2009).

(iii) *National ethical guidelines and standards to guide ethical review*

The NCST (2004) Guidelines for Ethical Conduct of Biomedical Research Involving Human Subjects in Kenya (otherwise referred to as NCST 45), establishes a framework for determining if a research proposal is ethical (Harvard School of Public Health, 2008). These guidelines provide pragmatic direction on the structure and functioning of ERCs (Grant et al., 2009).

The Kenya National Guidelines for Research and Development of HIV/AIDS Vaccines were enacted by the Ministry of Health in 2005. These guidelines were developed by the Kenya National HIV/AIDS Vaccines Sub-Committee to provide a framework for developing and evaluating HIV/AIDS vaccines.

(iv) *Laws to protect trial participants*

While there is no specific legal framework governing clinical research and the rights of trial participants in Kenya, many of the rights in the Constitution, statutory laws, and the common law have relevance (Grant et al., 2005; Grant et al., 2009). In Kenya, "the Constitution is the supreme law and is applicable throughout Kenya. Any law, either written or unwritten, which is inconsistent or which contravenes the Constitution is void to the extent of its inconsistency" (Grant et al., 2005, p.67). Embodied in the Constitution of Kenya, is, *inter alia*, the right to privacy and freedom from discrimination.

The recent HIV and AIDS Prevention and Control Act, yet to be operationalized, is a comprehensive piece of legislation that deals with HIV-related matters. In terms of the rights of research participants, Part IX of the Act contains explicit provision that biomedical HIV/AIDS-related research on human subjects cannot be embarked upon unless this research meets the requirements set out in the Science and Technology Act (section 39) (Grant et al., 2009). The written informed consent of each participant is required for such research; and

where an individual is a minor, the written consent of a parent or legal guardian is required. During the consent process the trial participant must be adequately informed of the aims, methods, anticipated benefits and the potential hazards and discomforts of research (section 40) (Grant et al., 2009). This new Act also contains provisions relating to protection from HIV/AIDS-related social harms and discrimination; privacy and confidentiality; access to healthcare services; and the conduct of HIV-testing (Grant et al., 2009). This Act also includes provisions relating to the age of consent to research and various medical procedures.

The Kenyan Children's Act, specifies the age of majority and includes provisions related to guardianship. The NCST 45 guidelines also include provisions regarding the specific conditions under which research can be conducted with children (Grant et al., 2009).

(v) *Mechanisms to monitor and enforce legal rights and ethical standards*

In Kenya, bodies affiliated to the Medical Science Advisory Research Committee are mandated by the Science and Technology Act to monitor and review the progress in research protocols on an annual basis (Grant et al., 2005; Grant et al., 2009).

The Public Health Act makes provision for the Minister of Health to, on the advice of the Central Board of Health, institute an inquiry into the manner in which public health research such as HIV vaccine trials are being conducted at a research institute, should concerns arise (Grant et al., 2005; Grant et al., 2009).

Trial participants have the right to have their complaints addressed through civil law processes, in terms of Kenyan common law. The HIV and AIDS Prevention and Control Act establishes an HIV and AIDS Tribunal to resolve any disputes or issues arising from the Act (excluding criminal matters) (section 26)..

Complaints regarding the violations of codes of professional and clinical practice in the conduct of research can be lodged with the Medical Practitioner's Board. Some NGOs may also be prepared to assist persons to uphold their rights (Grant et al., 2009).

2.5 The Ethical-legal framework for research in Malawi

To date, one HIV vaccine trial has been conducted in Malawi (see: www.iavi.org).

[Note: Much of the information in this section is taken from the draft country report for a 2009 AAVP-ELH legal audit (Andanda, 2009)]

(i) *Scientific, ethical and policy-making structures to regulate research*

The National Research Council of Malawi (NRCM) provides the general framework for research in Malawi. The NRCM is a statutory body within the purview of the Office of the President and Cabinet (OPC). As a professional arm of the OPC on matters relating to research, the NRCM is mandated with the promotion and coordination of research, science and technology in Malawi. All health-related (and other) research falls within this body's jurisdiction (NRCM, 2007). The NRCM is also responsible for the development of national research policy (Harvard School of Public Health, 2008). The NRCM, in consultation with relevant stakeholders, is also mandated with setting norms and standards for research through the development of national regulations, guidelines and procedures for research in the country (NRCM, 2002; Harvard School of Public Health, 2006-2008) and "[s]ectoral ministries and institutions are encouraged to develop their own sector-specific research guidelines and policies to work in tandem with NRCM's umbrella regulations, guidelines and policies" (Harvard School of Public Health, 2006-2008: Malawi).

The Pharmacy, Medicines and Poisons Board (established in 1988 under The Pharmacy, Medicines and Poisons Act) is the national drug regulatory authority. All clinical trials testing medicines intended for human use are required to register the product and the trial with this board. The Board does not have power of review and is not involved in research. However, registration is mandatory for all studies involving pharmaceuticals that are not on the national list of approved pharmaceuticals, for licensing and monitoring purposes (Harvard School of Public Health 2006-2008).

Various other bodies which form part of the ethical-legal framework for research and HIV vaccine-related research in Malawi are described in some detail in Andanda (2009). These include:

- The Bioethics Research Unit**,** which falls under the Department of Community Health and conducts research on various topics in the area of Bioethics as well as providing advice to various stakeholders;
- The Ministry of Health, which sets health policy relating to HIV/AIDS; the Ministry of Health HIV/AIDS Unit, which implements health sector response to HIV/AIDS as well as works to ensure the success of HIV/AIDS programs;
- The National AIDS Control Program which implements the health sector response to HIV/AIDS; the Cabinet Committee on HIV/AIDS Prevention and Care*,* which sets up relevant policy and provides political direction to the National AIDS Commission and also furnishes 'the NACP with political guidance, policy approval and advocacy';
- The National AIDS Committee (NAC), a multi-sectoral endeavour, to provide the NACP with policy guidance as well as technical support for its programmes;
- The National AIDS Control Committee, which functions *inter alia* to implement HIV/AIDS education and prevention programs;

- The National AIDS Commission – This is in the office of the President and co-ordinates the national multi-sectoral response to HIV/AIDS;
- The National AIDS Secretariat (NAS), which coordinates the national response to HIV and AIDS.

All clinicians conducting research must be registered with a medical professionals council, overseeing their domain of practice.

(ii) *Competent bodies for the ethical review of research*

Research Ethics Committees (RECs) in Malawi are mandated by the NRCM to review and monitor health research. There are no specific policies or guidelines onthe establishment and constitution of RECs in Malawi. Currently there are two NRCM accredited RECs: the National Health Sciences Research Committee (NHSRC) and the College of Medicine Research and Ethics Committee (COMREC). Both NHSRC and COMREC report to and are monitored by NRCM. All studies with human participants conducted within the country must be reviewed by one of these two committees (Harvard School of Public Health 2006-2008).

(iii) *National ethical guidelines and standards to guide ethical review*

The NRCM has developed Procedures and Guidelines for the Conduct of Research in Malawi. Both the NHSRC and COMREC have their own guidelines and standard operating procedures which are within the parameters of the NRCM Guidelines (Harvard School of Public Health 2006-2008).

The NHSRC and the COMREC guidelines for submission and review of proposals include:

1. Summary Guidelines for Writing a Research Proposal (NHSRC);
2. Research Guidelines' (COMREC);
3. Terms of Reference and Functions (COMREC)

(iv) *Laws to protect trial participants*

While there is no dedicated legislation in Malawi dealing with the rights of trial participants, the *Constitution of Malawi* (Chapter IV) and the *Human Rights Act* entrench the rights of citizens of Malawi, to, *inter alia*, informed consent to research participation; privacy and confidentiality; protection from discrimination on any basis; and the right to redress/ compensation for harm.

There are no specific laws relating to research with children. However, the *Child Welfare Act* and the *Child Welfare and Youth Policy* identify children as a vulnerable group, in need of particular protection. The Constitution lists children as all persons under the age of sixteen and states in section 23 that children should be protected from any treatment that is hazardous, or

will interfere with their education or will be harmful to their physical, mental or spiritual, or social development.

(v) *Mechanisms to monitor and enforce legal rights and ethical standards*

The NHSRC and COMREC have 'monitoring sub-committees' which are responsible for the ongoing review and monitoring of research (Andanda, 2009). At specified intervals (usually annually) investigators are required to submit reports to these committees. The Ethics Committees from time to time arrange field visits to study sites in order to ensure regulatory compliance. These Committees also have Compliance Officers who are supposed to monitor research. The NHSRC and COMREC are also required to investigate 'all reports of protocol or ethical violations'. Where there is adequate proof of a violation, the researcher may be directed to terminate the study and compensate subjects (Harvard School of Public Health 2006-2008: Malawi).

Medical Rights Watch, an NGO, also plays an important role in monitoring the rights of research participants. In addition, the Malawi Human Rights Commission may also look into research with an interest to protect the rights of participants. Professional medical bodies have statutory powers to discipline members who act unethically.

2.6 The Ethical-legal framework for research in Zambia

To date, two HIV vaccine trials have been conducted in Zambia (see: www.iavi.org)

[Note: Much of the information in this section is taken directly from the draft 2009 legal audit and the draft country report for a 2009 AAVP-ELH legal audit (Andanda, 2009)]

(i) *Scientific, ethical and policy-making structures to regulate research*

In Zambia, the Pharmaceutical Regulatory Authority (established by the Pharmaceutical Act) regulates medicines intended for human use and also provides for the control of medicines and herbal medicines. It is required that all products intended for clinical testing are registered with this authority, and that all clinical trials which will lead to the development of a product requiring registration must be registered with this authority.

The National HIV/AIDS/STI/TB Council**,** established in terms of the National HIV/ AIDS/ STI/ TB Council Act, is responsible for the co-ordination, development, monitoring and evaluation of the national effort for the prevention and combating of the spread of HIV, AIDS, STIs and TB. The functions and powers of the Council include the development of 'a national HIV, AIDS, STI and TB research agenda and strategic plan' which includes the search for a cure for HIV and AIDS, as well as collaboration 'with other research institutions in relation to HIV, AIDS, STI

and TB' (Andanda, 2009, p. 39). The Tropical Disease Research Centre Act creates a Tropical Disease Research Centre and Board which is responsible for conducting research and training in tropical diseases and related matters.

The National Council for Scientific Research Act establishes the National Council for Scientific Research (NCSR). The NCSR is mandated with the co-ordination and promotion of scientific research which meets the country's development plans. The functions of the NCSR are also to advise the government on national scientific research policy and activities within Zambia; to co-ordinate scientific research and activities within Zambia; to determine priorities in the national research programme, particularly in relation to development plans. All research institutions must be registered with the NCSR (Zarzan, 2009 in Andanda, 2009).

(ii) *Competent bodies for the ethical review of research*

The University of Zambia School of Medicine has established a Research and Ethics Committee which is responsible for reviewing and granting permission for undertaking research in the southern part of the country and the Tropical Diseases Research Board, also has an Ethics Committee which is responsible for the northern part of Zambia (Zarzan, 2009 in Andanda, 2009).

The functions of these RECs are to review research protocols/proposals, monitor and evaluate the conduct of research and address and complaints that arise through investigation (Zarzan, 2009 in Andanda, 2009).

(iii) *National ethical guidelines and standards to guide ethical review*

Zambia does not have national ethical guidelines to guide research nor are their guidelines to guide HIV vaccine research.

(iv) *Laws to protect trial participants*

There is no dedicated legislation dealing specifically with the rights of trial participants. The Constitution of Zambia includes, *inter alia*, provisions for the right to life, freedom, privacy, and protection from discrimination. It also includes a provision of the right of young persons to be protected from exploitation.

(v) *Mechanisms to monitor and enforce legal rights and ethical standards*

In Zambia at present there is no specific body which actively monitors and enforces legal rights and ethical standards. The RECs do not have the capacity for this.

Trial participants can seek legal redress for violations of their constitutional rights in the law courts. The Human Rights Commission may intervene on behalf of trial participants to enforce

their rights.

3. AIMS AND OBJECTIVES:

The principal objective of this study is to survey the extent to which HIV vaccine trial investigators are aware of and comply with national legal and ethical guidelines and human rights principles.

Research questions:

1. How aware are HIV vaccine trial investigators in Africa of existing ethical-legal frameworks (including human rights principles) which govern research in their respective countries?
2. How do researchers implement these provisions/principles?
3. What ethical-legal training would researchers, conducting HIV vaccine trials in the identified countries, consider most necessary?

4. METHODOLOGY:

Ethics approval was obtained from the University of KwaZulu-Natal, Faculty of Humanities, Development and Social Science research ethics committee.

4.1 Sample

This research was conducted via email surveys or telephone interviews with HIV vaccine trial investigators. Respondents in this study were selected via purposive or snowball sampling techniques, where initial contacts referred us to other respondents. Contact details for respondents were accessed from an existing AAVP database of researchers conducting HIV vaccine research in Africa and by searching key websites. Seven potential respondents from South Africa, 10 potential respondents from Kenya, three potential respondents from Zambia and one potential respondent from Malawi agreed to complete the questionnaire. Of these, two respondents from South Africa completed the email questionnaire; two respondents opted for the telephone interview and another two responded in brief (one byemail and one telephonically); three respondents from Kenya completed the questionnaire and two indicated that on review they could not complete it; two respondents from Zambia completed the questionnaire; and one respondent from Malawi completed the questionnaire. Overall 12 participants responded to the email survey [57 % response rate] (Table 1).

Table 1: Number of potential versus actual respondents by country

Country	Potential	Actual
South Africa	7	6*
Kenya	10	3
Malawi	3	2
Zambia	1	1
Total	21	12

*2 email questionnaires; 2 telephonic interviews; 2 in brief (email and telephone). The 2 brief questionnaires have not been included in the review of data.

4.2 Procedure

This research was originally conceptualized as an email survey to be sent to HIV vaccine trial investigators in countries whose ethical-legal frameworks governing research were perceived as strong e.g. South Africa and Kenya, and those whose frameworks were perceived as weaker, e.g. Zambia and Malawi. An information sheet (Appendix 2) outlining the study was sent to potential respondents. The email questionnaire (Appendix 1) was sent to those who expressed interest in completing the survey. Many of those who initially expressed interest in participating did not return the survey and did not respond to either of two follow-up emails.. In addition, initial responses indicated that the survey was difficult to complete, so the email survey was adapted to questions for a semi-structured interview. Key informants were canvassed for the telephone interviews – two respondents from South Africa agreed to telephone interviews.

Given the fact that initially following a follow-up email only three questionnaires were returned, the responses were vague, and in response to indications about the difficulty of the questionnaire, it was agreed that respondents who had not yet returned the questionnaire would be provided the option of telephone interviews. Those who had not yet returned the questionnaire were contacted via email with the offer of a telephone interview. Most respondents indicated that they would still prefer to complete the questionnaire electronically, and three key investigators in South Africa opted for the telephone interview. As such, the questions were adapted to cluster into particular issues and focussed more on implementation and researchers' requirements for ethical-legal training than an awareness of where provisions could be found.

4.3 Instruments

An email questionnaire (Appendix 1) consisting of both open- and closed-ended questions was sent to researchers who agreed to participate in the study. This questionnaire aimed to elicit information about respondents' awareness and implementation of ethical-legal provisions and

frameworks governing clinical research. It also aimed to establish potential gaps in researcher understanding of this framework, as well as what training around these frameworks might be most beneficial for researchers working in the identified countries.

Questions from the email survey were used as the basis for the semi-structured telephone interviews.

4.4 Data analysis

The questionnaires returned, as well as information from telephonic interviews, were grouped into country responses. They were then collated and compared, and an analysis was undertaken.

5. RESULTS:

The questionnaire asked respondents if they had specific knowledge of provisions in laws or policies dealing with certain areas that are important for trials (Table 2). Respondents were asked to mark yes, no or unsure. If yes, they were further asked to provide specific information on where the provision was from.

The purpose was to determine, firstly, if the investigator had knowledge of the particular ethical-legal principle and if so, where the knowledge was from. This was an attempt to establish if they followed international or national laws or guidelines.

Table 2: Investigators' self-reporting of knowledge of international and national guidelines/policies

	South Africa	Kenya	Malawi	Zambia
International guidelines frameworks mentioned	Yes	Yes	Yes	Yes
National guidelines/policies mentioned	Yes	Yes	Yes	Yes
Constitution mentioned	Yes, once when dealing with discrimination	Yes, once when dealing with age of consent	No	No

5.1 Country analysis: South Africa

It was clear that there was no standard agreement on what guidelines and laws cover the particular provisions. It appeared that researchers rely heavily on one guideline and use it as the justification for the various provisions (See for example respondent 1 in Table 3). In addition, rights that are clearly in the Constitution such as bodily integrity and human dignity were not cited by the respondents. The Constitution was mentioned only once by one respondent when considering the issue of discrimination.

Table 3: Responses from South Africa

	Respondent 1	**Respondent 2**	**Respondent 3**	**Respondent 4**
Specific provisions				
Autonomy	ICF/GCP	Guidelines for Good Practice in the Conduct of Clinical Trials in Human Participants in SA and Medical Research Council Guidelines on Ethics in Medical Research: General Principles	National Health Act, SA Department of Health Guidelines	DoH guidelines, Health Act
Human dignity	ICF/GCP	As above		
Confidentiality	ICF/GCP/EC	As above	Not sure where specifically found	Health Act, GCP
Age of consent to medical procedures	Unsure	Children's Act	Children's Act	S71 Health Act, Child Act Sexual Offences Act
Age of consent to research	SA GCP/ICH GCP	Good practice guidelines and MRC	Children's Act	
HIV testing	SA National Guidelines	Good practice guidelines	Children's Act, unsure about testing in adults	
Blood and tissue samples	Unsure	National Health Act	Tissue Act	Blood and Tissue Act, Ethics

	Respondent 1	Respondent 2	Respondent 3	Respondent 4
Specific provisions				
				Committees, GCP
Storage and future use of blood and tissue samples	ICH GCP	National Health Act	Tissue Act	
Regulation of research	SA and ICG GCP	Declaration of Helsinki	Yes, not sure exactly where	
Payment of research participants	Medicine's Control Council	Medicine's Control Council	MCC	GCP, previously MCC
Obligations to report neglect, abuse and criminal activities to relevant authorities	GCP and EC	Unsure	For children, Children's Act	Family Violence Act
Protection of the rights of research participants	GCP and EC	Good practice guidelines and MRC		
Dealing with adverse effects if harmed during trial	GCP and EC	Clinical Trial Compensation Guidelines/ABPI	ICH-GCP and SA national guidelines, MCC	GCP, MCC
Ethical review of research	GCP and EC	Good practice guidelines and MRC	Acts establishing NHREC	GCP, MCC
Informed consent	GCP and EC	As above	Guidelines	
Termination of trials	GCP and EC	Good Practice Guidelines and GCP		
Dealing with withdrawal of participants from trials	GCP and EC	Good Practice Guidelines	ICH-GCP	GCP
Dealing with eligibility and accessibility to drugs post-trial	GCP and EC	Declaration of Helsinki	Unsure	Ethics review process
Dealing with protection from discrimination during trial	GCP and EC	Unsure	Constitution – primary resource for dealing with discrimination ICH-GCP CFR	

	Respondent 1	Respondent 2	Respondent 3	Respondent 4
Specific provisions				
Dealing with protection from discrimination after trial	GCP and EC	Unsure	Constitution – primary resource for dealing with discrimination ICH-GCP CFR	
Dealing with regulatory approval of effective products	GCP and EC	MCC	National Health Act	No clear guidelines regarding approval

5.2 Country Analysis: Kenya

It is clear that there was no standard agreement on what guidelines and laws cover the particular provisions. It appeared that researchers rely heavily on one guideline as the justification for the various provisions (See for example respondent 1 in Table 4). In addition, the Constitution was only mentioned by one respondent, related to age of majority.

Table 4: Responses from Kenya

	Respondent 1	Respondent 2	Respondent 3
Specific provisions			
Bodily integrity	No	National Council for Science and Technology (NCST)	Unsure
Autonomy	No	NCST	Unsure
Human dignity	KEMRI Ethics Committee	NCST	AIDS vaccine research guidelines
Confidentiality	As above	NCST	As above
Age of consent to medical procedures	As above	NCST	Constitution
Age of consent to research	As above	NCST	Constitution
HIV testing	HIV /AIDS Prevention and Control Act	National guidelines on HIV testing, Ministry of Health	National guidelines for VCT
Blood and tissue samples	KEMRI import/export policies	NCST	Unsure
Storage and future	As above	NCST	Unsure

	Respondent 1	Respondent 2	Respondent 3
Specific provisions			
use of blood and tissue samples	KEMRI Ethic Committee		
Regulation of research	KEMRI Ethics Committee KEMRI IRB Kenya Medicine and Poison Board	NCST	Approval requirements
Payment of research participants	KEMRI Ethics Committee	NCST	Not specific
Obligations to report neglect, abuse and criminal activities to relevant authorities	As above	NCST	No
Protection of the rights of research participants	As above	NSCT	ICH
Dealing with adverse effects if harmed during trial	As above	NCST	Unsure
Ethical review of research	As above	NCST	Yes
Informed consent	As above	NCST	ICH
Termination of trials	KEMRI IRB	NCST	Unsure
Dealing with withdrawal of participants from trials	KEMRI Ethics Committee	NSCT	Unsure
Dealing with eligibility and accessibility to drugs post-trial	Kenya Medicine and Poisons Board	NCST	Unsure
Dealing with protection from discrimination during trial	KEMRI Ethics Committee	IRB	No
Dealing with protection from	KEMRI Ethics Committee	IRB	No

	Respondent 1	Respondent 2	Respondent 3
Specific provisions			
discrimination after trial			
Dealing with regulatory approval of effective products	Kenya Medicine and Poisons Board	Kenya Pharmacy and Poisons Board	No

5.3 County Analysis: Malawi

The responses from Malawi relied heavily on 'guidelines' without providing more details on what they were or where they come from (Table 5).

Table 5: Response from Malawi

	Respondent 1
Specific provisions	
Bodily integrity	
Autonomy	Guidelines and regulations of the Act
Human dignity	As above
Confidentiality	As above
Age of consent to medical procedures	Unsure
Age of consent to research	Guidelines and regulations of the Act
HIV testing	HIV Policy
Blood and tissue samples	Guidelines and regulations of the Act
Storage and future use of blood and tissue samples	Guidelines
Regulation of research	Guidelines of Pharmacy Act
Payment of research participants	Guidelines
Obligations to report neglect, abuse and criminal activities to relevant authorities	
Protection of the rights of research participants	
Dealing with adverse effects if harmed during trial	Guidelines and the Act
Ethical review of research	In guidelines

Informed consent	In guidelines
Termination of trials	In guidelines and regulations of the Act
Dealing with withdrawal of participants from trials	In Guidelines
Dealing with eligibility and accessibility to drugs post-trial	No
Dealing with protection from discrimination during trial	Unsure
Dealing with protection from discrimination after trial	No
Dealing with regulatory approval of effective products	In the Act and Regulations

5.4 County Analysis: Zambia

Since there is no clear framework in Zambia, respondents relied heavily on standard operating procedures and general principles, without referring to a particular provision or guideline (Table 6).

Table 6: Responses from Zambia

	Respondent 1	**Respondent 2**
Specific provisions		
Bodily integrity	Unsure	
Autonomy	Standard operating procedure (SOP)	All researchers required to observe dignity and freedom of participants in research
Human dignity	Human subjects research training, SOP on human subject education programme (HSEP) IRB	*Not answered*
Confidentiality	SOP on protection of volunteer privacy	Informed consent process assures that all information collected during research will not be divulged
Age of consent to medical procedures	Not specified but note that age of consent is 18	Age of consent is 16
Age of consent to research	SOP on obtaining informed consent	

HIV testing	SOP on couple's HIV VCT	Procedures for obtaining consent is in place and all researchers specify the process before approval given by REC
Blood and tissue samples	Unsure	Consent form, permission to transport from REC
Storage and future use of blood and tissue samples	SOP on procurement, storage and transport of samples	
Regulation of research	ICF, protocol, REC	
Payment of research participants	Informed consents	REC
Obligations to report neglect, abuse and criminal activities to relevant authorities	Unsure	Criminal law
Protection of the rights of research participants	Informed consents, REC	
Dealing with adverse effects if harmed during trial	SOP on SAE	Regulations in place
Ethical review of research	SOP on informed consent	REC
Informed consent	SOP on informed consent	
Termination of trials	Informed consent	REC to be informed, participants to be informed
Dealing with withdrawal of participants from trials	Informed consent	At beginning of study, participants clearly informed
Dealing with eligibility and accessibility to drugs post-trial	Study specific protocol	Protocol
Dealing with protection from discrimination during trial	Unsure	
Dealing with protection from discrimination after trial	Unsure	

Dealing with regulatory approval of effective products	Unsure	Pharmacy Regulatory Agency

6 DISCUSSION AND REFLECTION:

This study was initially conceived with the primary objective to survey the extent to which HIV vaccine trial investigators are aware of and comply with ethical-legal and human rights frameworks at local level. As such, a detailed email survey was developed that aimed to elicit responses to (1) existing ethical-legal provisions and human rights principles that impact on the conduct of HIV prevention trials in country, (2) whether the trial investigator was aware of the details of these provisions/principles, (3) how these provisions are procedurally implemented, and (4) the type of ethical-legal training that would most benefit HIV vaccine researchers.

The legal provisions in the survey covered areas such as informed consent, compensation for trial-related harm, ethical and regulatory review, protection of participants from discrimination, post-trial access, payment, HIV testing, confidentiality and age of consent. In an effort to elicit whether respondents were aware of where the provisions were found in national laws and ethical frameworks, an email questionnaire was considered most appropriate.

An information sheet was sent to participants and 21 respondents expressed an interest in participating in the study. On receipt of the questionnaire, several respondents noted that the questionnaire was difficult to complete due to their general lack of awareness of the specific laws governing research. Two also indicated that they would not be able to complete the questionnaire, given a lack of this specific knowledge, and withdrew from the study.

For those respondents who did return the surveys, many items in the questionnaire were not completed, particularly those pertaining to the provisions that govern research in country and how these are implemented at sites. This provided an important indicator that many respondents were not aware of the specific laws governing research within their respective countries. In many cases, international ethical guidelines were cited, rather than local guidelines. Good Clinical Practice was often listed as the only framework guiding research for many of the domains described above. This does suggest a lack of awareness of locally applicable laws. However, in Zambia, where there are no national guidelines or standards for research, this response may be appropriate.

Further, respondents heavily relied on one or two guidelines to cover the various

provisions/principles.

Few of the respondents mentioned the Constitution of the country in which they were conducting trials. This is significant because the Constitution is the supreme governing law of any country, and everyone is bound by the provisions contained therein. If researchers are not aware of the Constitution, they may be in breach of human rights protections and this can lead to serious issues in terms of potential liability for harm caused.

UNAIDS (2007) suggests that a survey of all protective laws and regulations applicable to a trial site should be conducted prior to the initiation of an HIV prevention trial and where such a survey has not been completed, HIV prevention trials should not be conducted. While this suggests that investigators would need to have some awareness of the applicable laws, the question of whether or not researchers would actually need to know where specific laws are found in order to do this is raised. Also, would GCP, which outlines the general ethical-legal principles according to which trials must be conducted, not be sufficient to offer protection to trial participants? Furthermore, who should be responsible for conducting such an audit? These are matters which invite further investigation and discussion.

Given the complexity of the ethical-legal frameworks for research, and the fact that in many countries there are no dedicated laws regulating research and protecting clinical trial participants (these are found in many different pieces of legislation), most respondents suggested that there was a need for some sort of ethical-legal training of researchers working in these countries. Some however questioned the value of additional training to raise awareness of the laws, when researchers should receive this generic overview of the ethical-legal issues and international standards at least from GCP training. Respondents identified areas of clinical research around which there is a need for ethical-legal training. Several suggested that broad, generic training regarding the ethical-legal frameworks for research applicable at each site would be useful for junior research staff, in order for them to gain an awareness of these. Others identified specific issues on which they felt researchers would benefit from training. These included: submissions for ethical review and the regulatory review process; research with vulnerable groups such as children and adolescents, men who have sex with men (MSM), and women in patriarchal societies; blood and tissue specimen storage and future use; researchers' roles in the prevention of stigma and discrimination; the payment of research participants; dealing with trial-related harms and compensation for trial related injury; mandatory reporting and disclosure obligations; and sponsor/investigator responsibilities to participants post-trial.

The identification of these specific areas requiring ethical-legal training, in conjunction with views expressed by respondents in the telephone interviews suggests that researchers felt

that they have an overview of the legal and ethical framework through GCP training, and that they would benefit more from specific issues-focused training, for example on research with adolescents or children. In addition to this, respondents to the telephone interviews noted that in many cases the ethical-legal provisions for addressing the areas identified as challenging (listed above) were sometimes contradictory and difficult to interpret, and that researchers were often left with no pragmatic solutions to the dilemmas that they face. Respondents suggested that training which aims to assist researchers in navigating the complexity of the ethical-legal framework and its application to specific issues would be beneficial. Workshops conducted by staff of the HIV Vaccine Ethics Group (HAVEG) around the inclusion of minors in research in South Africa, were used as good examples of problem-focused ethical-legal training for researchers.

Several respondents identified the *Directory of the Legal Rights of Child and Adolescent Research Participants* - developed in collaboration between the HIV/AIDS Vaccines Ethics Group (UKZN), the Desmond Tutu HIV Centre (UCT) and the Peri-natal HIV Research Unit (Wits), as a tool to guide protocol development and review of research with minors, and which includes all research and non-research related laws that could impact on research with minors – as a valuable resource in enhancing investigator awareness of, and capacity for navigating, the ethical-legal framework for research.

An interesting observation is that respondents who noted that they had undergone this HAVEG training and made used of the *Legal Directory*, were able to respond more completely and comprehensively to the questions in the survey – they were able to provide accurate information regarding the ethical-legal framework in South Africa and to describe in detail the content of the provisions how they would go about complying with them.

7 LIMITATIONS:

With relatively few responses (57% response rate), it is difficult to generalize findings. However, the responses, the low rate of return of the questionnaires, and the feedback from respondents can be interpreted also as an indication that this is a difficult area for trial investigators. This adds weight to the argument that appropriate ethical-legal training for investigators is needed.

We found that better responses were obtained via telephone interviews as these provided respondents to opportunity to clarify concerns and to explain their positions. Given more time and resources, future studies of this nature might consider telephone interviews as a better method.

Given that the ethical-legal frameworks are arguably complex and that this is an area in which researchers lack familiarity, future work examining investigator understandings of country-specific ethical-legal frameworks, and developing appropriate resources and training materials, is critical. The question of whether or not investigators need to know these laws at all or whether this understanding would rather be a duty of the local REC, are also worth considering.

8 CONCLUSION:

Overall, respondents in this study were generally aware of and reported compliance with the provisions outlined in GCP. Responses, however, indicated that investigators are frequently not aware of the locally applicable ethical-legal frameworks for research in the countries in which they work. Many suggested that generic ethical-legal training may not necessarily be pragmatically useful and that what was needed was training targeted at specific issues. While these concerns are valid, it is precisely with appropriate and practical training on the applicable laws in country that many of these concerns will be addressed.

With proper ethical and legal training, researchers will be given the practical tools to deal with many of the dilemmas they face (such as dealing with children in trials). In addition, importantly, ethical and legal training is a protective factor for the researchers themselves; if they know about what the law says in country, they can abide by it and not place the trial, or indeed themselves, at any risk of violating the laws.

9 RECOMMENDATIONS:

1. A reliable ethical-legal audit of the ethical-legal framework (including all relevant policy and legal documents) for research in each of the countries hosting HIV prevention research should be conducted and made available as a resource document for researchers.
2. In addition to the broad ethical training received during GCP training, all trial investigators should be trained on the particular legal, ethical and human rights provisions at local level before commencing any trials in country. This training should also be expanded to community members to ensure that participants and community members are able to hold investigators accountable. UNAIDS could perhaps consider supplementing their ethical guidelines with some legal information for each host country.
3. Investigators should be canvassed for areas of the ethical-legal framework with which they have difficulty, and for particular challenges they are facing.

4. Development of legal directories, following the model of the HAVEG/DTHC/PHRU legal directory, to assist investigators to respond pragmatically to ethical-legal challenges should be encouraged and supported. For example, a directory relating to the ethical-legal framework for research with other vulnerable groups, such as MSM could be developed; or for pragmatically considering and responding to concerns around human tissue storage could be considered.
5. Periodic issues-driven ethical-legal training, to complement the general training GCP and in country training, such as that provided by HAVEG, should be encouraged and expanded.

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12. APPENDICES

12.1 APPENDIX 1: AAVP Legal Survey: Questionnaire

Please be aware that your participation in this study is entirely voluntary, and that by completing and returning this questionnaire you acknowledge that you understand the information in the attached letter and consent to participate in this study.

Please understand that there are no right or wrong answers to the questions below. While some may pertain to issues you have not previously considered, we nevertheless ask that you try to think about them and answer them as best you can. We hope to use this data to develop resources which respond to the needs of researchers working in your country.

Background information

Name (optional)	
Organization (optional)	
Country	
City	
Trial	
Trial phase	
Any other relevant information	

Legal and Policy Framework

Please answer these questions to the best of your ability. If you are unsure about the answer, please write 'unsure', rather than leave any question blank.

What international laws or policies guide your work (or work conducted in your country), if any? (Please provide title and details of any laws, policies or provisions)

What regional laws or policies guide your work (or work conducted in your country), if any? (Please provide title and details of any laws, policies or provisions)
What national laws or policies guide your work (or work conducted in your country), if any? (Please provide title and details of any laws, policies or provisions
What specific provisions are there in place to deal with clinical trials in your country, if any? (Please provide details of any laws, policies or provisions)

In the table below, we list some common provisions in laws and policies dealing with HIV and AIDS and medical experimentation.
If your laws/policies include similar provisions, please mark 'YES' and specify in which laws and policies these provisions are found.
If not, please mark 'NO'.
Please provide comments on the provisions and indicate how they are implemented.
Please mark 'UNSURE' if you do not have enough information to say 'YES' or 'NO'.

Provision(s) dealing with:	**Yes (if so, indicate where it is found)**	**No**	**Unsure**	**How do you implement the provision(s) (if at all)?**	**Comments (please indicate what the provisions say etc.)**
Bodily integrity					
Autonomy					
Human dignity					
Confidentiality					
Age of consent to medical procedures					
Age of consent					

Provision(s) dealing with:	Yes (if so, indicate where it is found)	No	Unsure	How do you implement the provision(s) (if at all)?	Comments (please indicate what the provisions say etc.)
to research					
HIV testing					
Blood and tissue samples					
The storage and future use of blood and tissue samples					
The regulation of research					
The payment of research participants					
Obligations to report neglect, abuse and criminal activity to relevant authorities					
The protection of rights of research participants					
Dealing with adverse effects, if harmed during trial					
The provision for ethical review of research					
Informed consent					

Provision(s) dealing with:	Yes (if so, indicate where it is found)	No	Unsure	How do you implement the provision(s) (if at all)?	Comments (please indicate what the provisions say etc.)
Termination of trials					
Dealing with withdrawal of participants from trials					
Dealing with eligibility and accessibility to drugs post-trial					
Dealing with protection from discrimination during trial					
Dealing with protection from discrimination after trial					
Dealing with regulatory approval of effective products					

Please list any other relevant provisions dealing with clinical trials in your country.

Please add any further comments that you may have regarding the legal and policy framework and clinical trials:

What sort of ethico-legal training do you feel would most benefit you and other HIV vaccine researchers, conducting research in the region?

12.2 APPENDIX 2: Information Sheet

Hello,

We are two researchers working with the African AIDS Vaccine Programme (AAVP), based at the University of KwaZulu Natal. We both have backgrounds in Psychology and social science research.

What is the purpose of this study?
This study aims to gain insight into researchers' awareness and implementation of the legal provisions governing HIV vaccine trials in their countries of work. The overall purpose of this study is to develop legal training and resources for use by various stakeholders.

What will this research involve?
The researchers will be approaching researchers involved in HIV vaccine research and will be asking questions researchers' awareness and implementation of the laws governing clinical trials.

Why have you been chosen?
You have been asked to participate because of your involvement in HIV vaccine research.

Do I have to take part?
No. You can refuse to take part. Even if you agree, you can change your mind at any time.

What do you need to do?
If you agree to participate in this study, we will ask you to respond in writing to an email questionnaire (this shouldn't take you more than an hour to complete).

What will happen to the recorded data?
If you agree to participate in the email questionnaire, when you return your email survey to us, we will remove and unlink any identifying data like your name and email address. Your personal data will not be stored with your email survey. The data will be kept for 5 years then destroyed Only authorised research staff will have access to your data.

How will the results be reported?
The results will be written into a resource document for stakeholders involved in prevention research And will be used to develop legal training resources. They may also be written into a peer-reviewed publication. Confidentiality of your personal and institutional identity will be maintained. No identifiable details of individuals or organisations will be released, only

averaged information.

If you have any questions about this study you can contact either Zaynab Essack at +27332606164 or essack@ukzn.ac.za or Jenny Koen at +27332605566 or koenj@ukzn.ac.za. Farhana Zuberi, who is overseeing this study can be contacted at zuberi@mweb.co.za. Professor Doug Wassenaar (PI of AAVP) can be contacted +2733 2605373 or e-mail at wassenaar@ukzn.ac.za .

The research ethics committee of the University of KwaZulu-Natal has approved this study. The approval number is HSS/0675/08.