

The accountability of states for human rights abuses by non-state actors during preventive HIV vaccine efficacy trials in Africa

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Introduction

Human rights instruments confer an obligation upon states to take effective measures to prevent violations of the human rights of persons within their territories.¹ This obligation was reiterated before the Inter-American Court on Human Rights² in the case of *Velasquez Rodriguez v Honduras*:³

An illegal act which violates human rights and which is initially not directly imputable to a State can lead to international responsibility of the State, not because of the act itself, but because of the *lack of due diligence to prevent the violation* or to respond to it as required by the Convention.

The requirement of *due diligence* obliges states to prevent, investigate, punish and remedy human rights violations committed by non-state actors.⁴ Although international law considers states as its primary subjects, it increasingly holds states indirectly liable for the human rights abuses of non-state actors.

The paper draws upon the jurisprudence of the African Commission on Human and Peoples' Rights to investigate the accountability of states for human rights abuses by non-state actors during preventive HIV vaccine efficacy trials in Africa. It is divided into four parts: after an introduction, clinical research to establish HIV vaccine efficacy and the influence of globalisation upon the clinical research endeavour are examined. The possible exploitation of research participants is also analysed. Next, two communications before the

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¹See, eg, art 2(3)(a) ICCPR; art 2(e) CEDAW; art 2 African Charter on Human and Peoples' Rights.

²Art 33 American Convention on Human Rights; art 106 OAS Charter. See Nowak *Introducing the international human rights regime* (2003) 193.

³*Velasquez Rodriguez v Honduras* Inter-American Court on Human Rights Ser C No 4 1988; (1989) 28 *ILM* at par 172 (my emphasis).

⁴*Id* at pars 173-174.

African Commission on Human and Peoples' Rights are investigated in order to establish the accountability of states in Africa for human rights abuses by non-state actors. Finally, conclusions and general comments are proffered.

Arguments on the application of international human rights law to non-state actors have been canvassed more eloquently by others,⁵ so they will not be revisited here.⁶

Vaccines against HIV, clinical research and globalisation

Introduction

Sub-Saharan Africa is far the region worst affected by the HIV and AIDS epidemic. Two thirds of all adults and children with HIV globally live in sub-Saharan Africa, amounting to almost twenty-five million people.⁷ Further, 2,1 million Africans died of AIDS in 2006, totalling seventy-two per cent of all AIDS deaths globally.⁸

Within sub-Saharan Africa, southern Africa is the worst off – thirty-two per cent

⁵See eg Alston (ed) *Non-state actors and human rights* (2005) 3-36; 37- 89; Clapham *Human rights obligations of non-state actors* (2006) 25-83; Muchlinski 'Human rights and multi-nationals: Is there a problem?' (2001) 77 *International Affairs* 31.

⁶Andrew Clapham writes that 'the [application of human rights law] to the private sphere has implications for the ways in which we conceive human rights generally' (Clapham n 5 above at 1). Clapham outlines three broad approaches to the question whether non-state actors be held accountable for human rights abuses. The first insists that states are the only bearers of human rights obligations under international law and that the obligations of non-state actors are dealt with as questions of the relevant government's obligation to ensure respect for human rights. This view holds existing human rights law as sufficient in that it already demands that governments protect everyone from those who infringe their human rights. A second approach suggests that governments increasingly are irrelevant and that new ways of understanding transnational justice and global law are needed to respond to globalisation. Clapham favours a third approach, arguing that some of the obligations under public international law, traditionally applied only to states, should apply to non-state actors. He 'recognise[s] the role of non-state actors and their influence without suggesting that they have achieved the role of law-maker'. He points out that the existing general rules of international human rights law, created and acknowledged by states, fix on non-state actors so that they be held accountable for violations of this law. Clapham advances several reasons for this view, amongst others, that international law attaches individual criminal responsibility for certain acts committed by individuals, such as slavery, war crimes and torture; that international law attaches to non-state actors irrespective of their link to the state (Clapham n 5 above at 29); that there are certain entities apart from states and individuals that already bear rights and obligations under international law (such as the UN) (Clapham n 5 above at 26-30); and also, that states are bound by international law to ensure that the corporations respect the duties defined in international treaties. In this regard, Clapham cites the Bamako Convention on the Ban of the Import into Africa and the Control of Transboundary Wastes within Africa as ensuring that corporations respect the duties defined in international treaties. The Bamako Convention demands that African states promulgate national legislation which imposes criminal sanctions on *all persons* involved in violations of the Convention (Clapham n 5 above at 31-32).

⁷UNAIDS *AIDS epidemic update* (2006) 6.

⁸*Ibid.*

of all people living with the virus are in southern Africa, and thirty-four per cent of all AIDS deaths in 2006 occurred in this region.⁹ The following table outlines the prevalence of HIV infection among adults in southern Africa:¹⁰

Botswana	24.1%
Lesotho	23.2%
Swaziland	33.4%
Mozambique	16.%
Zimbabwe	20.%
Namibia	19.%
Malawi	14.%
South Africa	18.%

Despite initial optimism, scientists acknowledge that it is improbable they will develop a cure for AIDS within the next decade. This pessimistic outlook, together with the absence of an effective, low-cost, non-toxic and long-term-efficacious treatment,¹¹ the lack of effective prevention strategies,¹² and the prevalence of HIV among economically and socially powerless groups,¹³ makes it critical that an effective preventive vaccine be developed.

⁹*Id* at 3.

¹⁰*Ibid.*

¹¹In this regard, see Weiss and Weiss 'The emergence of human immunodeficiency viruses and AIDS' in Smith *et al* (eds) *New challenges to health: The threat of virus infection* (2001) 147. The development of HAART (highly active anti-retroviral therapy – which combines three antiretrovirals) has indefinitely prolonged the lives of countless people living with HIV and AIDS, but the therapy is often toxic, costly and difficult to administer. Furthermore, new studies indicate that triple-therapy-resistant variants of HIV are developing (see, eg, Harrigan *et al* 'Predictors of HIV drug-resistance mutations in a large antiretroviral-naïve cohort initiating triple antiretroviral therapy' (2005) 191 *The Journal of Infectious Diseases* 339-34).

¹²Prevention strategies that are being investigated include anti-HIV microbicides, male circumcision, and pre-exposure prophylaxes. However, anti-HIV microbicides and pre-exposure prophylaxes are still in the early stages of development (Ramjee 'Microbicides and other prevention technologies' Paper delivered at the XVI International HIV/AIDS Conference, Toronto, Canada, 13-18 August 2006). Similarly, male circumcision does not seem to offer the potential of halting the epidemic (see Nienaber unpublished LLD thesis University of Pretoria (2007) 44-47).

¹³Several studies have shown a correlation between poverty and HIV infection (Barnett and Whiteside *AIDS in the twenty-first century: Disease and globalization* (2002) 124-156, 159-181, 182-195; Van Niekerk 'Moral and social complexities of AIDS in Africa' in Van Niekerk and Kopelman (eds) *Ethics and AIDS in Africa: The challenge to our thinking* (2005) 53-70. Barnett and Whiteside comment at 167: 'Thus relative wealth reduces vulnerability at all levels from the individual to the nation. These resources are not purely financial; they may include skilled labour, or access to care; even a strong, cohesive and compassionate civil society'.

Vaccines are generally safe, effective and inexpensive ways to prevent disease.¹⁴ Clinical trials to test the efficacy of various candidate preventive HIV vaccines are underway in many parts of Africa.¹⁵ A successful preventive HIV vaccine should be effective, safe and affordable.¹⁶ A preventive HIV vaccine will be considered successful if it either prevents infection (known as sterilising immunity), or prevents the disease.¹⁷ If neither of the above is likely, a third possibility is that the successful vaccine will slow down or delay the progression of the disease from infection to death.¹⁸ In other words, the vaccine will succeed in lowering the viral load in the blood of infected persons for a considerable period. The third possibility indirectly decreases the transmission of the disease:¹⁹ the vaccine has a limited effect on the health of the vaccinated person (as she will become ill eventually), but, potentially, a significant effect on the epidemiology of HIV within the community.²⁰

¹⁴Schoub *AIDS and HIV in perspective* (1994) 183. As has been the case with viral diseases such as smallpox and poliomyelitis, the development of an effective vaccine offers the only hope of halting or slowing the HIV and AIDS epidemic. Also see Ada and Ramsay *Vaccines, vaccination, and the immune response* (1997); Cohen *Shots in the dark: The wayward search for an AIDS vaccine* (2001); and Collier and Oxford *Human virology* (2000).

¹⁵See AVAC *AIDS Vaccines: The next frontiers* (2006) 21-25.

¹⁶Janse van Rensburg 'Vaccine design and making vaccines for South Africa' (2002) 20 *CME* 577; Weidle *et al* 'HIV/AIDS treatment and HIV vaccine trials for Africa' (2002) 359 *The Lancet* 2264; Schoub 'Vaccination as an intervention against viral diseases: Will this work for HIV?' (2002) 20 *CME* 561. The endpoint of a therapeutic HIV vaccine trial is that the vaccine succeeds in ameliorating the disease by eliciting an immune response in the infected person (see Janse van Rensburg at 580; Schoub at 561).

¹⁷For most infectious diseases, sterilising immunity is the endpoint. In the case of sterilising immunity, the body is able totally to eliminate the virus, infection is prevented, and there are no signs and symptoms of the disease. Many scientists believe that it is not possible to develop an HIV vaccine that will prevent infection (see Janse van Rensburg n 16 above at 579; Weidle *et al* n 16 above at 2264; Schoub n 16 above at 561; Van Harmelen and Williamson 'HIV complexity: Challenges in vaccine development' (2000) 20 *CME* 569-570. Once a person is infected with HIV, the virus remains in that person's body, as it integrates itself into the person's DNA.

¹⁸Janse Van Rensburg n 16 above at 579; Weidle *et al* n 16 above at 2264; Schoub n 16 above at 561. The asymptomatic period of the disease will be prolonged, and there will be no or few symptoms (Janse Van Rensburg n 16 above at 579-580).

¹⁹A high viral load is a risk factor for HIV transmission.

²⁰This is known as a 'surrogate endpoint'. Janse Van Rensburg n 16 above at 579; Weidle *et al* n 16 above at 2264; Schoub n 16 above at 561. The Meeting summary of AIDS vaccine trials: considerations for Phase III trial design and endpoints, held in 2001 in the USA, outlined the following as 'surrogate' or replacement endpoints in HIV preventive efficacy trials in a case where neither sterilising immunity, nor the prevention of disease is achieved by the candidate HIV vaccine:

Virologic endpoints: a) Decreased plasma viral load set-point, or b) decreased plasma viral load below some biologically significant set-point and, in addition, increased duration of the effect for a meaningful time period (eg, more than one year).

Immunologic endpoints: a) Maintenance of the CD4 T-cell count (eg, >350 cells/ μ L), or b) decreased rate of CD4 T-cell decline.

Clinical endpoints: a) Decrease in the number of HIV-infected vaccinated subjects requiring ARV treatment, or b) increase in the time interval from infection to initiation of antiretroviral treatment.

Epidemiological endpoints: a) Decrease in sexual transmission rates by vaccinated subjects who become

HIV vaccine development

Vaccine efficacy is measured during Phases II and III vaccine trials. Phase III vaccine efficacy trials are large-scale, double blind, placebo-controlled, randomised clinical trials. Efficacy is measured statistically: a situation in which those participants who have had the HIV preventive vaccine have a significantly lower incidence of HIV infection than those receiving the placebo.²¹

During a Phase III efficacy trial, the possibility of adverse effects is also examined.²² Large numbers of volunteers take part, usually more than a thousand.²³ Because the efficacy of the candidate vaccine needs to be established, these volunteers should be at high risk for infection and are drawn from communities with a high incidence of HIV.²⁴

The risks and benefits inherent in HIV vaccine trial participation have been discussed frequently.²⁵ For the sake of completeness, these risks are summarised below. As the potential benefits of participation are of less concern to the current discussion, they are not included here.²⁶

A guiding principle that all human subject research has to comply with in order to be considered ethical and legal, is that there should be a favourable balance between risk and potential benefit.²⁷ Risks borne by participants in

HIV-infected subsequent to vaccination, or b) decrease in maternal-infant transmission rates for women who become HIV-infected subsequent to vaccination. In these situations, the clinical benefit may be to others rather than to the vaccinated subject.

From the above it is clear that it will be necessary to keep track of vaccine trial participants over a long period to evaluate these surrogate markers. Also, should participants be treated with ARVs, this process of evaluation could be complicated.

²¹What is considered to be 'statistically lower' is a matter for debate. VaxGen's completed vaccine trials in Thailand and the USA were looking at a reduction in the level of HIV infection by at least 30% at a statistically significant level. This means that an efficacy of more than 30% would be seen 95 times out of 100 (Farham 'The trials of testing', on file with author).

²²SS Abdool Karim 'Conducting HIV vaccine trials in South Africa' (2002) 20 *CME* 589.

²³The VaxGen Phase III trial involved 5009 volunteers.

²⁴In communities with a low HIV incidence rate, many more participants have to be enrolled in the trial in order to achieve statistical validity. Such trials are necessarily more expensive.

²⁵See, eg, UNAIDS *Ethical considerations in HIV preventive vaccine research* (2000) 28; Graham and Wright 'Candidate AIDS vaccines' (2003) 33 *New England J of Medicine* 1335; Slack *et al* 'Implications of the ethical-legal framework for adolescent HIV vaccine trials – report of a consultative forum' (2000) 96 *SA J of Science* 293.

²⁶For more on the benefits of HIV vaccine efficacy trial participation, see Janse Van Rensburg n 16 above at 579; Weidle *et al* n 16 above at 2264; Schoub n 16 above at 561.

²⁷Guideline 9.12.4.1 of the Medical Research Council guidelines: The probability of harm resulting from an activity and to its magnitude. *Risk* often stands for the combined probabilities and magnitude of several potential harms, whether psychological, sociological or physiological in nature. It should be noted that even inactivity may be associated with some risk and that every intervention, however simple it may be, involves some degree of risk. Risk includes the consequence of a breach of confidentiality and also risks to others, through the use of scarce

HIV preventive vaccine efficacy trials are physical, psychological and social in nature. As yet, it is unclear which of these risks will materialise during Phase III trials.²⁸

Adverse auto-immune reactions to the vaccine and the worsening of established infections

Participation in HIV preventive vaccine efficacy trials exposes participants to the risk of adverse auto-immune reactions to the vaccine and to the possibility that the participant will suffer from a more severe infection should she become infected with HIV.²⁹ Fears with regard to adverse auto-immune reactions relate to the fact that HIV's gp160 contains several regions (such as HLA-DR and interleukin-2) with sequences homologous to those of cellular proteins (especially those found on human CD4 cells).³⁰ It is feared that vaccination will stimulate auto-immune reactions against the body's own CD4 cells.³¹ This theory is borne out by the fact that HIV-infected persons show a high incidence of auto-immune reactions.³²

The possibility that HIV vaccination could worsen illness, if the trial participant becomes infected with HIV subsequent to vaccination, has been mentioned as a possible risk to participation.³³ To date this risk has not materialised, although there is some evidence that it is the case *in vitro*.³⁴ Further, with regard to this risk there is the possibility that a trial participant may have a greater risk of developing an established infection upon being exposed to HIV than others.³⁵

Someone already infected with HIV, when vaccinated, may develop a more serious and severe infection.³⁶ This may happen in cases where the participant is in the early stages of infection before sufficient antibodies have been produced to

resources for research that might otherwise be used for patient care.

²⁸It should be remembered that the risks of HIV preventive vaccine efficacy trials differ according to vaccine design and trial design. Some vaccines are safer than others; some trial designs may have more adverse effects than others, such as those using placebos. The social and health status of the individual taking part in the trial also may contribute to the probability and magnitude of the risk.

²⁹Graham and Wright n 25 above at 1335.

³⁰*Ibid.*

³¹*Ibid.*

³²*Ibid.* So far, low levels of CD4-antibodies have indeed been detected in vaccine trial participants (see, eg, S Keay *et al* 'Anti-CD4 anti-idiotypic antibodies in volunteers immunized with rgp160 of HIV-1 or infected with HIV-1' (1992) 8 *AIDS research on human retroviruses* 1091). See also the commentary on the article by Veljkovic *et al* below.

³³Graham and Wright n 25 above at 1335.

³⁴As above.

³⁵UNAIDS n 25 above at 28.

³⁶Slack *et al* n 25 above at 293.

show up on standard ELISA assays. The person is diagnosed as HIV negative, whereas, in fact, she is HIV positive, and then inoculated.

Adverse reactions to the vaccine itself

Other physical risks to HIV vaccination are adverse reactions to the vaccine itself,³⁷ pain, skin irritations, fever, and malaise.³⁸ HIV vaccination may require repeated inoculations, each in turn producing these adverse effects.

Live vaccines

Live vaccines³⁹ carry the risk that the vaccine virus may mutate sufficiently to revert to its virulent form and produce HIV infection. Although pre-clinical research is being done on live vaccines, there is at present no indication that these vaccines will be tested on humans.⁴⁰ However, should this occur, trial participants will be exposed to even more serious risk of harm.⁴¹

Immune tolerance

Participation in a preventive HIV vaccine efficacy trial may result in immune tolerance which, in turn, will prevent the trial participant from being successfully immunised against HIV in the future.⁴² This is a potentially serious risk, as it might mean that the participant will not be able to be given a subsequent, more effective vaccine.⁴³

Stress, anxiety and depression

Psychological risks to participants in HIV preventive vaccine efficacy trials include stress, anxiety and depression due to having to discuss intimate sexual issues with trial administrators, and the stress inherent in being subjected to repeat HIV testing.⁴⁴

Sexual relationships may become strained

Participation in HIV preventive vaccine efficacy trials might cause strain in the participant's sexual relations with others, especially when the participant's sexual partner (mistakenly) believes that the participant can infect others with the virus.⁴⁵

³⁷Such as an allergic reaction to one of its components.

³⁸UNAIDS n 21 above at 28.

³⁹As their name indicates, live (attenuated) viruses are 'alive' and able to replicate in the vaccinated person.

⁴⁰See Janse Van Rensburg n 16 above at 579; Weidle *et al* n 16 above at 2264; Schoub n 16 above at 561.

⁴¹*Ibid.*

⁴²Slack *et al* n 25 above at 293.

⁴³*Ibid.*

⁴⁴UNAIDS n 25 above at 29.

⁴⁵*Ibid.*

Increased risk-taking behaviour

Another potential risk of participating in HIV preventive vaccine efficacy trials is increased risk-taking behaviour by trial participants, caused by an (erroneous) belief that the candidate vaccine will protect them from infection.⁴⁶ This belief may be particularly dangerous in cases where trial participants belong to the placebo group.

Cultural isolation

Trial participants from a culture and belief system other than that under which the trial is designed and who are therefore exposed to alien scientific concepts, may experience stress and anxiety.⁴⁷

False-positive HIV test results

After being vaccinated, participants will test HIV-positive on standard ELISA assays even though they are not infected with HIV. This could have serious consequences for participants' prospects of successfully taking out insurance, finding employment, and so on. Some writers have rejected these fears of discrimination based on positive HIV antibody tests. They argue that a standard immunoblot can easily distinguish real HIV infection (which should show antibodies to all HIV's proteins) from vaccine-induced HIV antibodies (to the envelope proteins alone).⁴⁸ However, as vaccine science progresses, and vaccine designs become more complex, it is unlikely that immunity produced by the more complex DNA or vector vaccines will be easily distinguishable from true HIV infection in antibody laboratory tests.⁴⁹

Negative perceptions and stigmatisation

Not only will HIV preventive vaccine efficacy trial participants *test* positive on standard HIV-antibody tests, but they may be perceived by a misinformed public to *be* HIV positive. Participants in Phase III trials are usually high-risk individuals and this perception may cause them to be stigmatised and discriminated against. The communities from which these participants are drawn may be similarly stigmatised.

Although many vaccine scientists are quick to allay fears concerning the safety of vaccines, others are not so hasty, stressing the risks outlined above. For example, Veljkovic *et al*⁵⁰ raise serious concerns about preventive HIV

⁴⁶See Celentano *et al* 'Willingness to participate in AIDS vaccine trials among high-risk populations in northern Thailand' (1995) 9 *AIDS* 1079.

⁴⁷UNAIDS n 25 above at 29.

⁴⁸Francis *et al* 'Candidate HIV/AIDS vaccines: Lessons learned from the world's first phase III efficacy trials' (editorial review) (2003) 17/2 *AIDS* 151.

⁴⁹*Ibid.*

⁵⁰Veljkovic *et al* 'Safety and ethical considerations of AIDS vaccine' (2004) 23 *International Rev of Immunology* 465-486.

vaccine safety. They draw attention to the fact that, initially, the AIDS Research Advisory Committee in the USA commented in their report (on Phase III HIV-1 gp120/160 vaccine trials) that they ‘should not be conducted at this time in this country’.⁵¹ This decision not to conduct Phase III efficacy trials was based on the ‘chance that tested HIV vaccines will compromise the immune system and make the recipient more vulnerable to infection’.⁵² Despite this, ‘an advisory committee to WHO ... recommended that large-scale Phase III of these HIV vaccine candidates should be allowed to proceed in developing countries’.⁵³ This recommendation was based on the argument that ‘the desperate situation posed by the AIDS epidemic justifies acceptance of the so-called “small risks” involved’.⁵⁴

When this specific gp120/160 vaccine later proceeded to Phase III trials in Thailand, the initial fears expressed about its safety were proven justified. Researchers reported that the vaccine ‘acted as a decoy for the immune system ... increasing the likelihood of infection as well as disarming the immune system ... increasing the likelihood of rapid disease progression, which is seen in later-infected vaccinees’.⁵⁵

Another widely used vaccine strategy, also criticised by Veljkovic *et al*, is the use of live recombinant vectors to carry vaccine proteins into the human body.⁵⁶ Veljkovic *et al* express fears that, when combined with HIV-1 gp 120/160, these recombinant vectors can mutate in the human body to cause dangerous infections.⁵⁷ Even if the probability of this happening is very low, it is not nil, posing a grave risk to HIV vaccine trial participants.⁵⁸

Veljkovic *et al* further caution against the use of a VEE vector vaccine, such as the one used in the HVTN 059/AlphaVax vaccine to be tested in South Africa.⁵⁹ They express several reasons for concern about a VEE-based vaccine, not least of which is the fact that, according to reported data, the viral family to which VEE belongs is inherently recombinogenic in nature.⁶⁰ Moreover,

⁵¹*Id* at 466.

⁵²*Ibid.*

⁵³*Ibid.*

⁵⁴*Ibid.*

⁵⁵In this regard, see Locher *et al* ‘Antibody and cellular immune responses in breakthrough infection subjects after HIV type 1 glycoprotein 120 vaccination’ (1999) 71 *AIDS research* 1685.

⁵⁶Veljkovic *et al* n 50 above at 467.

⁵⁷*Id* at 467.

⁵⁸*Ibid.*

⁵⁹See See AVAC n 15 above at 21-25.

⁶⁰Veljkovic *et al* n 50 above at 472, quoting Weaver *et al* ‘A comparison of the nucleotide sequences of eastern and western equine encephalomyelitis viruses with those of other alphaviruses and related RNA viruses’ (1993) 197 *Virology* 375-90 and Rummenapf *et al* ‘Aura

they caution against other viral vectors used in vaccines, such as the herpes simplex virus vector,⁶¹ poxvirus (or vaccinia) vectors⁶² and HIV antigens found in plants.⁶³

The question to be answered is whether Veljkovic *et al* are being overly conservative, even alarmist, advocating caution when everybody else is forging ahead with large-scale preventive HIV trials in high-risk populations, or whether their warnings reflect an element of real danger (however small). At present it is unclear which of the perils they warn against, or the risks outlined above, if any, will materialise during HIV vaccine efficacy trials in Africa. However, it is clear that some of these risks, at least potentially, are very serious – and one of the virologists' warnings has manifested in harm to preventive HIV vaccine trial participants.⁶⁴ Inevitably, this example leads to the conclusion that the risks attendant upon preventive HIV vaccine trial participation in Africa may be more serious than is openly admitted.

Globalisation and clinical research

Clinical research demonstrates international collaboration, for example, multi-centre studies in which clinical trials are conducted in more than one country or if the sponsor is from one country (usually developed) and the principal investigator and trial participants are from another (usually less developed) country. It is likely that at least some HIV vaccine efficacy trials in Africa will be conducted in this way.⁶⁵

International pharmaceutical corporations increasingly conduct clinical trials in the developing world. Africa, in particular, offers large numbers of treatment naïve research participants, making it possible to obtain a speedier result which, in turn, leads to the accelerated approval of new drugs.⁶⁶ Sponsors of clinical research tend to search out the least expensive, least burdensome, regulatory environment with the lowest liability exposure, in order to avoid litigation in the event of injury to participants.⁶⁷ In many countries in Africa, there is little, if any, legislation or even regulation

virus is a New World representative of Sindbis-like viruses' (1995) 208 *Virology* 621-633. 'Recombinogenic', as the term indicates, implies an ability to 'recombine'.

⁶¹Veljkovic *et al* at 472.

⁶²*Id* at 473.

⁶³*Id* at 476.

⁶⁴As described by authors referred to in n 50 above.

⁶⁵In this regard, see AVAC n 15 above at 21-25. A single HIV vaccine has completed Phase III trials (by VaxGen).

⁶⁶Ford and Tomossy (2004) 1 *Law, Social Justice and Global Development* 3.

⁶⁷As above; eg, Malawi, Tanzania and Zambia lack legally binding informed consent procedures (see Meier 'International protection of persons undergoing medical experimentation: Protecting the right of informed consent' (2002) 20 *Berkeley J of International L* 533, fn 124).

governing clinical trials.⁶⁸ Meier writes that ‘African nations vie to minimize regulation on the conduct of medical research. They fear that legislation, and resulting lawsuits, could have a chilling effect on beneficial research efforts’.⁶⁹ Furthermore, in some host countries, ‘corruption often prevents [research ethics committees] from protecting the interests of experimental subjects’.⁷⁰

The potential for exploitation

Often poverty, a lack of resources, gender inequality and a lack of access to health care, are the order of the day in communities with a high incidence of HIV infection. Because of the presence of these factors, such communities are vulnerable to exploitation in research: this is a commonly voiced criticism of clinical research in developing countries..⁷¹ Accusations that African research participants are indeed exploited during clinical research, have been many, amongst others, the Zidovudine (AZT) trials to prevent mother to child transmission of HIV in Uganda;⁷² Pfizer’s Trovan experiments in Nigeria,⁷³ and the Tenofovir trials in Cameroon and Nigeria.⁷⁴ The potential for exploitation in clinical research is heightened in many countries in Africa where there is a lack of access to health care and other resources.⁷⁵

The UN guideline document, ‘Ethical considerations in HIV preventive research’, points out that it is important to identify the *particular* aspects of a social context

⁶⁸Kelleher writes: ‘Because their impoverished governments would otherwise be unable to provide medical treatment to their citizens, host countries – African nations in particular – have no legislative protection for subjects of clinical trials. Researchers in such countries, faced with dire medical conditions, understaffed hospitals, language and cultural barriers, and research subjects who would otherwise have no access to medical treatment, thus find it expedient to violate the minimum ethical standards for the protection of human subjects’ (Kelleher ‘The pharmaceutical industry’s responsibility for protecting human subjects in clinical trials in developing nations’ (2004-2005) 38 *Columbia J on L and Society* 67).

⁶⁹Meier n 57 above at 532.

⁷⁰*Id* at 533.

⁷¹It is certainly not true that communities in which these factors are present are at all times vulnerable to exploitation in research, or that communities which display the opposite characteristics are immune to exploitation. Vulnerability in this context is rather a matter of degree. Because of their characteristics, some communities are more vulnerable to exploitation than others. (Macklin *Double standards in medical research in developing countries* (2004) chs 1, 3 and 4; Resnik ‘Exploitation in biomedical research’ (2003) 24 *Theoretical medicine* 233.)

⁷²See Lurie and Wolfe ‘Unethical trials of interventions to reduce perinatal transmission of the Human Immunodeficiency Virus in developing countries’ (1997) 337 *New England J of Medicine* 853, and Angell ‘The ethics of clinical research in the Third World’ (editorial) (1997) 337 *New England J of Medicine* 847.

⁷³See Carr ‘Pfizer’s epidemic: A need for international regulation of human experimentation in developing countries’ (2003) 35 *Case Western Reserve J of International L* 15.

⁷⁴Mills *et al* ‘Designing research in vulnerable populations: Lessons learnt from HIV prevention trials that stopped early’ (2005) 331 *British Medical J* 1403.

⁷⁵See Nienaber n 12 above at 136-139 and WHO *World Health Statistics 2006* (2006).

that create conditions for exploitation or increased vulnerability for participants. It outlines characteristics which are considered to create the ‘conditions for exploitation or increased vulnerability’.⁷⁶ These are governmental, institutional or social stigmatisation or discrimination on the basis of HIV status;⁷⁷ an inadequate ability to protect HIV-related human rights, and to prevent HIV-related discrimination and stigma, including those arising from participation in a HIV vaccine trial; social as well as legal marginalisation of groups from which participants might be drawn, such as women, intravenous drug users, men who have sex with men and sex workers; the limited availability, accessibility and sustainability of health care and treatment options; the limited capacity of individuals or groups in the community to understand the research and informed consent processes, or be able to give their informed consent freely in the light of prevailing class, gender, and other social and legal factors.⁷⁸

Most, if not all, of these characteristics may be present at potential Phase II and III preventive HIV vaccine efficacy trial sites in Africa: some to a greater extent than others. However, it should be noted that the presence of these characteristics does not altogether rule out the possibility of ethical research taking place – they merely point to the *potential* for exploitation.⁷⁹

Non-state actors and vaccine research in Africa

A regulatory framework for the protection of research participants is established by international ethical guidelines, such as the Nuremberg Code, the Council for International Organizations of Medical Sciences’ International Ethical Guidelines for Biomedical Research involving Human Subjects, and the Declaration of Helsinki.⁸⁰ However, ethical guidelines often fail to protect clinical research participants sufficiently, resulting in their injury and death.⁸¹ In such cases, research participants need to gain access to a forum in which they can hold international pharmaceutical corporations liable for the loss suffered.

Should they wish to bring an action under international law, arguing that the research sponsor or pharmaceutical corporation violated a norm of

⁷⁶UNAIDS at n 25 above.

⁷⁷*Id* at 23-24. See guideline point 7 (and its commentary) of the Declaration of Helsinki (2000 rev) and guideline 13 of the CIOMS guidelines which outline similar characteristics.

⁷⁸*Ibid.*

⁷⁹Ruth Macklin expresses a similar view, see Macklin ‘Bioethics, vulnerability, and protection’ (2003) 17 *Bioethics* 475-477: ‘being vulnerable to exploitation need not result in being exploited’.

⁸⁰See Levine *Ethics and regulation of clinical research* (1986) 12-13; 425-427 for more on the history and promulgation of these codes of ethics.

⁸¹This is mainly due to the fact that international ethical guidelines lack effective enforcement mechanisms. In this regard, see Meier n 67 above at 513 and Nienaber n 12 above at ch 4. Also see Roman ‘US medical research in the developing world: Ignoring Nuremberg’ (2001-2002) 11 *Cornell J of L and Public Policy* 441.

international law, HIV vaccine research participants face serious practical⁸² and procedural difficulties. Court action against Pfizer, brought by Nigerian families who allegedly suffered loss during Pfizer's Trovan research in Nigeria in 1996,⁸³ demonstrates some of these difficulties. The plaintiffs in the case argued that a US court had to hear the case because Pfizer has its headquarters in New York,⁸⁴ and that an action brought in Nigeria would likely be decided against them due to the Nigerian government's complicity in the Trovan trial and the partiality and corruption in the Nigerian courts.⁸⁵

Although the US District Court agreed in September 2002 that it had jurisdiction to hear the case, it exercised its discretion not to do so, requiring the plaintiffs to attempt to sue Pfizer in Nigeria, so granting Pfizer's motion to dismiss the action on the basis of *forum non conveniens*.⁸⁶ In Nigeria, the proceedings were withdrawn⁸⁷ when 'it became clear that they were not likely to get justice in Nigeria after their case was adjourned more than 14 times'.⁸⁸

Even should they overcome difficulties of this nature, wronged HIV vaccine trial participants will still need to demonstrate that the international pharmaceutical corporation responsible for their abuse, is a subject of international law or that it is bound by international law. This obstacle relates to the traditional notion that states and their agents alone are held accountable under international law.⁸⁹

Another forum is open to HIV vaccine trial participants who have been wronged during clinical research: instead of instituting action directly against the international pharmaceutical corporation, they may access the various international human rights treaty monitoring bodies which monitor compliance

⁸²Related to the financial and other resources necessary to institute transnational court actions.

⁸³In this regard, see n 73 and WHO Disease Outbreak News <http://www.who.int/disease-outbreak-news/n1996/feb/n19feb1996c.html> (15 December 2006).

⁸⁴Ford and Tomossy n 66 above at 3; Kelleher n 68 above at 89.

⁸⁵*Ibid.*

⁸⁶*Ibid.*

⁸⁷*Zango v Pfizer* (FHC/K/CS/204/2001) (Kano Federal High Court).

⁸⁸Ford and Tomossy n 66 above at 4, quoting 'News' (2003) 326 *British Medical J* 899. In October 2003, the US Court of Appeals for the Second Circuit vacated the 2002 New York decision on the motion to dismiss and remanded the matter to the District Court to determine whether it was corruption or delay of the sort alleged by the plaintiffs that precipitated the dismissal or withdrawal of the Nigerian action (Ford and Tomossy at 5). In the interim, the Nigerian case once again has been instituted: see 'Nigeria sues drug giant over children's deaths' *Legalbrief Today* (2007-06-05) available at http://www.legalbrief.co.za/index.php?page=Legalbrief_Today (5 June 2007); 'Nigeria sues drug giant for billions' *IOL* (2007-06-04) available at http://www.iol.co.za/index.php?set_id=1&click_id=68&art_id=nw20070604_215319170C882035 (5 June 2007).

⁸⁹This notion is being challenged by claim that many international corporations wield more economic (and hence, political) power than do many states. See eg Muchlinski 'Human rights and multinationals: Is there a problem?' (2001) 77 *International Affairs* 31.

with states' human rights obligations under international law.⁹⁰ The African Charter on Human and Peoples' Rights (African Charter)⁹¹ in article 4 states that 'human beings are inviolable', and that 'every human being shall be entitled to respect for his life and integrity of his person'. Article 5 ensures that every 'person shall have the right to liberty and to the security of his person'. Even though research participation is not mentioned, these two provisions of the African Charter can be utilised in support of the notion that HIV vaccine trial participants give free and informed consent to research participation. Research without such consent violates the integrity and security of the person.⁹²

It is not only informed consent that is at issue. Research which harms the person or which is exploitative can also be regarded as violating the integrity and security of the person. It is submitted that research as in the case of Pfizer in Kano, Nigeria, in which Pfizer treated children for spinal meningitis with the experimental drug Trovan, violates article 5 of the African Charter. At the time the drug was tried in Nigeria, Trovan had never been tested on children, and, earlier that year, had been withdrawn from US markets due to its serious side-effects.⁹³ No matter the urgency, existing, proven medication alone should have been used.

Article 16 provides that 'every individual shall have the right to enjoy the best attainable state of physical and mental health'.⁹⁴ And, state parties are to 'take the necessary measures to protect the health of their people and to ensure that they receive medical attention when they are sick'.⁹⁵ HIV-related clinical research, whether state-sponsored or not, is a measure which aims to protect the health of Africa's people, and, thus, fulfils the duty assigned by this article.

The African Commission on Human and Peoples' Rights (African Commission) is responsible for the implementation of the African Charter.⁹⁶

⁹⁰In the past actions have been brought in the United States against pharmaceutical corporations under the Alien Tort Claims Act 28 USC 1350 (see *Abdullahi v Pfizer* No 01 Civ 8118, 2002 WL 31082956 (SDNY Sept 17 2002)).

⁹¹The African Charter was adopted on 27 June 1981 in Banjul, The Gambia, and entered into force on 21 October 1986. It has been ratified by all 53 member states of the Organization of African Unity (OAU), and functions within the institutional framework of this organisation. In May 2001 the OAU was replaced by the African Union (AU).

⁹²Note that this paper does not deal with other treaties within the African system, such as the African Charter on Rights and Welfare of the Child and the Protocol to the African Charter on Human and Peoples' Rights on the Rights of Women in Africa. In this regard, see Nienaber n 12 above at ch 4 and Nienaber 'The utility of international human rights law on informed consent in the protection of clinical research participants in Africa: "The road less travelled"' (2007) 22 *SAPR/PL* 422.

⁹³See Carr n 73 above at 15.

⁹⁴Art 16(1) African Charter.

⁹⁵Art 16(2) African Charter.

⁹⁶According to art 45(4) of the African Charter it must also perform any other tasks 'which may be entrusted to it by the Assembly of Heads of State and Government'. See also Gumedze

It must promote human (and peoples') rights in Africa,⁹⁷ it must protect these rights,⁹⁸ and it must interpret the provisions of the African Charter.⁹⁹

The following section relies on the jurisprudence of the African Commission to demonstrate that states may be held indirectly accountable for abuses by international pharmaceutical corporations undertaking HIV vaccine trials in Africa.

THE JURISPRUDENCE OF THE AFRICAN COMMISSION ON HUMAN AND PEOPLES' RIGHTS

Despite numerous abuses of the rights of research participants in Africa,¹⁰⁰ no communication related to research participation, or the right not to be subjected to medical experimentation without informed consent, has reached the African Commission on Human and Peoples' Rights.¹⁰¹ Nevertheless, two communications, in particular, are noted, in which the African Commission establishes general principles potentially relevant to the protection of HIV vaccine trial participants in Africa. They are *SERAC v Nigeria*¹⁰² and *Free Legal Assistance Group v Zaire*.¹⁰³

The communication in *SERAC v Nigeria* concerns concerted violation by the Nigerian state of numerous articles of the African Charter, including article 2, 4, 14, 16, 18(1), 21 and 24. These rights were violated by the activities of a (government-controlled) oil company, the Nigerian National Petroleum Company (NNPC), the majority shareholder in a consortium with Shell Petroleum Development Corporation, in an oil-producing part of Nigeria known as Ogoniland. The oil company's activities caused wide-scale contamination, degradation and devastation of the area's air, water and soil resources. For example, numerous oil spills occurred in the proximity of Ogoni villages, with serious consequences for the short and long-term health of the inhabitants, such as respiratory ailments, increased risk of cancers, neurological and reproductive problems.¹⁰⁴

In finding that violations had occurred, the African Commission argues the indivisibility of the different generations of rights, and emphasises that all three generations of rights entail positive and negative duties.¹⁰⁵ Internationally

'HIV/AIDS and human rights: The role of the African Commission on Human and Peoples' Rights' (2004) 4 *African Human Rights L J* 181.

⁹⁷ Arts 30 and 45(1) African Charter.

⁹⁸ Arts 30 and 45(2) African Charter.

⁹⁹ Art 45(3) African Charter.

¹⁰⁰ Touched upon in par II(v) above.

¹⁰¹ Neither has such a communication reached any of the UN bodies.

¹⁰² *Social and Economic Rights Action Centre (SERAC) v Nigeria* (2001) AHRLR 60 (ACHPR 2001).

¹⁰³ *Free Legal Assistance Group v Zaire* (2000) AHRLR 74 (ACHPR 1995).

¹⁰⁴ *Social and Economic Rights Action Centre (SERAC) v Nigeria* at par 2.

¹⁰⁵ *Id* at par 44 (my emphasis).

accepted ideas of the various obligations engendered by human rights indicate that all rights – both civil and political and social and economic – generate at least four levels of duties for a state that undertakes to adhere to a rights regime, namely the duty to *respect, protect, promote* and *fulfil* these rights. These obligations apply universally to all rights and entail a combination of negative and positive duties.

The Commission quotes from various international human rights law precedents¹⁰⁶ and remarks:¹⁰⁷

Governments have a duty to protect their citizens, not only through appropriate legislation and effective enforcement, but also by protecting them from *damaging acts that may be perpetrated by private parties* ... This duty calls for *positive action* on the part of governments in fulfilling their obligation under human rights instruments.

These comments are significant in respect of the position of participants in clinical trials in Africa undertaken by international pharmaceutical corporations. The Commission reiterates that the relevant articles of the African Charter impose an obligation on governments to take (positive) measures (in terms of art 24) to prevent pollution and ecological degradation, to promote conservation, and to ensure an ecologically sustainable development and use of natural resources.¹⁰⁸ By analogy, the other rights in the African Charter, such as in articles 4, 5 and 16, create obligations of this kind on African governments to prevent abuses of research subjects in clinical research, which they can do only if they take proactive measures to ensure these rights.

Further, according to the theory of implied rights, the right to be free from medical experimentation without participants' informed consent may be considered to be implied in the other rights in the African Charter. Therefore, articles 4 and 5 of the African Charter, may be used to support the notion that HIV-related clinical research participants give free and informed consent to research participation: research without such consent violates the integrity and security of the person.

The *SERAC* communication concerned article 21 of the African Charter as well: article 21(1) reads, '[a]ll peoples shall freely dispose of their wealth and natural resources. This right shall be exercised in the exclusive interest of the people ...' Assuming a correspondence in the communication between the violation of this guarantee and the exploitation by colonial powers of Africa's

¹⁰⁶The Commission eg referred to *Velasquez Rodriquez v Honduras* n 3 above and *X and Y v Netherlands* (ECHR).

¹⁰⁷*Social and Economic Rights Action Centre (SERAC) v Nigeria* at par 57 (my emphasis).

¹⁰⁸*Social and Economic Rights Action Centre (SERAC) v Nigeria* at par 52 (my emphasis).

material resources and its peoples, the African Commission found that Nigeria had violated that right by allowing the oil companies to undertake oil explorations in Ogoniland. The Commission claims: 'colonial exploitation has left Africa's precious resources and people still vulnerable to foreign misappropriation'.¹⁰⁹ In the same way, clinical research which exploits its human resources could be regarded as a violation of article 21, as not being in the 'exclusive' interest of Africa's peoples. The Commission adds:¹¹⁰

The drafters of the Charter obviously wanted to remind African governments of the continent's painful legacy and restore co-operative economic development to its traditional place at the heart of African society.

In endeavouring to develop a vaccine for HIV/AIDS, the collaborative effort between international corporations and African researchers and corporations should be mutually beneficial. A collaborative partnership, for example, would be one which offers training and the development of research capacity in under-resourced African counties. A research endeavour to which participants do not give free and informed consent, by definition, is exploitative.

In *Free Legal Assistance Group v Zaire*¹¹¹ the African Commission dealt with a communication resulting from severe violations during a civil war in Chad. The finding, which identifies a duty on the part of the state to 'protect' civilians against violations by non-state actors, is directly relevant to the position of HIV vaccine trial participants. In cases in which a government's own forces are not responsible for the killings committed by other (non-state) actors, it is not absolved of responsibility if it fails to prevent or takes no action to investigate allegations about assassinations and other killings.

The traditional view holds that, in principle, international human rights law binds states alone, as states are the parties to international agreements and, therefore, the conduct of other parties is not within the ambit of international human rights law. However, states have a responsibility to protect the rights of their populations against violations by others. On the finding in the above case, Viljoen comments: 'Going beyond the duty to "respect", the Commission also interpreted rights in the Charter to entail a "positive obligation" to "protect" and "fulfil" ... [the *Free Legal Assistance Group* communication] exemplifies the duty (or 'positive obligation') of the state to "protect" civilians against violations by non-state actors.'¹¹²

It is a matter of urgency that clinical trials be undertaken to find an efficacious vaccine against HIV. Yet, some of the risks of participation in vaccine

¹⁰⁹*Social and Economic Rights Action Centre (SERAC) v Nigeria* at par 56.

¹¹⁰*Ibid.*

¹¹¹Note 103 above.

¹¹²Viljoen *International human rights law in Africa* (2007) forthcoming.

research, potentially, are serious. Many preventive HIV vaccine efficacy trials will involve internationally collaborative research efforts by international pharmaceutical corporations and scientists in host countries in Africa. In many instances, the regulatory frameworks in African countries are inadequate to cope with HIV vaccine trials. Similarly, international ethical guidelines governing clinical research lack effective enforcement measures.¹¹³ Furthermore, aspects of African economic, social and political contexts, such as poverty, women's inequality, stigmatisation and poor access to health care, increase, not only certain communities' vulnerability to HIV infection, thereby accelerating the spread of the disease, but also their vulnerability to exploitation and abuse during HIV vaccine efficacy clinical trials. Because of these factors, the potential exists for the exploitation of participants in HIV vaccine trials.

The African Commission's jurisprudence in the two communications discussed above shows that the African Charter imposes positive obligations on states to act to protect individuals and groups against private actors, including international pharmaceutical corporations. States which ratify the African Charter have a duty to fulfil the rights guaranteed in the Charter. These rights include the right to freedom and security of the person, which can be read as prohibiting indignities committed during clinical trials in Africa.

The failure to act to prevent, investigate or punish human rights abuses committed by non-state actors will result in a finding that the state has failed in its international human rights obligations. Therefore, African states have an indirect accountability in the case of human rights abuses committed by international pharmaceutical corporations. Government compliance with the spirit of articles 4, 5 and 16 of the African Charter includes establishing an appropriate and effective regulatory environment in which HIV vaccine trials take place, so ensuring the safety of participants.

¹¹³In this regard, see Nienaber n 12 above.