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## HIV Vaccine Trial Participation in South Africa – An Ethical Assessment

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### ABSTRACT

Trial participation in the proposed HIV Vaccine Trials in South Africa is discussed in the context of the ethical tension that exists between international ethical research standards and local standards of care and cultural norms in the Third World. The important concepts of informed consent, risk-benefit ratio and fair treatment of trial participants are interpreted differently in traditional, rural African communities, where a moderate form of communitarianism referred to as “*Ubuntu*” or “communalism” is still prevalent. Research is an altruistic endeavor that benefits communities and societies as a result of risks taken by individuals. Universal ethical guidelines that are highly individualistic and fail to emphasize communalism may represent serious problems for the sort of research needed in Africa today.

*Key Words:* Africa, ethics, HIV vaccine trials

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### I. INTRODUCTION

With more than 16,000 new people infected daily throughout the world, HIV/AIDS is clearly an illness of global importance and is a major priority for the world community. An effective preventive HIV vaccine could be a powerful tool in the struggle against the expanding HIV pandemic. However, such a vaccine would have to be tested in clinical trials using human subjects in the absence of a suitable animal model. HIV vaccine trials began 10 years ago in the United States and Europe and are now increasingly being planned and

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implemented in developing countries (Guenter, Esparza, & Macklin, 2000, p. 37).

Recruiting volunteers for these trials is critical to the success of the endeavor, yet it is fraught with scientific, social, political and ethical concerns, especially when the target communities live in the Third World and funding is from affluent countries. The decision to participate in research is likely to be influenced by a wide range of factors. It is critical to determine what information is to be given to potential subjects or guardians to enable them to make an informed decision. A vital component of such patient information is the risk-benefit ratio that determines the ethical acceptability of clinical research. In AIDS vaccine research, however, the half of the equation that deals with risk is “virtually unknown.” There is no data about the potential for risks such as “vaccine-induced immunotoxicity or antibody-induced enhancement of infection” (Tacket & Edelman, 1990, p. 356).

In anticipation of the launch of HIV vaccine trials worldwide, guidelines have been developed to protect the rights of those participating in international vaccine trials. As noted in the Declaration of Helsinki of 2000, “concern for the interest of the individual must always prevail over the interests of science and society.” Accordingly individual informed consent becomes of central importance to investigators and trial sponsors in trying to develop effective vaccines, study the effective use of expensive anti-retroviral treatment, or treat participants in developing countries who become infected during the trials.

The problem inherent in any research is that one must balance the rights of the individual and group benefit, in this case not only societal good but global good. In some cases there can be a conflict between what benefits the individual and what promotes the societal good. Many of the principles of African “Communitarianism” or “*Ubuntu*,” which exists in various forms especially in rural, traditional South African communities, seem to be in stark contrast to the more individualistic principles of the West yet are beginning to be influenced by western individualism (Constitution of the Republic of South Africa 1996, Chapter 2 – Bill of Rights), and this is reflected in the way research is being conducted. This will be illustrated by ethical concerns central to the HIV vaccine trials, and its relevance in the African context will be discussed. Ultimately, the idea that an appeal to “*Ubuntu*” might be our only hope of conducting ethical HIV vaccine trials that will respond to the pandemic of HIV/AIDS in South Africa will be explored.

## II. RESEARCH IN DEVELOPING COMMUNITIES: HIV VACCINE TRIALS AND CONSENT IN THE THIRD WORLD

Some charge that developing communities around the world are sometimes seen as excellent candidates for medical research largely because people in these communities tend to be poor, malnourished, illiterate and desperate. Lurie and Wolfe wrote of earlier HIV vertical transmission trials, “Residents of impoverished, postcolonial countries, the majority of whom are people of color, must be protected from potential exploitation in research. Otherwise, the abominable state of health care in these countries can be used to justify studies that could never pass ethical muster in the sponsoring country” (Lurie & Wolfe – 1997 Public Citizen’s Health Research Group). In the aftermath of these controversial HIV Vertical transmission trials, HIV Vaccine Trials are now emerging as the next major ethical challenge in South African research circles. Basic ethical principles need to be applied, interpreted and specified within different cultural settings (Barry, 1988, p. 1083). The Nuremberg Code and its progeny require that participation in biomedical research be based on “freedom of *individual choice* with no element of coercion or constraint.” This may prove to be a problematical standard in the Third World where *personal choice* is extremely limited, because in many African cultures the concept of personhood differs substantially from that in Western cultures. One’s tribe, village or social group defines personhood. In certain African societies, selfhood cannot be extricated from a dynamic system of social relationships, both of kinship and of community as defined by the village (Barry, 1988, p. 1083). South African philosopher Augustine Shutte, in his work on “*Ubuntu*,” explains that the dominant form of contemporary European thought is materialist in character and a human community is seen as a collection of separate individuals. He refers to this as the “mechanistic theory of society” with the individualist version of this theory underlying liberalism and capitalism. On the other hand, the African concept of personhood differs: persons exist only in relation to other persons. According to him, in all African languages, there is the local variant of the Nguni saying “umuntu ngumuntu ngabantu” – a person is a person through persons. Each individual member of the community sees the community as *themselves*, as one with them in character and identity (unpublished data). Under such circumstances, it is easier for traditional African communities to see research as an altruistic endeavor as opposed to an endeavor for personal benefit only. Similarly, in Ugandan culture, the wishes of the individual are often

subordinated to those of the immediate or extended family. As such, participation of an individual in biomedical research may depend on the acquiescence or consent of another family member (Loue, Okello, & Kawuma, 1996, p. 49). The concept of family consent is not peculiar to Africa alone. It is an important concept in Japanese culture as well. As such, the principle of autonomy, as it exists in its traditional North American paradigm, is not entirely applicable to Japanese culture. Instead, Edmund Pellegrino refers to “something close to autonomy” that is respected in the context of Japanese society (Akabayashi, Fetters, & Elwyn, 1999, pp. 296–301). Similarly, ancient Chinese medical ethics, established on the foundations of Confucian ethics, emphasizes a respectful attitude towards one’s patients based on an unconditional value for human life, but does not include respecting their autonomous choices (Tsai, 1999, pp. 315–321). It is thus clear that where the notion of persons as individuals is not dominant, the consent process may shift from the individual to the family or community (Christakis, 1988, p. 34).

Thus, an investigator seeking informed consent from individual persons in such settings may need to approach community elders for their consent before attempting to obtain informed consent from individual persons (Barry, 1988, p. 1083). The person acknowledged to be a “community leader” would vary from one culture to another and from one investigator to another. In some cases they would need permission to approach individuals to seek their participation. Since the consent of the individual is sought, this would not be incompatible with Western models. What would be incompatible, however, would be where no one needed to ask the individual person because the tribal leader’s authorization was *sufficient* for studies carrying risk. Rather what is typically different in Africa is the need for family consent in addition to individual consent in biomedical research. One might need a waiting period before an informed consent form is signed so this could be discussed with family or elders. Yet this waiting period can often be problematic since it might involve returning to the region, costly transportation and loss of time. Furthermore, the nature of the information regarding the trial may be misrepresented and it is possible that informed consent will not be obtained. However, with no suitable alternatives, a waiting period remains an option when obtaining informed consent in Africa.

In short, it may be a problem to understand who will be giving consent (the person, family or elders) in addition to the sort of review needed in the West. Let us assume, however, that we know this. The next set of problems concerns trying to convey adequate information. During a workshop held in South

Africa to discuss ethical issues in HIV vaccine trials in September 1998, Oliver Ransome, the medical ombudsman, outlined some standard prerequisites for obtaining and documenting informed consent. One should have an information sheet for potential subjects, a third party adviser, and time to reflect as well as the actual written consent. The details on the information sheet should include the overall purpose of the research "in comprehensible language." Confidentiality should be stressed and it should be clear that the subject is free to decline or withdraw. Questions should be invited. However, in South Africa, with very high rates of illiteracy, such a sheet may be inappropriate to use. In a similar workshop in Uganda, it was established that with their currently "high rate of illiteracy, many prospective research participants would be unable to read a form and understand it" (Loue et al., 1996, p. 50). This would also have serious implications for obtaining the "written consent" referred to by Ransome.

Illiteracy coupled with language barriers in Africa make the description of AIDS-related studies difficult. When concepts like germ theory, viruses and vaccines are alien, it is indeed challenging to establish what is sufficient information for informed consent. Ron Bayer (HIV Centre, New York) also expresses concern regarding the explanation of "complicated scientific methods such as randomization, placebos, vaccine inefficiency, the fact that participation in one trial may exclude future participation in trials of more effective vaccines and discrimination linked to participation" (Bayer, 1998, p. 5).

An interesting problem with language was illustrated in the HIV Vertical Transmission Trials conducted on pregnant women in South Africa in 1997. The placebo drug used in these trials was translated as being a "spaza" drug or a "chuff-chuff" drug (Prabhakaran, 1997, p. 5). While a "chuff-chuff" drug is understood to be a "pretend" drug, the word "spaza" is a colloquial term generally meaning "half the real thing" or pretence of the real thing. In no way are they associated with the concept of inertness inherent in a placebo. As such, the use of the term "spaza" to describe a placebo is clearly misleading.

In addition to the problems of supplying adequate information for informed consent, one must also ensure that the potential subject or guardian who gives consent does so voluntarily and competently. These too present problems in the third world where research participants are usually poor, desperate and dependent. Consider problems with voluntariness. Research participants should be able to choose freely amongst alternatives and also have a right to refuse to participate. In a research setting, manipulation rather than

coercion or persuasion tends to occur. In the context of decision-making in health care, informational manipulation tends to be the key form of manipulation employed. Misleading research participants, as in the case of using the word “spaza” to describe a placebo, is a form of deception that is clearly inconsistent with autonomous choice. Attractive offers such as free medication or extra money can leave persons without any meaningful choice apart from accepting the offer largely because such persons are constrained in a desperate situation. Whatever we may decide to call this, it is widely held that offers of this magnitude to a person in desperate need is inherently exploitative and is not consistent with autonomous choice.

In South Africa, it is general research practice that trial participants are paid \$6 per trial visit that is intended to cover costs for transport and meals for the day. Including this amount in the informed consent document is problematic in poor communities where people would consent to such research for half this amount of money. Research methodology and statistical validity may also be adversely influenced by follow-up visits if patients are offered payment for these visits. The development of “side-effects” might be very attractive if one is aware that one will be paid for all “illness visits” to a trial site.

Looking specifically at the ethical design of an AIDS vaccine trial in Africa, Christakis warns researchers that

it is difficult to avoid coercing subjects in most settings where clinical investigation in the developing world is conducted. African subjects with relatively little understanding of medical aspects of research participation, indisposed toward resisting the suggestions of Western doctors, perhaps operating under the mistaken notion that they are being treated, and possibly receiving some ancillary benefits from participation in the research, are very susceptible to coercion. Their vulnerability warrants greater care in procuring consent and necessitates greater sensitivity to protect this class of research subjects. (Christakis, 1988, p. 35)

Research conducted in Durban, South Africa to assess whether informed consent for HIV testing in a South African hospital was truly informed and voluntary yielded interesting results. Of the 56 women studied, 88% felt compelled to participate, even though they were assured that their participation was entirely voluntary. 28% of the women “perceived the research to be integral with the service at the hospital and agreed to the HIV test because they thought that refusal would compromise their care. This subtle coercive

element may stem from the social context of a hospital where the health professionals are held in high regard.” When patients have little recourse to other medical care, they may have no choice but to participate in a research study conducted at the only tertiary hospital at their disposal. It is highly probable that informed consent sought under such circumstances might be “less than voluntary.” This study concluded that “subtle and unexpected elements of coercion can reside in the perceptions (real or imagined) held by patients recruited into a research project in a medical care setting” (Abdool Karrim, Abdool Karrim, Coovadia, & Susser, 1998, p. 640).

A discussion on informed consent would be incomplete without examining the important precondition of competence. In biomedical contexts a person has been viewed as competent if able to understand a therapy or research procedure, to deliberate regarding major risks and benefits, and to make a decision in light of this deliberation (Beauchamp & Childress, 1994, p. 136). The label of “incompetence” has traditionally been applied to children, the mentally retarded, people with major psychiatric illnesses and those with delirium or dementia. Such people are regarded as vulnerable research subjects because they lack capacity to give informed consent and because they depend on others to protect them (Kopelman, 1994, p. 2291). Little attention has been paid to the millions of people in developing countries, like South Africa, who due to poverty, malnutrition and lack of opportunities for education are either illiterate or uneducated. Coupled to this are the constraints of cultural belief systems especially where causation in illness is concerned. To these people, many concepts in science and medicine are alien and they often have to undergo an enormous paradigm shift in order to understand and deliberate about the complexities of Western biomedical research. This group of people also falls into the category of “vulnerable research subjects” because fear, ignorance or pressure may account for their agreement to participate. Too little protection of these subjects risks their exploitation; too much protection risks unjustified paternalism (Kopelman, 1994, p. 2292).

At the risk of the latter charge, I believe that it is highly probable that in many cases of biomedical research in the developing world, subjects, although adult and not mentally impaired or retarded, do not fulfil all the criteria for competence outlined above. Often, subjects do not understand what they have been told about a complicated and foreign research protocol and when they do not understand they are not competent to decide whether to accept or reject their involvement in such a setting. The capacities necessary for such under-

standing include “a memory for words, phrases, ideas and sequences of information.” Furthermore, the

chance nature of the occurrence of risks and benefits highlights the importance of the ability to understand causal relations and the likelihood of various outcomes. Finally, it may be important for patients to be able to understand not only what they are told, but also that they have a critical part to play in the decision-making process. Deficits in attention span, intelligence and memory may detract from these abilities. (Appelbaum & Grisso, 1988, p. 1636)

It is not my intention to suggest that all people from developing communities are incompetent and hence cannot give informed consent to participate in research conducted in the third world. This would deprive such subjects of their decision-making rights and would represent a serious infringement of liberty. Rather, it is possible that a position of “limited competence” exists in many instances.

In the aftermath of the apartheid era in South Africa, many people who are completely competent still relinquish their decision-making rights to authority figures, be they doctors, researchers or both. This is accentuated when researchers and study participants belong to different racial groups and where asymmetrical power relationships, based on the previous apartheid system, exist. Enormous efforts are required on the part of the medical profession and researchers to create the level of understanding necessary to meet the criteria of competence. Coupled with this is a need for empowerment of many patients, who, as a result of decades of oppression, have never learned how to exercise their decision-making rights.

It is evident from this discussion on the procurement of informed consent from prospective participants in HIV vaccine trials that the concept is riddled with intricacies. The precise demands of the principle of autonomy are largely unsettled and remain open to interpretation and specification.

### III. WHAT RISKS WILL BE FACED BY PARTICIPANTS IN AN HIV VACCINE TRIAL?

To begin with, adverse effects of the vaccine itself may occur as with other vaccines in current use, such as pain or infection at the injection site, fever or



allergic reactions. A study conducted in Thailand among high-risk populations to assess willingness to participate in AIDS vaccine trials found that vaccine side effects were considered to be important barriers to trial participation (Celentano et al., 1995, p. 1079).

More specifically, with an HIV vaccine, participants are likely to be concerned about actually developing HIV disease from the vaccine. With the current use of genetically altered or killed viruses, this risk is unlikely. The current subunit vaccine candidates, which employ genetically engineered proteins from the HIV envelope – with a piece of the virus being used – are likely to allay much anxiety (Jonston, 1998, p. 1). However, participants' fears are likely to magnify as vaccine developers incorporate the use of whole killed or live attenuated virus. Already, scientists are becoming impatient to test live attenuated virus vaccines! However, leading clinicians are still hesitant regarding the safety of such vaccines. The majority opinion at present is that “there is just not enough evidence that a live-attenuated HIV-1 vaccine is safe-or effective” (McCarthy, 1997, p. 1082).

Even with current genetically engineered vaccines, while it is possible that disease will be prevented, infection might still occur. Few of the candidate HIV vaccines appear promising for preventing infection, and the expectation that HIV vaccines will in fact prevent infection is yielding, in the scientific community, to the hope that they may prevent disease (Bloom, 1998, p. 186). In reality, when the first AIDS vaccine trials were launched in the United States and Thailand in 1998, using the HIV envelope protein gp120 in a vaccine called AIDSVAX, two outcome measures were to be assessed: “infection by HIV and viral load in those infected.”

Furthermore, the possibility of vaccine failure is very real and the occurrence of “breakthrough HIV infections” or disease cannot be excluded. This particular risk to the subject needs to be assessed in the context of the different types of trials that are performed. It is reasonable to assume that the risk of developing HIV infection during the course of phase 1 or 2 trials by low risk participants will be far greater than the risk taken by people entering phase 3 trials, already at high risk by virtue of lifestyle or other predisposing factors (Jenkins, Temoshok, & Virochsiri, 1995, p. 171). Where the HIV vaccine is concerned, in South Africa, phase 1 and 2 trials will have to be conducted here as these vaccines are specifically directed against the clade C virus.

Researchers will have an obligation to provide anti-retroviral treatment to subjects who become infected during the course of the trials. Scientists and researchers are concerned that treatment with anti-retroviral drugs will

compromise the ability of the trial to measure the efficacy of the vaccine in preventing disease (Bloom, 1998, p. 186). A critical measure of the success of an AIDS vaccine trial would be whether the vaccine lowers the “viral load” in people who get infected. Anti-retroviral treatment will also lower the viral load. If many of the participants who become infected begin taking potent anti-retroviral drugs, reduction in viral loads due to the vaccine cannot be assessed. Scientists fear that it will become impossible to design a “scientifically valid” trial if there is widespread use of anti-retroviral drugs. The head of the biotech company VaxGen, that launched the first efficacy trials of an AIDS vaccine in the United States, argued that not everyone would start treatment immediately, and because researchers would be taking blood from participants every 24 weeks or so, they should be able to make at least one viral load measurement in many untreated people who become infected (Cohen, 1998, p. 22). Delaying drug treatment until viral loads can be measured, as is implicit in the trial design by VaxGen, however, only adds to the complex ethical problems already inherent in treating participants who develop HIV infection during the trials. This delay in treatment will pose problems in the developed world where it will be ethically required that individuals in vaccine trials who have acquired HIV infection will be offered anti-retroviral therapy as soon as possible. A delay in treatment will not be tolerated in the West. The standard of care in the developing world is clearly “no treatment for HIV/AIDS.” This will also obviate the ethical dilemma of delaying treatment to measure viral load.

The question of the duty to treat trial participants with anti-retroviral drugs if they develop infection during the trials remains largely unanswered. During a workshop in South Africa in 1998, the issue was skirted, stating that this issue would be left up to the host country to decide. An idea of what is likely to happen in South Africa may be extrapolated from the Thai trial funded by VaxGen, where neither the company nor the cash-strapped Thai government plans to give treatment to people who become infected (Cohen, 1998, p. 23).

Various “social harms” may burden participants in a vaccine trial. Participants might be identified as high risk for AIDS, or might be mistakenly assumed to have AIDS. A Thai study has shown that 24–49% of participants believed that their partners would refuse to have sex with them after immunization (Celentano et al., 1995, p. 1079). Discrimination based on HIV antibody status may occur in a number of settings – acceptance into the military, the job corps, the peace corps or the foreign service; the purchase of insurance; permission to immigrate or travel abroad or incarceration (Hodel, 1994,

p. 256). While it is possible to distinguish between HIV positive results from a vaccine as opposed to natural infection, many potential participants and others might be unaware of this. Testing HIV positive after the vaccine will be perceived as a significant risk.

The possibility of being included in a control group in the trial, where a placebo will be used instead of the HIV vaccine, will create further problems. Researchers in Philadelphia have already reported that interest in participating in a vaccine trial dropped from 47% to 24% when the possibility of using a placebo was mentioned (Jenkins et al., 1995, p. 37).

Finally, a further risk inherent in an HIV vaccine trial is the possibility of increased risk-taking behavior by participants who mistakenly believe that they have been protected by the vaccine.

#### IV. WHAT ARE THE BENEFITS, IF ANY, TO TRIAL PARTICIPATION?

As scientists weigh the potential benefits of conducting a trial against the potential risks, so too will individual participants and target communities weigh relevant data before deciding to participate. This risk-benefit calculus will ultimately be informed by social values. This is of special relevance to the Third World where in communities already

burdened by violence, drugs, alcohol, unemployment, urban decay and the like, the AIDS epidemic has merely exacerbated an already arduous burden of day-to-day survival. For many inner city residents the threat of random gunfire easily exceeds the somewhat less immediate threat of HIV infection, a risk profile that is difficult for outsiders to appreciate. (Hodel, 1994, p. 255)

This sentiment is echoed by South African social anthropologist, Virginia van der Vliet:

Increasingly, those affected are the poor in urban ghettos, illegal migrants, drug users, street children, prostitutes, or the impoverished people in Third World countries. They are not unacquainted with the savagery of life. For them, AIDS is just an additional problem, often faced with their customary fatalism. Fatalism is no protection against AIDS. (1996, pp. 77–78)

It is against this backdrop of fatalism that one needs to assess whether the development of a protective vaccine against AIDS will be perceived to be of overwhelming benefit to the Third World.

Subjects may be motivated to join a trial either on altruistic grounds or on grounds of personal benefit. A few studies have been conducted to date to assess the motivation of people to participate in trials. In one such study in Thailand, purely altruistic motives were unrelated to willingness to participate (Jenkins et al., 1995, pp. 40–41). Similarly, in another survey of 2180 Thai people, 62% found that the principal inducement to join a trial was health insurance (Celentano et al., 1995, pp. 1079–1082).

Where HIV vaccine trials are concerned, the risk-benefit ratio is situated in a rather precarious position. Participants have little to benefit personally from such trials and potentially much to lose! In a French vaccine trial, only 57 of 645 persons who had expressed initial interest by mail actually enrolled in the trial. Other surveys have found that under the relatively hypothetical condition of being asked to join a phase 2 or 3 HIV vaccine trial, levels of willingness have ranged from 37% to 84% (Jenkins et al., 1995, p. 37).

Studies that have gone beyond asking the simple question of whether participants would be willing to join a trial have found that interest dropped dramatically when specific trial features or procedures were explained. Research on intravenous drug users in the New York City area found that the percentage of “very interested” potential volunteers dropped from 50% to 17% after they received information normally contained in a consent form. Another study found that 73% of those approached in Baltimore were interested in participation, although this figure dropped to 49% after the issue of testing HIV antibody-positive as a consequence of immunologic response to the vaccine was discussed (Jenkins et al., 1995, p. 37). Both studies were conducted on people at high risk to develop HIV infection!

Interestingly, studies are also finding that willingness to participate in these trials is associated with lower levels of education. In a Thailand study of 255 participants, high school-educated respondents were more willing to participate than university graduates (Jenkins et al., 1995, p. 39). One wonders whether this choice not to participate by more educated respondents is not the result of a more accurate appreciation of the risk-benefit ratio inherent in these trials, namely the high risk-low benefit scenario.

Given full details of the risks and benefits of an HIV vaccine trial, participants will either exercise their right of refusal to participate or will agree to participate only if the benefit is maximized in terms of personal

incentives, in particular, health care, in the developing world. A crucial factor to be considered is that in order for the benefits to outweigh the risks in the trial of an HIV vaccine, an individual would have to be at some risk of HIV infection. The necessity of being at risk therefore has scientific and ethical import.

## V. JUSTICE, CONSENT AND THE HIV/AIDS PANDEMIC

The principle of justice or fairness requires that the benefits and the burdens of research be equitably distributed among individuals or communities. No single group can be required to bear a disproportionate share of the risk or be favored with a disproportionate share of the benefits (Loue et al., 1996, p. 51). Under the principle of justice, research subjects should be chosen “for reasons directly related to the problem being studied,” and not “because of their easy availability, their compromised position, or their manipulability.” As a result, the “practical concerns that make an AIDS vaccine trial easier to conduct in Africa do not alone constitute sufficient justification to use Africans as subjects. Only the scientific concerns related directly to the problem of establishing the ability of a vaccine to prevent HIV infection are relevant” (Christakis, 1988, p. 36).

Where HIV/AIDS is concerned, it is evident that this disease is rampant in Africa. As a result, it may be unavoidable that a higher degree of research risk is tolerated in order to deal with the problem and this may even be socially sanctioned. However, this does not mean that Westerners should “indiscriminately benefit from research conducted in Africa if Africans are systematically subjected to excess research risks with the prospect of deriving but little benefit” (Christakis, 1988, p. 36).

Obviously, however, the entire world stands to gain from the development of an effective vaccine. In keeping with the principle of justice, those who stand to benefit from the vaccine should also bear the burden. Hence, the research risks should be fairly distributed as should the benefits. Vaccine development trials need not be restricted to the African continent. In Africa, economic constraints may prevent adequate distribution of such a vaccine. The benefits to Africans are thus “only hypothetical unless there is a financial commitment by the developed world to provide the vaccine. In this light, it would be frankly unethical to subject Africans to a disproportionate share of the research risks” (Christakis, 1988, p. 36).

CIOMS Guideline 15 on Externally Sponsored Research requires that any trial “must be responsive to the health needs of the host country. . . . Any product developed through such research (should) be made reasonably available to the inhabitants of the host community or country at completion of successful testing” (Bloom, 1998, pp. 186–187). This is also a requirement of the latest version of the Declaration of Helsinki (October 2000).

A contingency of any trial of an AIDS vaccine in Africa by Western scientists should thus be to provide access to the technology once it is developed – possibly in the form of free or subsidized vaccine (Christakis, 1988, p. 36).

In South Africa, this well established principle has been violated. In 2001, four years after the completion of trials in which shorter courses of anti-retroviral treatment for HIV infected pregnant women were found to be effective, millions of eligible women still go without treatment. Anti-retroviral treatment has been recently and selectively introduced at a few antenatal clinics only in South Africa (Dr. Mark Cotton, pediatrician, Tygerberg Hospital, South Africa – personal communication).

In a paper published in the *American Journal of Public Health*, this issue is discussed openly. The outcome of the trials performed on impoverished populations around the world was clearly not the delivery of the necessary drugs to these developing countries. Instead, the purpose was “to provide information that the host country can use to make a sound judgement about the appropriateness and financial feasibility of providing the intervention” (Annas & Grodin, 1998, p. 561). Good intent in the absence of a sound plan to provide the intervention, once proven to be effective, is no justification for the performance of such research. Annas and Grodin go on to say that

Unless the intervention being tested will actually be made available to the impoverished populations that are being used as research subjects, developed countries are simply exploiting them in order to quickly use the knowledge gained from the clinical trials for the developed countries’ own benefit. If the research reveals regimens of equal efficacy at less cost, these regimens will surely be implemented in the developed world. If the research reveals the regimens to be less efficacious, these results will be added to the scientific literature, and the developed world will not conduct these studies. (1998, p. 561)

Once again, with the proposed vaccine trials, South Africa has not clarified that it will only conduct these trials on condition that a definite plan is in place

to acquire the vaccine for widespread use, if it proves to be effective. Of note, however, is the fact that South Africa has decided not to conduct trials using a clade B vaccine that has already been developed in the United States. This viral subtype is not common in sub-Saharan Africa but it is the predominant clade in North America where homosexual transmission of HIV is common. In South Africa, with a predominantly heterosexual transmission of disease, the predominant subtype is clade C. South African researchers have opted to develop an appropriate clade C vaccine for experimentation here (Makgoba, 1998, p. 10).

Yet another way in which subjects could be exploited for research and the principle of justice violated involves encouraging trial participants to continue practicing other preventative measures after the vaccine has been administered. It will be difficult to assess vaccine efficacy if they suddenly change their habits. These interventions could diminish the ability of the study to detect a difference between true vaccine recipients and controls by decreasing the incidence of HIV infection in all participants for reasons unrelated to vaccine status (Christakis, 1988, p. 34). On the other hand, failing to stress these preventative measures could result in a greater risk of contracting HIV infection, especially if the vaccine proves to be ineffective. To circumvent this problem, a larger study group would be required to detect the relatively smaller measured influence of the vaccine. As a result, more individuals will be exposed to the experimental vaccine and the cost of the trials will be higher. It will also take longer to get statistically significant results. To prevent this potential harm to participants and in all fairness to them, it is imperative that researchers continue to promote preventative measures.

## VI. TRIAL PARTICIPATION – THE TENSION BETWEEN LIBERALISM AND COMMUNITARIANISM

Research guidelines and principles that guide human investigation need to be interpreted and applied within different cultural settings. As Beauchamp and Childress note,

making respect for autonomy a trump moral principle, rather than one moral principle in a system of principles, gives it an excessive value. . . In many clinical circumstances the weight of respect for autonomy is minimal, and the weight of nonmaleficence or beneficence is maximal.

Similarly, in public policy, the demands of justice can easily outweigh the demands of respect for autonomy. (1994, p. 181)

There are, of course, tensions once one agrees that the principles of beneficence, non-maleficence, justice and autonomy have no one ranking. This is true in Africa when we consider morally justified research.

In South Africa, as we emerge from a history where the rights of the vulnerable and poor have been negated in the service of apartheid, the preference for a subject-oriented view, where research is concerned, is a logical choice. Our new democratic order, our Constitution and Bill of Rights bear testimony to individual rights. Yet the importance of the needs of the community cannot be ignored. Medical research is seen as one of the essential goods in a society and is therefore vital to the survival of such a society (Ackerman & Strong, 1989, pp. 166–179). Christakis comments that an African might find it “difficult to see how the interests of the subject conflict with the interests of the society except, of course, if the society is not his own.” In traditional Africa, in keeping with the concept of “*Ubuntu*,” the interests of the subject and of society are necessarily congruent. People see themselves as “potential persons” who become fully human to the extent that they are included in relationships with others (Shutte – unpublished data).

Scientifically, South Africa is an ideal site for HIV vaccine research. Yet, the HIV Vaccine Trials pose a grave and significant risk to the individual who may subsequently have little to gain. Under such circumstances, statistically significant trial participation can only be ensured by an appeal to altruism – “*Ubuntu*” in the African context. In this regard, the interests of science and society are seen as one with the interests of the individual. Interdependence and connectedness is a prominent feature of traditional African society. In such a setting, trial participation and hence medical research will be possible. Appeals to “*Ubuntu*” will be difficult since liberalism and notions of personal rights are becoming entrenched in Africa. In rural Africa, an appeal to “*Ubuntu*” could succeed in harnessing trial participation. However, in the developed areas of Africa, where individualism is spreading, this will not be possible.

## VII. CONCLUSION

Ethical principles and research guidelines try to balance individual rights with the good of the community. Ethical principles and research guidelines must be



adapted and applied to the community in which the research will be done, taking account of their traditions and honoring their practices. Affluent countries cannot presuppose that they understand how the concept of informed consent should be understood. If the principles which underpin the 2000 version of the Declaration of Helsinki are strictly adhered to, constraints on the rights of the individual will be impermissible and in the Third World, this would render research unethical and hence, impossible. The global population is not homogenous, and universality “obscures and obliterates the particularity and specificity of morality which is grounded in communal traditions” (Bernstein, 1982, p.137). It is therefore unnecessary for “every country to follow the practice of autonomy in all of its details in a fashion identical to that found in North America” (Akabayashi, Fetters, & Elwyn, 1999, p. 299). We need to “take into account local customs and traditions that should be respected and incorporated into the research process” as far as is possible (Loue et al., 1996, p. 51). Culturally relevant ethical issues need to be incorporated into existing frameworks to augment them with cultural sensitivity. However, changing the rules from time to time and from place to place to achieve the research aims of the West will be both unjustifiable and morally reprehensible.

Undoubtedly, the HIV Vaccine Trials in South Africa will pose a major ethical challenge to all involved. We must, however, be wary that in our haste to develop and test an HIV vaccine, we do not cause an ethical catastrophe that we will never be able to justify. It has taken a long time for the research community to recover from Tuskegee. May we never tread along that path again!

## REFERENCES

- Abdool Karim, Q., Abdool Karim, S.S., Coovadia, H.M., & Susser, M. (1998). Informed consent for HIV testing in a South African hospital: Is it truly informed and truly voluntary? *American Journal of Public Health*, 88(4), 637–640.
- Ackerman, T.F., & Strong, C. (1989). *A casebook of medical ethics*. New York: Oxford University Press.
- Akabayashi, A., Fetters, M.D., & Elwyn, T.S. (1999). Family consent, communication, and advance directives for cancer disclosure: A Japanese case and discussion. *Journal of Medical Ethics*, 25, 296–301.
- Annas, G.J., & Grodin, M.A. (1998). Human rights and maternal-fetal HIV transmission prevention trials in Africa. *American Journal of Public Health*, 88(4), 560–562.
- Appelbaum, P.S., & Grisso, T. (1988). Assessing patients’ capacities to consent to treatment. *The New England Journal of Medicine*, 319(25), 1635–1636.

- Barry, M. (1988). Ethical considerations of human investigation in developing countries: The AIDS dilemma. *The New England Journal of Medicine*, 319(16), 1083–1085.
- Bayer, R. (1998). What is informed consent? *Workshop on ethical issues in the conduct of HIV vaccine trials*. Durban, South Africa.
- Beauchamp, T.L., & Childress, J.F. (1994). *Principles of biomedical ethics* (4th ed.). New York: Oxford University Press.
- Bernstein, R.J. (1986). Nietzsche or Aristotle? Reflections on Alasdair MacIntyre's *After Virtue*. In: R.J. Bernstein (Ed.), *Philosophical profiles. Essays in a pragmatic mode*. Oxford: Basil Blackwell (Polity Press).
- Bloom, B.R. (1998). The highest attainable standard: Ethical issues in AIDS vaccines. *Science*, 279, 186–187.
- Celentano, D.D., Beyrer, C., Natpratan, C., Eiumtrakul, S., Sussman, L., Renzullo, P.O., Khamboonruang, C., & Nelson, K.E. (1995). Willingness to participate in AIDS vaccine trials among high-risk populations in northern Thailand. *AIDS*, 9, 1079–1083.
- Christakis, N.A. (1988, June/July). The ethical design of an AIDS vaccine trial in Africa. *Hastings Center Report*, 31–37.
- Cohen, J. (1998). No consensus on rules for AIDS vaccine trials. *Science*, 281, 22–23.
- Constitution of the Republic of South Africa. (1996). As adopted on 8 May 1996 and amended on 11 October 1996 by the Constitutional Assembly. Act 108 of 1996. Chapter 2 – Bill of Rights.
- Guenter, D., Esparza, J., & Macklin, R. (2000). Ethical considerations in international HIV vaccine trials: Summary of a consultative process conducted by the Joint United Nations Programme on HIV/AIDS (UNAIDS). *Journal of Medical Ethics*, 26, 37–43.
- Hodel, D. (1994). HIV preventive vaccine efficacy trials in the United States: An overview of target communities' concerns. *AIDS Research and Human Retroviruses*, 10(2), 255.
- Jenkins, R.A., Temoshok, L.R., & Virochsiri, K. (1995). Incentives and disincentives to participate in prophylactic HIV vaccine research. *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology*, 9, 36–42.
- Kopelman, L.M. (1994). Research policy/ III. Risk and vulnerable groups. *Encyclopedia of Bioethics* (2nd ed.). New York: Macmillan Free Press.
- Loue, S., Okello, D., & Kawuma, M. (1996). Research bioethics in the Ugandan context: A program summary. *Journal of Law, Medicine & Ethics*, 24, 47–53.
- Lurie, P., & Wolfe, S.M. (1997). Unethical trials of interventions to reduce perinatal transmission of the human immunodeficiency virus in developing countries. *The New England Journal of Medicine*, 337(12), 853–855.
- Makgoba, W. (1998). Should South Africa embark on clade B vaccine trials? *Workshop on ethical issues in the conduct of HIV vaccine trials*. Durban, South Africa.
- McCarthy, M. (1997). AIDS doctors push for live-virus vaccine trials. *The Lancet*, 350, 1082.
- Prabhakaran, S. (1997, October 3–9). Mothers give support to placebo trials. *Mail & Guardian*, 5.
- Ransome, O. (1998). What is informed consent? *Workshop on the ethical issues in the conduct of HIV vaccine trials*. Durban, South Africa.
- Shutte, A. *Ubuntu. The African vision*. Chapter Two. Unpublished book.
- Tacket, C.O., & Edelman, R. (1990). Ethical issues involving volunteers in AIDS vaccine trials. *The Journal of Infectious Diseases*, 161, 356.
- Tsai, D.F. (1999). Ancient Chinese medical ethics and the four principles of biomedical ethics. *Journal of Medical Ethics*, 25, 315–321.

- Van der Vliet, V. (1996). *The Politics of AIDS*. London: Bowerdean Publishing Company Limited.
- World Medical Association (2000). *Declaration of Helsinki*. Ethical Principles for Medical Research Involving Research Subjects Adopted by the 18th WMA General Assembly Helsinki, Finland, June 1964 and amended by the 52nd WMA General Assembly, Edinburgh, Scotland, October 2000.