

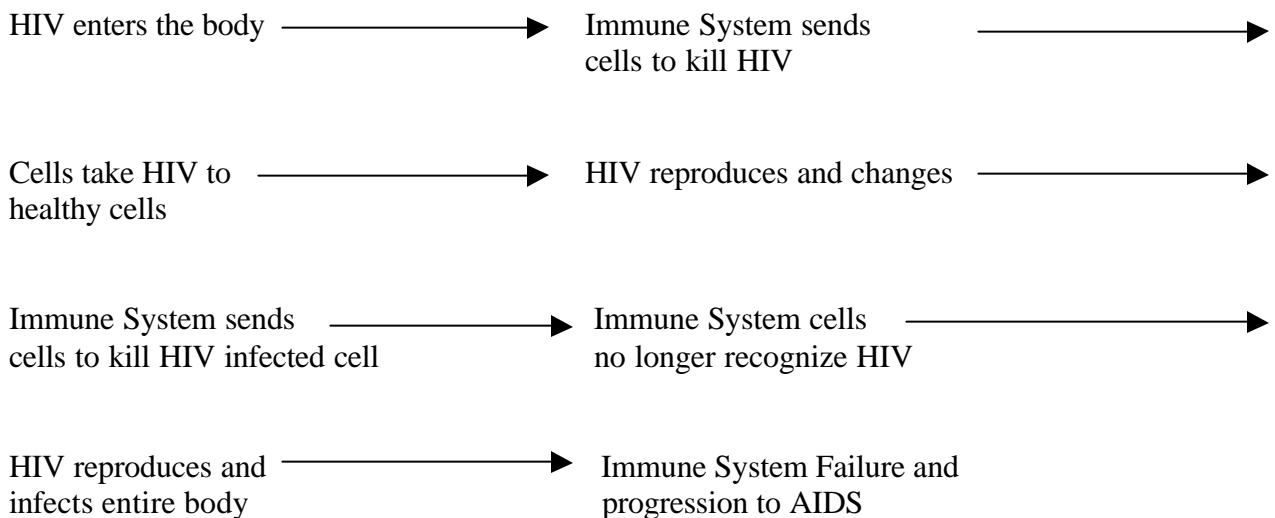
**GOOD ENOUGH TO USE FOR RESEARCH, BUT NOT GOOD ENOUGH TO BENEFIT FROM THE RESULTS OF THAT RESEARCH: ARE THE CLINICAL HIV VACCINE TRIALS IN AFRICA UNJUST?**

**I. Introduction**

A. What is HIV?

The HIV virus works by destroying an individual's immune system. HIV is contained in blood and certain bodily fluids. The most prevalent methods of infection are sharing needles or having unprotected sex with infected individuals. There are various different types of HIV because of the way HIV reproduces it changes rapidly, but suffice it to say that the type of HIV prevalent in the United States is different than the type in Africa. The progression of HIV is summarized in Chart 1 below.

**CHART 1: PROGRESSION OF HIV INFECTION**



B. Pandemic of HIV in Sub-Saharan Africa

Sub-Saharan Africa<sup>1</sup> is the region most affected by the HIV pandemic and where HIV is the leading cause of death. In fact, out of the 36.1 million HIV infections

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<sup>1</sup> Sub-Saharan Africa includes all of the countries of Africa except eight. The countries not included in Sub-Saharan Africa are the Western Sahara, Morocco, Algeria, Tunisia, Libya, Egypt, Sudan, and Eritrea. See University of California, San Francisco School of Medicine, The Center for HIV Information, Sub-Saharan Africa Map (2003), at <http://hivinsite.ucsf.edu> (last visited Feb. 4, 2004).

worldwide, 25.3 million, seventy-percent, are in Sub-Saharan Africa. Due to the significant number of Africans infected with HIV, many researchers and ethicists have focused their attention on granting Africa fair opportunity to have access to clinical HIV vaccine trials. But fair opportunity to participate in clinical HIV vaccine trials does not guarantee that Africans will benefit from the research because of the very nature of clinical trials.

### C. Clinical Trials

A clinical trial consists of a research study that uses human subjects to evaluate the efficacy of new drugs and treatments. The purpose of clinical trials is to develop new treatments to prevent or treat diseases. Although trials offer the prospect of benefits for the individuals participating in the trials, in reality many subjects do not receive a net benefit because the new drugs and treatments have unknown side effects and dangers. Rather, the benefit is to society. In an attempt to protect the lives of individuals participating in these trials, the United States and other nations developed ethical principles applicable to clinical trials. The three fundamental ethical principles are: Respect of Persons, Beneficence, and Justice. I will focus exclusively on the Justice Principle.

## II. **Justice**

Beginning in 1945, various organizations adopted codes of ethics for the protection of human research subjects. The most influential codes are the *Nuremberg Code*, the *Declaration of Helsinki*, and the United Nation's *Declaration of Human Rights*. In the United States, the requirements governing the protection of human subjects were codified in the Code of Federal Regulations in 1974 and later revisited in 1979 in the *Belmont Report*.

The broad doctrine of Justice has a limited application to clinical trials and is only found in the *Declaration of Helsinki* and the *Belmont Report*. According to these documents, Justice demands that the "society" that benefits from the results of the study must include individuals similar to those who participate in the study. In this context,

Justice addresses issues of a population's right to be treated equally, while Respect of Persons and Beneficence address the rights of individuals.

A. Helsinki Declaration (<http://www.wma.net/e/policy/b3.htm>) =>

The *Declaration of Helsinki*, drafted and adopted in 1964 by the World Medical Association, is a statement of ethical standards that were designed as a guide to physicians and others participating in medical research involving human subjects, in addition to the responsibilities imposed by their own countries. The *Declaration of Helsinki* states that, “[M]edical research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the results of the research.” Hence, the Justice principle should be used by researchers in evaluating who should participate in clinical trials by first identifying those populations that will benefit from the results of the trials. If the population will not benefit from the results of the research, then the researcher must choose subjects from another population. The incorporation of the Justice principle into one of the premier international documents regarding human rights and clinical trials demonstrates clearly the importance of the principle in protecting research subjects across the world. Unfortunately, the *Declaration of Helsinki* is not compulsory.

B. Belmont Report (The Belmont Report, 44 Fed. Reg. 23,192)

In the early 1970s, the U.S. Senate Committee on Labor and Human Resources held hearings on some of America's most egregious clinical trials, such as the Tuskegee Syphilis Study conducted from 1932 to 1972, in which poor African American men were denied access to standard treatment.<sup>2</sup> As a result of the hearings, Congress enacted the National Research Act of 1974, requiring the U.S. Department of Health, Education, and Welfare to develop and publish policies for the protection of human subjects in the Code of Federal Regulations and created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (Commission).

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<sup>2</sup> See generally, JAMES H. JONES, *BAD BLOOD: THE TUSKEGEE SYPHILIS EXPERIMENT* (1981).

The Commission drafted the *Belmont Report*, which was printed in the Federal Register in 1979, codified in 1986 in the Code of Federal Regulations, and now applies to all government research. According to the *Belmont Report*, Justice demands that all individuals be treated equally and that development of therapeutic devices and procedures provide equal advantages to the poor and the rich. The Justice principle prohibits the use of vulnerable populations as research subjects when the recipients of the benefits of the research are the rich. Thus, whenever research supported by public funds leads to the development of therapeutic devices and procedures, such research should not unduly involve vulnerable persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.

The United States has made a conscious effort to enforce these Justice requirements to prevent the manipulation and exploitation of vulnerable individuals in the United States; however, the application of this principle to studies funded and conducted by Americans in foreign countries has been negligible at best. Thus, one must ask what is the justification for making the Justice requirements relative to the location of the research, rather than the source of the funding and researcher? This question of ethical relativism is of great significance with respect to HIV vaccine trials because the scientific challenges of developing a vaccine for this genetically diverse disease make the Justice question even more difficult harder to answer.

### **III. Current HIV vaccine trials**

The purpose of clinical HIV vaccine trials is to develop a vaccine that will either prevent the disease, as in the case of the smallpox vaccine, or slow the progression of the disease, as is the case of the flu vaccine. To develop an effective HIV vaccine through clinical trials, researchers must complete three phases. Phase I is conducted using a small number of subjects to obtain information regarding the safety and effect of the candidate vaccine on human subjects. Information regarding the immune system's response to the subject, the effect of the vaccine on different populations, and the effect of different doses on the population is gathered from several hundred subjects in Phase II trials. Phase III, the final phase of vaccine clinical trials before the vaccine is patented or discarded, is used by researchers to determine the efficacy of the vaccine for preventing the disease by

following several thousand subjects. Under each phase of the trials, subjects are given a number of vaccine doses and then tested for HIV several months later. Currently, there are three phase I HIV vaccine trials being conducted in African countries: Botswana, South Africa, and Uganda.

A. Types of HIV vaccines being tested

There are many types of HIV vaccine being tested, but they can be separated into two main categories: prophylactic and therapeutic. A prophylactic vaccine will prevent HIV infection, while a therapeutic vaccine only delays or prevents progression of HIV to AIDS. Thus, if a prophylactic vaccine is developed individuals will only need to receive a number of shots but no other treatment to address HIV infection or AIDS. However, if a therapeutic vaccine is used individuals will need a number of shots plus access to HIV retroviral drugs.

B. The Structure of the clinical trials being conducted

1. **Botswana trial** => Funded by the U.S. government, the trial is using a vaccine based on a combination of the infection most prevalent in the United States and in Botswana but there is no guarantee of benefit
2. **South Africa** => Funded by the U.S. government, the trial is using vaccine based on a type of HIV infection prevalent in Africa but there is no guarantee of benefit
3. **Uganda** => Funded by a private company, the trial is using vaccine based on a type of HIV infection prevalent in Africa & agreement of access to drug

C. Justice

1. *What benefit must be bestowed upon the citizens of United States?*

Americans will benefit from HIV vaccine trials gaining gain access to an effective vaccine regardless of whether the vaccine is prophylactic or therapeutic because the United States has the health infrastructure to deliver either vaccine. Most vulnerable Americans will have access to the vaccine through Medicaid or through prison health programs. Moreover, because of the astronomical costs of providing retroviral drugs to people infected with HIV, many insurance companies may opt to pay for the vaccine to

save money. Thus, it seems that the Justice principle's requirement of fair access is met in the United States.

*What benefit must be bestowed upon the citizens of Africa?* The benefit to these African countries participating in the three HIV vaccine trials is the development of a vaccine that will prevent new HIV infections or decrease the number of deaths from AIDS. However, unlike the United States it is questionable whether the countries will be able to afford the vaccine. Researchers scoff at the requirement to provide individuals similar to those who participated in the research study access to the drug or vaccine when conducting research in countries that cannot afford the drugs or treatment.<sup>3</sup> Yet, there is no mention of a cost limitation to the principle of Justice in the Belmont Report. But is this realistic?

If a researcher cannot factor in a cost limitation in the provision of a benefit, will they continue to conduct research in Africa and other developing countries or simply stay in the United States? This depends on what constitutes a benefit to the population being studied. Does use of a drug constitute a benefit when the country's infrastructure is ill-equipped to deliver the drug to its citizens? It is undoubtedly clear that the benefit from trials conducted in the United States is the development of an effective HIV vaccine in the United States. However, because most African countries cannot afford and do not have the infrastructure to provide quality health care, is the development of a vaccine enough of a benefit to Africans to make the clinical trials in Africa ethical? Are researchers required to provide access to the vaccine in Africa as well as create the necessary infrastructure to distribute the vaccine, when this is not a requirement in the United States? Although researchers have been wrestling with these issues for decades, there is no consensus on how to address these ethical issues.

#### **IV. Conclusion**

The purpose of the HIV vaccine trials is to develop a vaccine that will prevent new HIV infections. To accomplish this end, researchers must find willing participants

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<sup>3</sup> Harold Varmus and David Satcher; *Ethical Complexities of Conducting Research in Developing Countries*, 337(14) NEW ENG. J. OF MED. 1003, 1003-4 (1997).

who will sacrifice their lives for the betterment of society. Furthermore, Justice requires that although research subjects bear the burden, the “society” that benefits from the results of the study must include individuals similar to those who participate in the study. Research subjects bear the burden, while society receives the benefit, but who is included in the “society” that will benefit from this research? Based on the legal requirements of human subject research in the United States, if research is conducted in the United States then it must benefit its citizens. This is not necessarily the case for trials conducted in Africa. Is this difference in treatment ethical? I would answer no.