

This article was downloaded by: [UNIVERSITY OF KWAZULU-NATAL]

On: 21 June 2012, At: 01:53

Publisher: Routledge

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



African Journal of AIDS Research

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/raar20>

The ethical and legal regulation of HIV-vaccine research in Africa: lessons from Cameroon, Malawi, Nigeria, Rwanda and Zambia

Pamela Andanda ^a, Paschal Awah ^b, Paul Ndebele ^c, Olanrewaju Onigbogi ^d, Daniel Udatinya ^e & Malala Mwondela ^f

^a University of the Witwatersrand, Private Bag 3, Wits 2050, Johannesburg, South Africa

^b Ipas, PO Box 5027, Chapel Hill, North Carolina, 27514, United States

^c University of Botswana, Office of Research and Development, Private Bag, UB00708, Gaborone, Botswana

^d Department of Community Health and Primary Care, University of Lagos, College of Medicine, PO Box 35950, Agodi, Ibadan, Nigeria

^e Rwanda Ministry of Health, PO Box 84, Kigali, Rwanda

^f Zambia AIDS Law Research and Advocacy Network (ZARAN), Plot No. 22, Katemo Road, Rhodes Park, PO Box 39088, Lusaka, Zambia

Available online: 31 Jan 2012

To cite this article: Pamela Andanda, Paschal Awah, Paul Ndebele, Olanrewaju Onigbogi, Daniel Udatinya & Malala Mwondela (2011): The ethical and legal regulation of HIV-vaccine research in Africa: lessons from Cameroon, Malawi, Nigeria, Rwanda and Zambia, African Journal of AIDS Research, 10:4, 451-463

To link to this article: <http://dx.doi.org/10.2989/16085906.2011.646660>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.tandfonline.com/page/terms-and-conditions>

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae, and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand, or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

The ethical and legal regulation of HIV-vaccine research in Africa: lessons from Cameroon, Malawi, Nigeria, Rwanda and Zambia

Pamela Andanda^{1*}, Paschal Awah², Paul Ndebele³, Olanrewaju Onigbogi⁴, Daniel Udatinya⁵ and Malala Mwondela⁶

¹University of the Witwatersrand, Private Bag 3, Wits 2050, Johannesburg, South Africa

²Ipas, PO Box 5027, Chapel Hill, North Carolina 27514, United States

³University of Botswana, Office of Research and Development, Private Bag UB00708, Gaborone, Botswana

⁴University of Lagos, College of Medicine, Department of Community Health and Primary Care, PO Box 35950, Agodi, Ibadan, Nigeria

⁵Rwanda Ministry of Health, PO Box 84, Kigali, Rwanda

⁶Zambia AIDS Law Research and Advocacy Network (ZARAN), Plot No. 22, Katemo Road, Rhodes Park, PO Box 39088, Lusaka, Zambia

*Corresponding author, e-mail: pamela.andanda@wits.ac.za

Ethical and legal frameworks are important for ensuring that the goals of scientific research are realised while at the same time the rights and welfare of human participants are adequately protected. A balance in attaining these two goals can be achieved if such frameworks provide for legally binding structures and processes to oversee, regulate, and monitor research on human participants according to accepted norms and standards. From 2007 to 2009, an ethical/legal audit, sponsored by the WHO/UNAIDS Ethics, Law and Human Rights Working Group of the African AIDS Vaccine Programme (AAVP ELH), was conducted in regard to five African countries (Cameroon, Malawi, Nigeria, Rwanda and Zambia) to determine whether these countries have adequate laws, ethical guidelines and policies in place to regulate HIV-vaccine research. This article discusses the findings of the audit with a view to highlighting key lessons that can be learnt from these countries. The article provides the context of the audit by highlighting its rationale, aims and methods. We discuss the general findings of the audit and the complex issues arising from HIV-vaccine research, specifically. Lastly, we propose specific ways in which the ethical/legal frameworks guiding research with human participants in these countries can be improved.

Keywords: Africa, clinical trials, country profiles, ethics, guidelines, health research, HIV/AIDS, legislation, policy

Background: Context of the five-country audit

Rationale for the audit

The current literature shows that there are an estimated 32.8 million people living with HIV globally, 68% of whom live in sub-Saharan Africa (UNAIDS, 2010). HIV has equally been identified as the most important infectious disease, with AIDS being the most common cause of death in Africa (Esparza & Bhamarapravati, 2000). The development and distribution of a safe and effective preventive HIV vaccine remains the best hope for ending the HIV pandemic (Kaleebu, Abimiku, El-Halabi, Koulla-Shiro, Mamotte, Mboup *et al.*, 2008). Consequently, Africa is increasingly being used as a site for clinical trials where people considered at risk of being infected with HIV can be included as participants in clinical research. To date, HIV-vaccine trials and/or HIV-vaccine-preparedness studies have taken place in Kenya, Uganda, Tanzania, Rwanda, Zambia, Botswana, South Africa, Cote d'Ivoire, Burkina Faso, Cameroon, Ethiopia, Gabon, the Gambia, Malawi, Nigeria, Senegal and Zimbabwe (AIDS Vaccine Advocacy Coalition, 2008).

Globally, the majority of participants in the clinical trials

conducted “to build evidence of safety and efficacy of medicines, to support an application for marketing authorisation for the period 2005–2008, came from developing countries, many of them in Africa” (Maïga, Akanmori & Chocarro, 2009, p. 7249) (cf. European Medicines Agency, 2008). Considering the nature and the volume of HIV/AIDS research conducted in Africa, it is generally understood that African countries need to develop a strong legal and ethical capacity to regulate local research on new drugs, as well as research in general. This is particularly important in the context of the research and development of an affordable, effective and locally relevant HIV-preventive vaccine. HIV-vaccine research, while regarded as a research priority by a number of African countries, poses many complex ethical and legal challenges which may be difficult to resolve in the absence of sound regulatory frameworks. The audit of the countries under discussion (see Andanda, Gxoyiya & Mahenge, 2010) was thus prompted because it is imperative to undertake research into the nature and extent of the health legislation and other laws regulating research in Africa, specifically the extent to which the legislation protects the rights of HIV-vaccine research participants. An

understanding of the ethical/legal framework for research in Africa will assist in identifying the strengths and weaknesses of the existing processes, and in developing plans to build strong, local ethical and legal capacities throughout Africa.

Purpose and objectives of the audit

The purpose of the audit was to examine the ethical/legal frameworks for research conducted in five African countries, namely Cameroon, Malawi, Nigeria, Rwanda and Zambia, in order to determine whether adequate laws, ethical guidelines and policies are in place to regulate HIV-vaccine research, specifically. The audit was intended to assist in the development of an advocacy and training plan pertaining to ethics, law and human rights, for developing the countries' capacity to strengthen the ethical/legal systems that guide research.

An ideal ethical/legal framework should foster the realisation of scientific goals while at the same time protecting the research participants. This is the measure with which we have gauged the adequacy of the countries' ethical/legal frameworks. Thus, the following were the primary objectives of the audit:

- 1) To establish the content of the laws and policies in Cameroon, Malawi, Nigeria, Rwanda, and Zambia relating to the ethical and legal structures and processes for the review, approval, and monitoring of health research and the registration of new drugs, as well as with reference to the rights of trial participants and the mechanisms to enforce those rights.
- 2) To establish whether the ethical/legal frameworks identified in the countries are able to support and guide HIV-vaccine development and research, either in terms of general legal and ethical principles or in terms of HIV-vaccine specific policies and guidelines.
- 3) To establish whether the frameworks protect and promote the rights of the participants in HIV-vaccine trials from the major ethical concerns raised by such research.
- 4) To compare and contrast the various models of ethical/legal frameworks in the five countries, in order to develop recommendations for ethical/legal frameworks as required.

Audit methods

Cameroon, Malawi, Nigeria, Rwanda and Zambia were chosen for the audit as they are countries where HIV-vaccine trials are currently taking place or planned for the near future and where legislation and policies are available in English. The questionnaire used in the previous legal audit by the Ethics, Law and Human Rights Working Group of the African AIDS Vaccine Programme (AAVP ELH) (see Grant, Lewis & Strode, 2005) was revised and sent to local contact persons involved in ethical or legal aspects of health research in each of the five African countries. The questionnaire was designed to elicit information and documentation relating to health, health research and/or HIV-vaccine-research legislation, policy or guidelines in the country. In addition, a desktop review, including an Internet search, was conducted on relevant health, health research and/or HIV-vaccine-research legislation, policy and

guidelines in the five African countries. Based on the results of the questionnaire and follow-up correspondence with the local contacts, as well as the desktop review, five country reports were developed. A final report (see Andanda *et al.*, 2010) was compiled based on the findings of the individual country reports.

Part 1: General findings of the five-country audit

Table 1 provides a summary of the countries' national regulatory authorities overseeing research. Each of the five countries that were audited has statutory and administrative bodies with the capacity to be involved in various aspects of the ethical/legal regulation of health-related research. Some of these are research bodies, while others are not directly involved in regulating research but could play a broader role in protecting and promoting the rights of trial participants within the ethical/legal framework. (Part 4 discusses the specific challenges that these countries face in the ethics review process.) All the countries except Zambia have National Health Research Ethics Committees (NHRECs). In Malawi and Rwanda, the NHRECs are responsible for reviewing and approving research, while in Cameroon and Nigeria these national committees oversee, register, and regulate local research ethics committees (RECs). All the countries have institutional RECs for the evaluation of research protocols to be implemented in the institutions concerned. In Zambia, the University of Zambia has three committees that approve all research on humans, countrywide.

The audit established that either statutory bodies or the RECs are given power to monitor ongoing research. However, in Zambia and Cameroon there are currently no mechanisms or statutory bodies to do this, while Nigeria, Rwanda and Malawi do have mechanisms in place to monitor clinical trials following approval of the research.

The audit established that the ethical/legal frameworks in the five African countries (Cameroon, Malawi, Nigeria, Rwanda and Zambia), although not ideal, would be able to support HIV-vaccine research while protecting the rights of research participants. The audit identified informed consent, post-trial access to effective vaccines, the adequacy of the ethics review process, and the monitoring of ongoing trials as ethically complex issues. (The details of the complexity of these issues themselves are discussed further on.) It is worth noting that Malawi and Rwanda have taken an additional step in their constitutions by specifically providing for informed consent for research; Table 2 provides a useful summary in regard to the issue. The specific manner in which the countries have dealt with inherent challenges in implementing informed consent is discussed in Part 4 of this article.

Part 2: Ethically complex issues of HIV-vaccine research in Africa

Conducting vaccine research in developing countries has correctly been described as complex (Emanuel, Wendler, Killen & Grady, 2004). The audit of the five countries' ethical/legal frameworks identified informed consent, post-trial access to effective vaccines, the adequacy of the ethics

Table 1: National regulatory authorities overseeing research in the five African countries audited

Cameroon	Malawi	Nigeria	Rwanda	Zambia
<p>Three government ministries regulate research involving humans:</p> <ul style="list-style-type: none"> The Ministry of Public Health, which has an Advisory and Strategic Board that sets priorities for health research and evaluates the implementation of research projects; The Ministry of Scientific Research and Innovation, which is responsible for the development, implementation and evaluation of government policy for scientific research and innovation; The Ministry of Higher Education, which supplements the role of the Ministry of Public Health. 	<p>The National Commission for Science and Technology (NCST) (formerly the National Research Council of Malawi) is responsible for the promotion and coordination of research in Malawi.</p> <p>All Research Ethics Committees (RECs) fall under the NCST and coordinate, review and monitor health-related research on behalf of the NCST. Currently, there are two RECs: the National Health Sciences Research Committee (NHSRC) and the College of Medicine REC (COMREC).</p> <p>While serving as a REC, the NHSRC also serves as a sectoral committee of the NCST.</p>	<p>The National Agency for Food and Drug Administration and Control (NAFDAC) is the national regulatory body responsible for the registration of new drugs and regulates clinical trials of new drugs.</p>	<p>The Ministry of Health is the highest authority that oversees health research in Rwanda. Its Pharmacy Task Force supervises the effectiveness and quality of pharmaceutical products.</p> <p>The ministry established the Rwanda National Ethics Committee (RNEC) in May 2003.</p> <p>The ministry is also affiliated with the Centre for Treatment and Research on AIDS, Malaria, Tuberculosis and Other Epidemics (TRAC Plus). TRAC Plus is in charge of health and research in matters relating to disease prevention, especially HIV, malaria, tuberculosis and leprosy.</p>	<p>The Ministry of Health oversees health research in the country.</p>

Table 2: Sources informing the right to informed consent in the five African countries audited (i.e. the right to take part in a trial only with voluntary informed consent) (from Andanda *et al.*, 2010, pp. 11–12)

Cameroon	Malawi	Nigeria	Rwanda	Zambia
<p>There is no legislation dealing specifically with informed consent to medical treatment and/or research. However, the constitution provides for: the right to liberty and security of the person, and the right not to be subjected to torture, cruel, inhuman or degrading treatment or punishment.</p>	<p>Section 19(5) of the constitution provides that no person shall be subjected to medical or scientific experiment without his/her consent. The constitution also states that every person has the right to freedom and security of the person, which includes the right to life and the right not to be subjected to torture, cruel, inhuman or degrading treatment or punishment. The PMPB Act of 1988 specifically provides for the right to informed consent.</p>	<p>The 'National HIV Vaccine Plan' contains national guidelines for the review and approval of HIV-vaccine studies; this includes the right to informed consent. Section 32(1) of the National Health Bill specifically provides for the right to informed consent.</p>	<p>Article 15 of the constitution provides that no one shall be subjected to experimentation without giving his/her consent. HIV-vaccine research initiators should also procure written informed consent from the trial participants as well as a signature from the trial participant's next of kin as a witness to the consent provided.</p>	<p>The constitution provides for protection from torture, inhuman or degrading punishment or other like treatment. It also provides for the right to personal liberty, and for the protection of young persons against physical or mental ill-treatment, all forms of neglect, cruelty and exploitation.</p>

review process, and the monitoring of ongoing trials as ethically complex issues.

The complexity of informed consent

Concerns about implementing informed consent in developing countries appear as a major issue in the current

literature. A recent survey of stakeholder perspectives on ethical challenges in HIV-vaccine trials in South Africa, for instance, established that informed consent was top among most stakeholders' concerns. They considered disempowerment and poor education to impact negatively on the participants' ability to understand the provided information and

give their consent (Essack, Koen, Barsdorf, Slack, Quayle, Milford *et al.*, 2010). These findings from a South African study are equally relevant for other African countries where HIV-vaccine trials are conducted.

The complexity of informed consent is compounded by inherent challenges in implementing informed consent in HIV/AIDS-related clinical trials in developing countries. A recent study on such challenges identified three main concerns (see Mystakidou, Panagiotou, Katsaragakis, Tsilika & Parpa, 2009). First, it is possible that participants will give their consent with the assumption that the doctor has their best interest at heart. Second, there seems to be “a clash of the scientific culture with the non-expert, traditional culture” (Mystakidou *et al.*, 2009, p. 49) (cf. Lindegger & Richter, 2000). Third, it has been argued that cultural barriers may make obtaining truly valid informed consent problematic in most African settings, thus precluding ethical research conduct (Annas & Grodin, 1998). Language has equally been identified as a problem in so far as there are no equivalent terminologies for some concepts of health research in some local languages (Dawson & Kass, 2005).

Providing post-trial access

Post-trial access is an issue that is clearly provided for in international ethics guidelines. Paragraph 33 of the World Medical Association's (WMA) Declaration of Helsinki (“the Declaration of Helsinki”) (WMA, 2008) for instance provides that “at the conclusion of the study, patients entered into the study are entitled to be informed about the outcome of the study and to share any benefits that result from it, for example access to interventions identified as beneficial in the study, or to other appropriate care or benefits.” This paragraph may seem straightforward, but in the context of resource-poor countries, challenging issues arise which should be addressed.

The wording of the above paragraph appears to advocate for the principle of reciprocity, in terms of which those who have participated in a trial should be given access to the beneficial intervention. The application of this principle in resource-poor countries has been questioned in so far as “only a fraction of HIV-infected people who need ART [antiretroviral treatment] are able to get it, and rationing is inescapable” (Merritt & Grady, 2006, p. 1791). Consequently, it does not seem just to give first priority to the research participants while equally needy compatriots are not provided for.

Since the paragraph does not specify who has the obligation to provide access to such intervention, assuming that the government of the host country attempts to apply the stipulations of this paragraph, the practical question, as Merritt & Grady (2006, p. 1793) correctly argue, is: “Might the country then deliberately revise its existing priorities to accommodate trial participants?” If this question were to be answered by any of the African countries under discussion, one would anticipate an obvious response because the audit of the five countries' ethical/legal frameworks revealed that the issue of post-trial access is not adequately addressed (Andanda *et al.*, 2010). As such the priorities would not be changed.

An alternative consideration could be based on Guideline 21 of the Council for International Organizations of Medical

Sciences (CIOMS) (2002) which places the obligation to provide post-trial access on the sponsors of the research. Again, Merritt & Grady (2006, p. 1793) have correctly observed that “the extent and sustainability of funders' responsibility for post-trial treatment over time...is an issue with practical and ethical complexities...”

The specific complexities of post-trial access can be glimpsed from the results of one study that identified the views of relevant stakeholders (i.e. REC chairs, investigators, and research participants) in a multinational HIV/AIDS study on post-trial access (see Pace, Grady, Wendler, Bebchuk, Tavel, McNay *et al.*, 2006). The study attempted to establish the respondents' views regarding to whom the products should be made reasonably available, at what cost, and by whom. It established that very few respondents thought that guaranteed post-trial access to drugs or interventions should be limited to the research participants. The REC chairs, for instance, responded that “access should be guaranteed for people in the country where the research was conducted” (Pace *et al.*, 2006, p. 840). “Both...REC chairs' and investigators' responses suggest[ed] shared responsibility for making a drug ‘reasonably available,’ with both groups indicating an important role for the host-country government” (Pace *et al.*, 2006, p. 841). The findings of that study essentially indicate that these complex issues are for the governments of the host countries to contend with.

Ethics review processes that prioritise the protection of participants, with consideration for the issues related to HIV-vaccine research

It is an established requirement that research protocols should be reviewed to ensure that the research meets internationally acceptable scientific and ethical standards, otherwise “it would be unethical for poorly designed research involving human beings to be approved, since data generated from such research would not contribute to the improvement of disease prevention or management” (Nyika, Kilama, Chilengi, Tangwa, Tindana, Ndebele & Ikingura, 2009, p. 189). Reviewing protocols for HIV-vaccine trials is more complex and challenging in so far as the research may involve international collaboration between resource-poor nations and organisations that are drawn from better-resourced countries (Milford, Wassenaar & Slack, 2006). RECs therefore require proper guidelines that can facilitate the protection of the rights of trial participants, apart from ensuring the scientific validity of the data.

The monitoring of research after approval

Paragraph 15 of the Declaration of Helsinki (WMA, 2008) states that RECs should have the right to monitor ongoing studies and it places an obligation on the researchers to provide monitoring information to the committee, especially information about any serious adverse events. The monitoring of ongoing clinical research is important because, as has correctly been argued, “Ethical approval alone does not necessarily ensure protection of the safety and welfare of research participants throughout the research...” (Nyika *et al.*, 2009, p. 189). Such monitoring requires adequate resources and trained RECs, but these are limited in most African committees (Nyika *et al.*, 2009).

Part 3: How countries have addressed complex challenges through their national ethical/legal frameworks

The audit established that the five countries have laws in place to protect all people, including HIV-vaccine trial participants. For instance, all the countries have constitutions that are supreme and protect basic human rights and freedoms, such as the right to life, the right to liberty, and the right to equality and non-discrimination. Malawi's constitution has human-rights provisions that deal with clinical research participants; Cameroon's constitution does not mention health or research participants' rights. In view of the different levels of ethical and legal developments in each country, this part discusses the extent to which each country has dealt with the complex ethical issues surrounding research involving human participants (the issues themselves were purposely discussed in Part 2).

Ethical/legal frameworks to guide HIV-vaccine research in the five countries

A notable characteristic of the ethical/legal frameworks in the five countries is their reliance on the given country's constitution as the supreme law to protect human rights. As shown in Table 2 the constitutional provisions in Cameroon, Nigeria and Zambia provide generally for the right not to be subjected to torture or cruel, inhuman, or degrading treatment or punishment, while the constitutions of Malawi and Rwanda provide specifically for the right not to be subjected to medical or scientific experiment without consent. The constitutional provisions in all the countries are adequate since the role of the constitution is to stipulate the fundamental rights upon which other substantive legislation should expound. All the countries have substantive legislation to regulate research on human participants.

In Cameroon, the constitution protects basic human rights and freedoms, such as the right to life, the right to liberty, the right to health, and the right to equality and non-discrimination. However, Cameroon's constitution does not specifically refer to health research but focuses on issues related to injuries. Moreover, the constitution does not deal with health rights or research participants' rights, and as such other statutory provisions are used. For instance, the country's penal code has provisions that punish cases of injury or harm to individuals. Section 228(2)(c) of the Penal Code (Law No. 65-LF-24 of 12 November 1965, and Law No. 67-LF-1 of 12 June 1967) provides that "whoever, rashly and in a manner liable to cause harm to any person... administers any drug or other substance" will be punished with imprisonment for a period of six days to six months. This section can be clearly relied on in cases of injuries in the course of research participation. Section 285(b) of the Penal Code equally provides that "the administration of any substance harmful to health" is deemed to be a use of force.

A similar legislative framework exists in Malawi, where the constitution empowers the Human Rights Commission and the Office of the Ombudsman, as well as other government organs (such as the police and courts), to protect human rights. Malawi's Human Rights Commission was established under the Human Rights Act of 1998, and it is responsible

for regulating the conduct of citizens regarding respect for the rights of others (Hatchard, 1999). The commission can also assist in cases where research participants' rights have been infringed, and the Office of the Ombudsman can assist in cases involving infringement by government institutions or workers. In Malawi, the Pharmacy, Medicines and Poisons Board Act (PMPB Act) has established the Pharmacy Medicines and Poisons Board (PMPB), a national regulatory board responsible for regulating research on drugs (Act No. 15 of 1988). The PMPB's technical committee is specifically responsible for reviewing research protocols; this committee is made up of members with expertise in pharmacy, bioethics, medicine, veterinary science, biostatistics and other fields. The technical committee is supported by the PMPB staff and inspectors who also assist in the technical evaluation of the protocols and products as well as in monitoring (through reviewing reports and field visits). Some of the technical committee members and inspectors have received training in reviewing and monitoring vaccine trials, which was provided by the World Health Organization in a bid to strengthen the capacities of regulatory bodies in ethical review and monitoring of clinical trials.

Malawi's PMPB is responsible for the registration, importation and licensing of medicines in that country. It also regulates clinical trials by issuing product licenses for test products and clinical-trial certificates. According to the legislation, persons intending to conduct clinical trials are required to obtain a product license for the product to be used in the trial as well as a clinical trial certificate. Any person who contravenes the provision is guilty of an offence and is liable to a fine or imprisonment.

Nigerian laws, which are enacted by the national assembly and senate, regulate research in that country. The implementation of policies related to research is localised in specific states of the federation. The constitution provides for fundamental rights, which can be used to protect the rights of research participants. For instance, section 33(1) protects the right to life while section 34(1)(a) provides that "no person shall be subject to torture or to inhuman or degrading treatment." In the context of research, the 'National Code of Health Research Ethics' (Nigeria Federal Ministry of Health, 2007) deals more comprehensively with specific issues, such as informed consent, confidentiality, the right to life, the right to dignity, fairness in choosing participants, protection from inhuman treatment, protection from exploitation, and compensation for harm. Furthermore, the Nigerian National Human Rights Commission (NHRC), which was established under Decree No. 22 of 1995, could be relied on to ensure the safety of research participants since it serves as the national ombudsman for research participants who cannot take their own cases to the courts.

RECs also play an important role in the protection of research participants in all the countries. Four of the countries have national RECs or equivalent bodies, except for Zambia where the University of Zambia REC and the independent Tropical Diseases Research Centre (TDRC) REC are responsible for reviewing, approving and monitoring research, including vaccine trials. The TDRC REC was created under the Tropical Diseases Research Act (Chapter 301) (see Ngandwe, 2005) while the University

of Zambia's other ethics committees are established by the university. Paragraph 4.3 of the university's 'Research Policy and Intellectual Property Rights' (University of Zambia, 2009) establishes RECs for Zambia at large; the mandate of these committees is to review research proposals for research-ethics compliance is not restricted to the University of Zambia researchers but also covers collaborative research with other institutions. So far the university has three RECs: Biomedical REC, Natural and Applied Sciences REC, and Humanities and Social Sciences REC.

The Zambian RECs are composed of members from multidisciplinary backgrounds. For instance, the Biomedical REC has representatives from the University of Zambia's schools of medicine, veterinary medicine, agricultural sciences, the university teaching hospital, the Institute for Economic and Social Research, the National Institute for Scientific and Industrial Research, the ministries of health and agriculture, the university's legal counsel, a religious leader, the general public, civil society, and the university's directorate of research and graduate studies. The Natural and Applied Sciences REC has representatives similar to the Biomedical REC, in addition to representatives from the schools of engineering and mines, the executive secretary of the National Science and Technology Council, and the Zambia Agricultural Research Institute, but ministries are not represented in this committee. The Humanities and Social Sciences REC has the same composition, in addition to representatives from the university's schools of humanities, education and law.

Appendix 2 of the University of Zambia's (2009) research policy stipulates the ethical requirements and standards for research. Only paragraph 1 of that appendix briefly deals with research on humans — for instance, that research procedures should be explained on an information sheet written in simple language that is easily comprehensible by the potential research participants who are expected to give informed consent before participating.

In Cameroon, the National Ethical Committee for Human Subject Protection in Research is responsible for reviewing research involving human participants. Apart from this committee, there are 14 ethics committees or Institutional Review Boards (IRBs) that can review research protocols. Of these, the Ministry of Health's Operational Research Unit, which acts as the regulatory authority on issues related to health research, claims to recognise only three: the National Ethics Committee, the Chantal Biya International Research Centre, and the University of Yaoundé Teaching Hospital Review Board. This situation raises concerns about the status and functionality of the remaining 11 committees or boards that are not recognised by the regulatory authority. Critics have found Cameroon's structure peculiar because "an institutional committee manages ethical issues at the national and international level instead of the official national committee appointed by the ministry of health" (Rwabihama, Girre & Duguet, 2010, p. 245).

Malawi currently has two RECs: the National Health Sciences Research Committee (NHSRC) and the College of Medicine Research and Ethics Committee (COMREC). COMREC is responsible for coordinating, reviewing and approving research conducted by staff and students within

the University of Malawi's constituent college, except for research of 'national importance.' The NHSRC reviews research proposals relating to the following categories of studies, which are classified as studies of national importance: vaccine trials, stem-cell research, cloning research, genetic studies, national health surveys and pharmaceutical studies involving significant safety issues (National Research Council of Malawi [NRCM], 2002). The two RECs report to the National Commission for Science and Technology (NCST) and include representatives of the NCST in their membership. The NRCM, NHSRC and COMREC have all issued guidelines on how research should be conducted and not specifically on how ethics committees should be established.

Hence, in Malawi, there are clear links between the NHSRC, COMREC and the NCST through cross-memberships. Linkages have also been established between the PMPB and other RECs, as the PMPB includes ethics committee members in the committee that is responsible for reviewing and monitoring clinical trials. The PMPB has brought non-complying researchers before courts of law. This initiative is being implemented in collaboration with COMREC and the NHSRC and NCST. Professional associations for doctors, nurses and other health professionals have statutory powers to discipline members who act unethically. Additionally, RECs can report researchers who are involved in unethical research to professional bodies for disciplinary action. 'The Malawi National HIV and AIDS Policy' also provides, *inter alia*, that people living with HIV or AIDS, whose rights have been infringed, be given "access to independent, speedy and effective legal and/or administrative procedures for seeking redress" (Ministry of Health, 2003, p. 14).

Nigeria's National Human Rights and Ethics Committee (NHREC) and the National Agency for Food and Drug Administration and Control (NAFDAC) are responsible for ethics reviews. The NAFDAC was established under Decree No.15 of 1983, which gives it the responsibility of regulating all injected and oral drugs as well as foods in the country, while the NHREC was established in 1996 under the National Human Rights Commission Decree No. 22 of 1995. These two agencies regulate research on both humans and animals. In addition, acts of the state legislature have created statutory bodies at the state level which enable many institutions to set up their own RECs. Institutional RECs in Nigeria are mandated by law to register and link up with the NHREC, which has the oversight function as the national regulatory body.

A more streamlined framework in Nigeria has recently been ushered in with the enactment of the National Health Bill by the Senate on 15 May 2008 and by the House on 26 February 2009 (West Africa Democracy Radio, 2011). Section 39(3) of the bill has re-established and defined the role of the NAFDAC, and section 33 has re-established the NHREC. Part IV of the bill deals exclusively with health research. Ethical issues that are related to research on humans are specifically provided for under section 32 of the bill. The constitution of the NHREC is statutorily backed by the bill, which sets out guidelines for the approval of all health research and the accreditation of local RECs. Ethical

review is a component of this process and such procedures must be followed in clinical trials. Members of the NHREC consist of a medical doctor, legal practitioner, pharmacist, nurse, at least two religious leaders, community health worker, one researcher in the medical field, one researcher in the pharmaceutical field, and three other persons of unquestionable integrity.

A key role of the NHREC in Nigeria is to monitor and ensure strict adherence to ethical guidelines. It equally regulates and coordinates institutional ethics committees (under Section 33[6] of the bill). It also determines the guidelines to be followed for the functioning of institutional health RECs. Professional bodies are empowered by Acts of the National Assembly to set up disciplinary committees to deal with professional misconduct by their members.

For purposes of reconciling the existence and roles of these institutional frameworks in Nigeria, especially the current ones mentioned in the preceding paragraphs, reference should be made to section 62(1) of the National Health Bill which provides that “anything done before the commencement of this [Bill] under a provision of any other relevant Act or regulation which could have been done under a provision of this [Bill] shall be regarded as having been done under the corresponding provision of this [Bill].”

Despite the existence of statutory agencies in Nigeria, the initiative for ethical conduct in HIV-vaccine research was taken over by the Federal Ministry of Health which, in 2001, commissioned researchers to draw up a ‘National HIV Vaccine Plan’ (Nigeria Federal Ministry of Health, 2001) to provide guidelines on HIV-vaccine research. Prior to this, the National Ethics Committee of the NAFDAC had overseen HIV-vaccine research in Nigeria. The plan aims at articulating a comprehensive, well-coordinated, long-term strategy for the development and evaluation of safe, immunogenic and efficacious preventive, therapeutic and perinatal HIV vaccines in Nigeria. It is also concerned with the development of policies and procedures for the planning, implementation, oversight, administration and evaluation of HIV-vaccine-related research in Nigeria, and for facilitating the conduct of scientifically and ethically appropriate HIV-vaccine trials in the country. The national plan has an annex that contains national guidelines for review and approval of HIV-vaccine studies, which includes the right to informed consent.

The Rwanda National Ethics Committee (RNEC) examines all human research projects conducted in Rwanda. The committee has issued comprehensive standard operating procedures (SOPs) (see Rwanda Ministry of Health, 2009). The RNEC is composed of no less than seven members, including: an expert in biomedical sciences, a lawyer, a clinician, a public health expert/biostatistician/epidemiologist, a philosopher/theologian/bioethics expert, and a representative of the community (SOPs, paragraph 5). A secretariat has been established to ensure the smooth functioning of the committee (SOPs, paragraph 6).

In Rwanda, the HIV, AIDS and STI Unit (formed as a merger of the Treatment and Research AIDS Centre [TRAC] and other programmes) continues to be part of the Centre for Treatment and Research on AIDS, Malaria, Tuberculosis

and other Epidemics (known as ‘TRAC Plus’) in the Ministry of Health. The unit is responsible for clinical aspects of research in the HIV and AIDS domain. It provides technical guidance and overall leadership in the areas of voluntary counselling and testing (VCT), prevention of mother-to-child transmission (PMTCT), HIV/AIDS-related care and treatment, epidemiological surveillance and research.

Apart from the RNEC, the National University of Rwanda has a committee for research screening and ethics clearance. It screens all research proposals that plan to use human participants and it either issues clearance or directs them to the RNEC. It deals particularly with studies intended to be carried out within the university or by university employees and it ensures that the research centres of hospitals as well as affiliated research institutes and centres enforce the international standards of scientific research, notably by means of information transmitted periodically to the university within the framework of affiliation contracts (see National University of Rwanda Research Directorate, no date).

Rwabihama *et al.* (2010, p. 246) have correctly argued that “the functionality of an ethics committee hinges on an efficient secretariat that serves as the clearing house for protocols.” Our discussion in Part 3 has shown that only Rwanda has a secretariat with clearly defined functions. The lack of a secretariat may impact negatively on the ability of the other countries to protect the rights of research participants there.

Part 4: The extent to which the frameworks have addressed areas of complexity in HIV-vaccine research

The discussion in this part will show the extent to which the countries’ ethical/legal frameworks are able to support and guide HIV-vaccine development and research, either in terms of general legal and ethical principles or in terms of HIV-vaccine-specific policies and guidelines.

The complexity of informed consent

The question of vulnerability is very important when it comes to informed consent. Malawi and Rwanda specifically address the concept of vulnerability in their guidelines, while the other countries address the issue of informed consent in a general manner. Table 2 provides information on the relevant frameworks providing for informed consent in the five countries.

In Nigeria, section 32(1)(b) of the National Health Bill provides that every instance of research investigation or experimentation involving a living person shall be conducted only with the written consent of the person subsequent to being informed of the objects of the research or experimentation and any possible effect on his or her health. Paragraph (d) of the ‘National Code of Health Research Ethics’ also comprehensively provides the important components that must be satisfied for valid informed consent (Nigeria Federal Ministry of Health, 2007).

In Malawi, the NRCM, NHSRC and COMREC recognise the existence of vulnerable persons and groups. These groups are highlighted in the guidelines of COMREC and the NHSRC and investigators are encouraged to be

cautious when conducting research that involves vulnerable populations or individuals (National Research Council of Malawi, 2002). Investigators are also required to justify the inclusion of such populations. The specified groups include children, adolescents, patients, prisoners and others who may be vulnerable to HIV infection. The Malawi 'National HIV/AIDS Policy' (Ministry of Health, 2003) also provides for measures directed at protecting the populations thought to be vulnerable to HIV infection.

In Rwanda, paragraph 22 of the SOPs (see Rwanda Ministry of Health, 2009) deals with information and informed consent requirements in detail. The procedures equally provide for groups that are categorised as vulnerable; these are listed in paragraph 12.8 as being children, pregnant women, refugees, prisoners, elderly persons, orphans, etc. Documentation on how the researcher will protect the rights and welfare of these special categories of the population should be provided to the REC. Paragraph 12.6 details the informed-consent process that researchers should comply with. Also, the consent form that provides potential participants information on the study has to be translated into the local languages (English, French and Kinyarwanda) for better comprehension by the participants.

As a precautionary measure, standard informed-consent forms in Cameroon have a clause that requires participants to report to the REC if certain procedures are not executed accordingly (information from in-country collaborator). However, most RECs in Cameroon have advocated for the formation of Data and Safety Monitoring Boards (DSMBs) for clinical trials, but these DSMBs rarely meet to assess the progress of trials. Experience shows that where the REC has requested provisions for monitoring and supervision, the exercise usually ends at the review stage without any field monitoring and supervision ever occurring.

Zambia has notably faced challenges in upholding the principle of informed consent. Two cases highlight these challenges. The first case relates to a six-month herbal-remedies trial involving 26 HIV-positive individuals (see Zambia AIDS Law Research and Advocacy Network [ZARAN], no date). The participants in the trial, who were mostly from a low-income bracket, were reportedly paid about US\$60/month for the duration of the trial. When some participants were unhappy with the way the trial was proceeding and threatened to withdraw, it is alleged that the principal investigator convinced them to stay by alleging that as a result of the trial they would become famous and wealthy. If the allegations are true, the principle of informed consent in this study was compromised. To date, the University of Zambia's REC has not resolved this matter. This case illustrates the challenge of limited ability to monitor research once it is approved as well as the problem of addressing allegations of unethical conduct.

The second case involves the microbicide trials conducted in Zambia (see Phiri, 2010). The case concerned the provision of adequate information to the participants and the communities in which the trials were conducted. There was negative publicity, alleging complaints about women who took part in the study becoming HIV-infected, as well as statements that the trials were not conducted ethically. However, after ZARAN and the Human Rights Commission

conducted their own investigations, it was established that the trials appear to have been conducted according to a protocol approved by the University of Zambia's ethics committee. Insufficient, however, was the information that was provided, particularly to the community members and to some extent to the research participants. Zambia thus offers a clear lesson on how exceptional care must be taken to ensure that informed consent is not compromised.

The complexity of post-trial access

The five countries audited were found to have addressed the issue of post-trial access very differently. The subject is not dealt with at all in the ethical/legal frameworks in Cameroon, Malawi and Zambia. Rwanda has attempted to address the issue, while Nigeria has comprehensive guidelines (which can be used to help other countries to adopt a similar approach).

Paragraph 12.3 of Rwanda's SOPs (Rwanda Ministry of Health, 2009) specifies that REC should consider "a description of any plans to make the study product available to the research participants following the research." However, the paragraph does not specify who is responsible for ensuring post-trial access to the study product. This certainly leaves the dilemma of whether or not the existing priorities should be revised to accommodate provision of access to trial participants.

In Nigeria, paragraph (s) of the 'National Code of Health Research Ethics' (Nigeria Federal Ministry of Health, 2007) stipulates the responsibilities of researchers, sponsors and institutions. Interestingly, subparagraph 6(iv) specifically places the obligation to provide post-trial access on the investigator, as follows:

The investigator must provide assurances that reasonable efforts shall be made to ensure that the benefits of research are made available to the community where the research was conducted. Details of any arrangement to ensure this shall be worked out by the researchers, sponsors, HREC [Health Research Ethics Committee], community leaders and community advisory committees (Nigeria Federal Ministry of Health, 2007).

This paragraph essentially implies that all stakeholders in the research must be involved in establishing the terms of post-trial access; thus, Nigeria provides a lesson that other countries can learn from. Certainly the difficulties inherent in dealing with this issue (as mentioned in Part 2) can be better dealt with — by all stakeholders — as envisaged in this paragraph. However, the host country's government still needs to take overall responsibility, and placing post-trial obligation on the sponsor is rather controversial and needs to be addressed carefully.

Ethical review processes that prioritise the protection of participants and consider issues related to HIV-vaccine research

As mentioned earlier, ethics guidelines alone are insufficient to guarantee the protection of research participants' rights. Consequently, for an ethics review process to guarantee ethical research, factors such as community engagement, education of the researchers about research regulation,

and the functionality of the ethics review committees are vital. Rwanda's ethics review process includes these factors, while the remaining four countries do not even have standard operating procedures or functional secretariats.

On this topic, Cameroon currently relies on a national HIV/AIDS policy to explain the rights of people living with HIV as well as the provisions that govern HIV-related research and development. However, such policies are not legally binding but only give some directives that may be optionally followed by researchers.

In Malawi, the PMPB Act sets out the approval procedure for clinical trials involving drugs, but there is no law that sets out the procedures to be followed for all health research. The PMPB issues clinical trial certificates and product licenses after reviewing the research proposal. In Malawi, the process of approving research is detailed in the guidelines of the NRCM, NHSRC and COMREC. This approach can be contrasted with section 5(1)(g) of Zambia's Pharmaceuticals Act of 2004, which established the Pharmaceutical Regulatory Authority to regulate and monitor the conduct of clinical trials on humans and animals. Part VII of the act addresses clinical trials and animal tests, yet it seems inadequate as it focuses mainly on the medicine being researched in the trial and not on the procedures/how the trial should be conducted. Section 49(1) of the act provides that:

A person shall not sell, supply, assemble, manufacture or procure the sale, supply, manufacture or assembly of any medicine for purposes of a clinical trial unless that person is the holder of a product license issued by the Authority, on such terms and conditions as the Authority may determine and which authorises that person to conduct clinical trials (Zambia's Pharmaceuticals Act of 2004).

It is unclear whether or not the issuance of a product licence is preceded by an ethics review process that ensures the safety of participants in the trial.

Section 34(1) of Nigeria's National Health Bill requires that every institution, health agency and health establishment where research is conducted establish or have access to a health REC that is registered with the National Health Sciences Research Ethics Committee. Additional guidelines are provided in the 'National HIV Vaccine Plan' (Nigeria Federal Ministry of Health, 2001), which prescribes the review of research proposals and protocols by the technical committee of the National Agency for the Control of AIDS (NACA) and the WHO/GPA Steering Committee on Vaccine Development. There is also a requirement for the formation of a monitoring team to oversee the implementation of all vaccine trials. The composition of an international Data and Safety Monitoring Board (DSMB) to monitor and analyse the data from all HIV-vaccine trials conducted in Nigeria in accordance with international best practices is also part of the national plan. There is little detail provided on the protection of HIV-vaccine trial participants, however.

Rwanda's standard operating procedures (SOPs) provide for a more elaborate process. Paragraph 12 specifies the elements that the committee must consider (see Rwanda Ministry of Health, 2009). One interesting element is the need for documentation on how the researcher will protect

the rights and welfare of special categories of the population that are categorised (in paragraph 12.8) as vulnerable. Training of personnel, committee members and the scientific community is overseen by the secretariat. Such training focuses on, *inter alia*, the protection of research participants. The stipulated review process considers the steps taken to consult communities during the course of designing the research, the influence of the community on the consent of the individual participants, and the proposed community consultation process during the course of the research (SOPs, paragraph 12.7).

Models for monitoring ongoing research

Three models for monitoring research are used by the five countries. Cameroon and Zambia operate on the basis of trust. Malawi and Rwanda have established monitoring and oversight committees, respectively, while Nigeria uses local advocacy groups to monitor ongoing research.

In Cameroon, the ministries of scientific research and innovations, higher education, and health have the power to monitor research, but they currently do not have the resources to do this because their terms of reference do not include the regulation of research. Consequently, RECs work on the basis of trust where researchers are to conduct research in accordance with international guidelines and national laws. However, there are instances of failure to review protocols and to seek informed consent. All investigators are required to submit periodic reports for monitoring by RECs and field visits by committee members as stipulated in the letters of approval, but this is seldom done (Rwomire & Nyamnjoh, 2007).

In Zambia, RECs are unable to monitor ongoing research adequately because of various challenges, such as the limited resources available to committees for monitoring research and poor or non-existent mechanisms for addressing cases of unethical conduct. Plans are underway to put monitoring mechanisms in place and committees have attempted to provide much-needed guidance to ensure that research is done in an ethical manner.

Each REC in Malawi has a subcommittee that is responsible for monitoring research. All investigators are required to submit annual reports for review. Occasionally, REC members visit study sites to ensure regulatory compliance. Each committee now has a compliance officer whose role is to monitor research by reviewing study documents and conducting site inspections. These officers have been trained in clinical-trial monitoring. The NHSRC, COMREC, NRCM and experts in relevant areas may review and monitor studies following the acceptance of research proposals of national interest. The NHSRC and COMREC are responsible for investigating cases of ethical violations. Where there is adequate proof of a violation, the researcher may be directed to terminate the study and compensate the participants (National Research Council of Malawi [NRCM], 2002).

Also in Malawi, the Medical Rights Watch (MRW), initiated in 2008 by medical students at the University of Malawi, is a rights advocacy group formed to champion the rights of patients and research participants and it also plays an important role in monitoring the handling of research

participants. Furthermore, the Human Rights Commission also assists with issues concerning the protection of research participants' rights.

Advocacy groups are used in Nigeria as well. Since the advent of the 'National HIV Vaccine Plan' in 2001, the Federal Ministry of Health has tried to involve community leaders and local advocacy groups in the conduct of HIV-vaccine trials. These groups help ensure that the informed-consent process is properly followed with prospective participants. For instance, the New HIV Vaccine and Microbicide Advocacy Society (NHVMAS) has been involved in monitoring research in new HIV-prevention technologies and HIV-vaccine research in Nigeria based on their experience in this field.

Rwanda's elaborate monitoring process stands out and can be used by other countries to develop similar approaches. Paragraph 10 of the SOPs (Rwanda Ministry of Health, 2009) specifically states that a REC is responsible for ensuring that the research projects it has approved are monitored and evaluated. The lead researcher is expected to submit an annual report to the committee on the following:

- current progress of the study or the results of studies already completed;
- information connected with maintaining data confidentiality;
- proof that the research protocol is being properly followed; and
- proof that each condition of the agreement has been observed.

One specific element that the committee is required to consider when approving protocols is "the adequacy of provisions that are made for monitoring and auditing the conduct of the research, including the constitution of a Data and Safety Monitoring Board (DSMB) or Oversight Committee" (SOPs, paragraph 12.1: Rwanda Ministry of Health, 2009).

Part 5: Summary and implications of the country audits

HIV-vaccine research seeks to address a problem of national importance for each of the five countries audited. The structures, measures and procedures that have been highlighted in this article are a clear sign that these countries are prepared to host HIV-vaccine trials and are ready to address complex issues related to the trials. Overall, some level of protection is available to participants who participate in clinical trials; meanwhile, RECs have been established to review and monitor research.

The findings of the five-country audit suggest that the research oversight systems in these countries are still evolving. There is an urgent need to enact laws that directly address the conduct of health research. There is also a need for clear policies and ethics guidance that address issues relevant to HIV-vaccine trials, specifically. Particular regard should be given to the situation of participants who become HIV-infected during the course of trials. In Malawi, there is currently an understanding among REC members and the Ministry of Health that such participants need to be given priority in accessing care. The guidelines of UNAIDS

(2007a) offer some guidance on this issue — which may be useful for RECs in Africa as countries develop their respective formal national positions. For example, Guidance Point 14 (UNAIDS, 2007a) states that all participants who acquire HIV infection during the course of a biomedical HIV-prevention trial should be provided with access to treatment using internationally recognised regimens. The guidance document further recommends that before the initiation of an HIV-preventive vaccine trial, all research stakeholders should come to an agreement through discussion and negotiation about the mechanisms to be used to provide and sustain such HIV-related care and treatment.

Particular attention should be paid to the involvement of children in research. For example, Malawi has a large population of orphans and vulnerable children and yet does not have a clear position on how consent involving such a population category in clinical trials should be sought.

Trial participants need to be empowered through education so that they become aware of their rights and the mechanisms for enforcing their rights. Toolkits for trial participants or individuals who are considering taking part in a trial would be helpful. The publication 'Good Participatory Practice: Guidelines for Biomedical HIV Prevention Trials' by UNAIDS (2007b) can be used for developing such toolkits.

Even though there are various pieces of legislation and structures in place that may be used to protect their rights, participants do not often use them due to lack of awareness. Most research in African countries is conducted among poor and less-educated communities. Therefore, explicit procedures are needed to guide the selection of research candidates, to ensure that undue inducements are avoided and that participants agreeing to participate in research do so based on complete information.

In order to address the challenges that face these countries in regulating HIV-vaccine research it is necessary to enact laws that 1) adequately protect the rights of research participants, and 2) strengthen the RECs through capacity-building and adequate resources for monitoring research. It is at least commendable that the five countries reviewed here have either started the process of enacting such laws or plan to do so. Specific ways in which the ethical/legal frameworks can be strengthened are proposed below.

Lessons learnt: How countries can improve their ethical/legal frameworks

There are both general and country-specific lessons that emerge from the various ethical/legal frameworks that the five countries audited have used to address challenges related to HIV-vaccine research.

First we can surmise that it is important to have a clear power structure of institutions or governing bodies that are responsible for creating and implementing ethical/legal frameworks. A good example of a clear and well-coordinated institutional structure exists in Malawi, where three committees (the PMPB, NHSRC and COMREC) work in a synergetic manner in reviewing clinical trial protocols.

Closely related to the issue of achieving a clear mandate is the need to ensure that the responsible institutions actually carry out their duties, particularly that of monitoring

ongoing trials following approval by a REC. We found that where monitoring information was provided by investigators, the information was generally not utilised for monitoring and field supervision. The prevailing situation forces RECs to work on the basis of trust, wherein it is expected that researchers will execute the research in accordance with international guidelines and national laws.

Second, having research ethics guidelines and institutional structures that are based on enabling legislation for ensuring compliance may be helpful for solving problems related to a lack of protection of trial participants' legal rights (which most of the countries under discussion experience). A good example can be taken from Nigeria's National Health Bill which has attempted to comprehensively address the relevant issues and established a proper framework for the registration and functions of RECs in the country.

Third, community engagement is vital for achieving public confidence in ethical/legal frameworks. An illustration of this lesson is the case of Zambia's microbicide trials which generated bad publicity and complaints, apparently due to inadequate information being provided to the participants and communities.

Several country-level recommendations can be made for strengthening the existing ethical/legal frameworks:

- 1) In Malawi there is a need to develop guidelines for structures and processes for the ethical review of research with human participants. These guidelines should be based on enabling legislation that takes cognisance of the complex issues related to HIV-vaccine research.
- 2) In Cameroon, an enabling legislation is equally required to facilitate the implementation of the National Health Research Ethics Guidelines since issues specific to HIV-vaccine research need to be addressed in the guidelines.
- 3) With the current positive developments towards developing a more streamlined ethical/legal framework, the situation in Nigeria will probably improve once the National Health Bill has received presidential assent. One specific point of improvement could be to include the rights of trial participants in the 'National HIV Vaccine Plan.'
- 4) Rwanda needs to establish a clear structure for the approval and monitoring of clinical trials. For instance, the status of its standard operating procedures needs to be clear — that is, whether or not they should they be applied by all RECs in the country, and on what basis, particularly given that they originate from the Ministry of Health.
- 5) Zambia should establish clear guidelines for research with human participants in order to ensure: adequate structures and processes for the ethical review of research; compliance with national ethical norms and standards; and broad participation in the RECs, including by social scientists and human-rights experts. Creating enabling legislation for guidelines for research review and membership to RECs is one possible solution. This can equally address the need for a complaints mechanism for participants who allege unethical conduct.

Conclusions

It is apparent that the ethical/legal frameworks in the five African countries, although not ideal, have attempted to address the challenges involved in conducting HIV-vaccine research. In principle, basic laws and ethical guidelines protect the fundamental rights of all people, including trial participants. However, the lessons mentioned here also demonstrate room for improvement. Other countries that are developing ethical/legal frameworks for HIV-vaccine research can benefit from the country-level recommendations mentioned above.

Acknowledgements — This work is based on contributions from in-country collaborators in each of the countries reviewed and is based on the best information available at the time. We are very grateful to Professor Douglas Wassenaar (University of KwaZulu-Natal, School of Psychology) and Nicole Mamotte (Project Coordinator, Ethics, Law and Human Rights Working Group of the African AIDS Vaccine Programme [AAVP ELH]) for their invaluable comments on earlier drafts. Preparation of the audit report on which this article is based received financial support from the WHO-sponsored AAVP based in Geneva. The ELH Collaborating Centre is an expert ethical advisory body to AAVP, established to provide independent advice to AAVP through the WHO/UNAIDS HIV Vaccine Initiative (WHO/IVR/HVI) regarding the development of AAVP research ethics. WHO/IVR/HVI and the WHO/AFRO ATM Division also provide secretarial and administrative support to AAVP. The above financial support notwithstanding, the views expressed are those of the authors and do not represent the views of any of the organisations listed above.

The authors — Pamela Andanda holds a master's degree in public law (LLM) from the University of Nairobi (Kenya) and a PhD in law from the University of the Witwatersrand (South Africa) where she is an associate professor in the School of Law.

Paschal Awah holds a PhD in medical anthropology from the Faculty of Medical Sciences at Newcastle University (United Kingdom). He also holds certificates in biomedical ethics from the Western Institutional Review Board (WIRB) (in Olympia, Washington State, USA) and the University of Washington in Seattle. Currently, he is a senior research advisor for the African Region with Ipas in Chapel Hill, North Carolina (USA).

Paul Ndebele holds a PhD in psychology from the University of KwaZulu-Natal (South Africa) and a master's degree in population studies and a bachelor's degree in sociology, both from the University of Zimbabwe. He is the assistant director of research ethics in the Office of Research and Development at the University of Botswana.

Olanrewaju Onigbogi holds an MBBS degree from the University of Ilorin (Nigeria) and an MPH from the University of Kuopio (Finland). He is a fellow of the Faculty of Public Health with the National Postgraduate Medical College of Nigeria. Currently, he is a lecturer at the University of Lagos (Nigeria).

Daniel Udatinya (MD) holds a degree in general medicine and surgery from the National University of Rwanda.

Malala Mwendela holds a bachelor's degree in development studies from the University of Zambia and is currently studying for a master's degree in public health at the University of the Western Cape (South Africa). She is the executive director of the Zambia AIDS Law Research and Advocacy Network (ZARAN).

References

- AIDS Vaccine Advocacy Coalition (AVAC) (2008) *AVAC Report 2008: The Search Must Continue*. New York, AVAC. Available at: <<http://www.avac.org/ht/a/GetDocumentAction/i/2338>>.
- Andanda, P., Gxoyiya, K. & Mahenge, O. (2010) *The Ethical-Legal Regulation of HIV Vaccine Research in Africa: A study of the regulation of health research in Cameroon, Malawi, Nigeria, Rwanda and Zambia to determine their capacity to protect and promote the rights of persons participating in HIV vaccine research*. A Report for the Ethics, Law and Human Rights (ELH) Working Group of the African AIDS Vaccine Programme (AAVP), commissioned by the World Health Organization (WHO).
- Annas, G.J. & Grodin, M.A. (1998) Human rights and maternal-fetal HIV-transmission-prevention trials in Africa. *The American Journal of Public Health* 88(4), pp. 560–563.
- Council for International Organizations of Medical Sciences (CIOMS) (2002) *International Ethical Guidelines for Biomedical Research Involving Human Subjects*. Geneva, World Health Organization/CIOMS.
- Dawson, L. & Kass, N.E. (2005) Views of U.S. researchers about informed consent in international collaborative research. *Social Science and Medicine* 61(6), pp. 1211–1222.
- Emanuel, E.J., Wendler, D., Killen, J. & Grady, C. (2004) What makes clinical research in developing countries ethical? The benchmarks of ethical research. *Journal of Infectious Diseases* 189(5), pp. 930–937.
- Esparza, J. & Bhamarapravati, N. (2000) Accelerating the development and future availability of HIV-1 vaccines: Why, when, where, and how? *The Lancet* 355(9226), pp. 2061–2066.
- Essack, Z., Koen, J., Barsdorf, N., Slack, C., Quayle, M., Milford, C., Lindegger, G., Ranchod, C. & Mukuka, R. (2010) Stakeholder perspectives on ethical challenges in HIV vaccine trials in South Africa. *Developing World Bioethics* 10(1), pp. 11–21.
- European Medicines Agency (EMA) (2009) *EMA Strategy Paper: Acceptance of Clinical Trials Conducted in Third-World Countries, for Evaluation in Marketing Authorisation Applications*. Doc. Ref. General-EMA/228067/2008, December 2008. London, EMA.
- Grant, C., Lewis, M. & Strode, A. (2005) *The Ethical-Legal Regulation of HIV-Vaccine Research in Africa: A study of the regulation of health research in Botswana, Ethiopia, Kenya, Tanzania and Uganda to determine their capacity to protect and promote the rights of persons participating in HIV-vaccine research* (Technical Report). Pietermaritzburg, South Africa, Ethics, Law, and Human Rights Working Group (ELH), African AIDS Vaccine Programme (AAVP).
- Hatchard, J. (1999) The Human Rights Commission Act, 1998. *Journal of African Law* 43(2), pp. 253–257.
- Kaleebu, P., Abimiku, A., El-Halabi, S., Koulla-Shiro, S., Mamotte, N., Mboup, S., Mugerwa, R., Nkengasong, J., Toure-Kane, C., Tucker, T., Wassenaar, D., Williamson, C. & Wolday, D. (2008) African AIDS Vaccine Programme for a coordinated and collaborative vaccine development effort on the continent. *PLoS Medicine* 5(12), pp. 1–5.
- Lindegger, G. & Richter, L.M. (2000) HIV-vaccine trials: critical issues in informed consent. *South African Journal of Science* 96 (June), pp. 313–317.
- Maïga, D., Akanmori, B.D. & Chocarro, L. (2009) Regulatory oversight of clinical trials in Africa: progress over the past 5 years. *Vaccine* 27(52), pp. 7249–7252.
- Merritt, M. & Grady, C. (2006) Reciprocity and post-trial access for participants in antiretroviral therapy trials. *AIDS* 20(14), p. 1791–1794.
- Milford, C., Wassenaar, D. & Slack, C. (2006) Resources and needs of research ethics committees in Africa: preparations for HIV vaccine trials. *IRB* 28(2), pp. 1–9.
- Ministry of Health [Malawi] (2003) *National HIV/AIDS Policy – A Call for Renewed Action*. October 2003. Lilongwe, Malawi, Ministry of Health.
- Mystakidou, K., Panagiotou, I., Katsaragakis, S., Tsiliika, E. & Parpa, E. (2009) Ethical and practical challenges in implementing informed consent in HIV/AIDS clinical trials in developing or resource-limited countries. *Journal of Social Aspects of HIV/AIDS (SAHARA-J)* 6(2), pp. 46–57.
- National Research Council of Malawi (NRCM) (2002) *Procedures and Guidelines for the Conduct of Research in Malawi*. Lilongwe, Malawi, NRCM.
- National University of Rwanda (NUR) Research Directorate (no date) *Ethics Clearance Operational Guidelines and Procedures*. Butare, Rwanda, NUR. Available at: <<http://www.researchdirector.nur.ac.rw/spip.php?article6>>.
- Ngandwe, T. (2005) 'Research ethics 'watchdog' planned in Zambia.' *Science and Development Network*, 1 February 2005. Online article: <<http://www.scidev.net/en/news/research-ethics-watchdog-planned-in-zambia.html>>.
- Nigeria Federal Ministry of Health (2001) *Nigerian National HIV Vaccine Plan, Draft August 2001*. Lagos, Nigeria, National Action Committee on AIDS (NACA).
- Nigeria Federal Ministry of Health (2007) *National Code of Health Research Ethics, 2006*. Abuja, Nigeria, National Health Research Ethics Committee of Nigeria (NHREC) and Federal Ministry of Health.
- Nyika, A., Kilama, W., Chilengi, R., Tangwa, G., Tindana, P., Ndebele, P. & Ikingura, J. (2009) Composition, training needs and independence of ethics review committees across Africa: Are the gate-keepers rising to the emerging challenges? *Journal of Medical Ethics* 35(3), pp. 189–193.
- Pace, C., Grady, C., Wendler, D., Bebhuk, J.D., Tavel, J.A., McNay, L.A., Forster, H.P., Killen, J. & Emanuel, E.J. (2006) Post-trial access to tested interventions: the views of IRB/REC chair, investigators, and research participants in a multinational HIV/AIDS study. *AIDS Research and Human Retroviruses* 22(9), pp. 837–841.
- Phiri, D. (2010) 'Microbicides clinical trial raises dust in Mazabuka.' *ZARAN News* [Zambia], January–March 2010, pp. 1 and 4.
- Rwabihama, J.P., Girre, C. & Duguet, A.M. (2010) Ethics committees for biomedical research in some African emerging countries: Which establishment for which independence? A comparison with the USA and Canada. *Journal of Medical Ethics* 36(4), pp. 243–249.
- Rwanda Ministry of Health (2009) *Rwanda Ministry of Health Selected Standard Operating Procedures (SOPs)*. January 2009. Kigali, Rwanda, Ministry of Health.
- Rwomire, A. & Nyamnjoh, F.B. (eds.) (2007) *Challenges and Responsibilities of Social Research in Africa: Ethical Issues*. Addis Ababa, Ethiopia, Organisation for Social Science Research in Eastern and Southern Africa (OSSREA).
- UNAIDS (2007a) *Ethical Considerations in Biomedical HIV Prevention Trials*. UNAIDS/WHO Guidance Document, UNAIDS/07.28E/JC1349E, July 2007. Geneva, UNAIDS.
- UNAIDS (2007b) *Good Participatory Practice: Guidelines for Biomedical HIV Prevention Trials*. UNAIDS/07.30E/JC1364E, November 2007. Geneva, UNAIDS.
- UNAIDS (2010) *UNAIDS Report on the Global AIDS Epidemic 2010*. Geneva, UNAIDS.
- University of Zambia (2009) *Research Policy and Intellectual Property Rights*. June 2009. Lusaka, Zambia, University of Zambia, Directorate of Research and Graduate Studies. Available at: <http://www.unza.zm/index2.php?option=com_docman&task=

doc_view&gid=75&Itemid=73>.

West Africa Democracy Radio (WADR) (2011) 'Nigeria: Senate passes national health bill amidst protest.' 20 May 2011. WADR.org, online article: <http://www.wadr.org/en/site/news_en/782/Nigeria-Senate-passes-national-health-bill-amidst-protest.htm>.

World Medical Association (WMA) (2008) *World Medical Association Declaration of Helsinki. Ethical Principles for Medical Research Involving Human Subjects*. Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964 [since amended]. Ferney-Voltaire, France, WMA.

Zambia AIDS Law Research and Advocacy Network (ZARAN) (no date) *Discussion and analysis of Zambia's herbal remedies trial: ethics and human rights in medical research trials*. Discussion Paper (unpublished). Lusaka, Zambia, ZARAN.