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Articles

***1127** 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?

Ruqaiijah Yearby [FNa1]

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Introduction

The epidemic of the Human Immunodeficiency Virus (HIV) infection in Sub-Saharan Africa, [FN1] the region most affected by the HIV pandemic and where HIV is the leading cause of death, is reaching insurmountable proportions. In fact, out of the 36.1 million HIV infections worldwide, 25.3 million, seventy percent, are in Sub-Saharan Africa. [FN2] Additionally, of the more than 15,000 people who are infected with HIV every day, ninety-five percent of the cases are in populations that live in developing countries such as those located in Sub-Saharan Africa. [FN3] 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.

***1128** A clinical trial consists of a research study that uses human subjects to evaluate the efficacy of new drugs and treatments. [FN4] The purpose of clinical trials is to develop new treatments to prevent or treat diseases. [FN5] 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. [FN6] Rather, the benefit is to society. [FN7] 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: [FN8] Respect of Persons, [FN9] Beneficence, [FN10] and Justice. These ethical principles prevent the manipulation and exploitation of research subjects for the benefit of society as a whole. Furthermore, these principles provide the framework for researchers in the United States and abroad regarding what is humane and what the acceptable risk is for research subjects to bear. [FN11] In the United States, these principles have been codified and are therefore compulsory. [FN12] Abroad, these principles are widely accepted and appear in documents of international ethical principles. [FN13] Of these ethical principles, this Article will focus on the Justice principle and its application to clinical trials.

***1129** The expansive doctrine of Justice encompasses the principles of fairness, equity, and equality. [FN14] This broad doctrine of Justice has a limited application to clinical trials in that it demands that the “society” that benefits from the results of the study must include individuals similar to those who participate in the study. [FN15] 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 an individual. Even though statements of Justice can be found in the ethical guidelines of most countries and medical organizations, [FN16] this Article will focus on the statement of Justice found in two of the most renowned statements of ethics: the United States's The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research (Belmont Report) and the World Medical Association's Declaration of Helsinki. [FN17] As this Article will show, however, some researchers have perverted the principle by consistently ignoring the requirements of Justice when conducting research in developing countries or regions such as Sub-Saharan Africa. [FN18] Individuals who participate in clinical trials in Africa bear the same burden that American research subjects bear but do not receive the same benefits. Thus, one must ask why Africans are good enough to use for medical research but not good enough to be included in the "society" that benefits from that research.

Illustrative examples of this problem are the clinical trials conducted by some American researchers to prevent the spread of HIV in Sub-Saharan Africa. In the late 1990s, researchers from the United States traveled to Sub-Saharan Africa and conducted drug trials. [FN19] Many of these trials involved testing the effectiveness of new treatments and developing a shorter length of treatment for drugs already in use to prevent mother-to-child HIV transmission. [FN20] Unfortunately, because of the astronomical cost of these new treatments and drugs, *1130 few Sub-Saharan African countries and citizens would have had access to these treatments and drugs. [FN21] Therefore, relatively few Africans afflicted with HIV directly benefited from the results of this research. [FN22] Many researchers and ethicists questioned why Africans should bear the burden of participating in the research when they did not benefit from the results of the studies. [FN23] In response to these questions, researchers asserted that exorbitant costs meant that "society" should only include those who could afford treatment once it was patented and packaged by corporations. [FN24] Moreover, some researchers argued that Justice applies to an individual's right to participate in clinical trials. [FN25] But who does the Justice principle protecting--individuals or populations?

In the case of the HIV drug trials, leading ethicists asserted that neither individual Africans nor the African population benefited from these trials. As a result of these problems and negative publicity, many of these studies were terminated before completion or the structure of the trials was changed because of the violations of individual and population rights. Nevertheless, neither researchers nor ethicists reached any consensus regarding the requirements of the Justice principle in clinical trials conducted in Africa and other developing countries. [FN26] Questions of who is included in the "society" that benefits from a particular study and whether the Justice principle may be limited by concerns related to cost are paramount issues that persist and need answering as researchers commence HIV vaccine trials in Africa.

The first HIV vaccine trial was conducted in Africa in 1987 by a French doctor who immunized himself and a small group of Zairians *1131 with an investigational HIV vaccine. [FN27] According to a New York Times article published at the time, the reason the study was conducted in Zaire was because "it was easier to get official permission [in Zaire] than in France," [FN28] not because the population would benefit from the trials. [FN29] Since that trial, only four other HIV vaccine trials have been conducted in Africa, three of which began in 2003. [FN30] The trials currently being conducted in Africa, unlike the drug trials in the late 1990s and the first HIV vaccine trial, are not inherently discriminatory in their practice. However, it is questionable whether Africans will benefit from these trials because, in part, researchers have not guaranteed Africans access to the HIV vaccine if it proves effective.

In the past, the Belmont Report and the Declaration of Helsinki would provide the framework to address this problem; however, now some of the HIV vaccine trials are funded by private industry and are exempt from these requirements. [FN31] For instance, the International AIDS Vaccine Initiative (IAVI), an international scientific organization, funds the HIV vaccine trial conducted in Uganda. [FN32] Neither the Belmont Report, which only applies to research funded by the U.S. government, [FN33] nor the Declaration of Helsinki, which applies to all international trials but is only advisory, [FN34] applies to that trial. Some scholars have suggested requiring researchers and funders to enter into

prior agreements with individual countries to negotiate the proposed benefits before the research begins; however, these agreements *1132 are not compulsory and provide no additional mechanism of enforcement beyond the advisory requirement of the Declaration of Helsinki. [FN35] The best way to ensure that the African populations that bear the burden receive a benefit is to draft and implement a compulsory international document of ethical protections enforced by an international organization.

This Article explores the ethical principle of Justice and its application to clinical trials in developing countries through the lens of the current HIV vaccine trials in Sub-Saharan Africa. Part II examines the history of the Justice principle as it pertains to clinical trials and answers the question of who should be included in the “society” that benefits from the results of the research. The benefits of the Justice principle, fair access to the results of clinical trials, are compared to the benefits of fair opportunity to clinical trials in Part III, which reviews the problems with past clinical HIV drug trials conducted in Sub-Saharan Africa. Part IV briefly surveys the current HIV vaccine trials underway in Africa, discusses some of the failures of researchers to apply the principle of Justice, and suggests a possible mechanism to ensure that future clinical trials conducted in Africa provide a benefit to a “society” that includes Africans.

II. The History of the Justice Principle and Its Application to Clinical Trials

The Justice principle encompasses fairness and equity. [FN36] Norman Daniels, a Professor of Ethics at the Harvard School of Public Health, states that Justice requires everyone be given a fair opportunity to resources including health care. [FN37] Aristotle defined Justice in terms of equality: equals must be treated equally and unequals must be treated unequally. [FN38] The French philosopher, Rosseau, said that because all men are born equal one must “treat all men [and women] with complete equality and justice will prevail.” [FN39] But how is Justice achieved? The principle of Justice is an active process used to remedy or prevent what would arouse a sense of injustice. [FN40] These same general principles of Justice are applied to protections of human subjects participating in clinical trials. There are two main documents that govern *1133 international clinical trials and espouse the requirements of Justice: the Belmont Report and the Declaration of Helsinki. [FN41] According to these documents, Justice requires that populations used for research be treated equally and fairly. [FN42] As a review of these documents shows, the application of this principle to clinical trials has a long, sordid history--internationally and in the United States.

The first discussion concerning the allocation of burdens and benefits of clinical trials appeared in the United States's Belmont Report. [FN43] 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 through 1972, in which poor African-American men were denied access to standard treatment. [FN44] As a result of the hearings, Congress enacted the National Research Act of 1974, which required the U.S. Department of Health, Education, and Welfare (HEW) [FN45] to develop and publish policies for the protection of human subjects in the Code of Federal Regulations. [FN46] In addition, Congress created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (Commission) [FN47] and imposed a moratorium on *1134 research conducted or supported by HEW until adequate protections for research subjects were developed. [FN48]

The duties of the Commission were to identify the basic ethical principles that should govern medical and behavioral research involving human subjects, advise the Secretary of HEW on what changes to make to HEW policies governing clinical trials, and draft final guidelines that would ensure that researchers conducted clinical trials in accordance with these ethical principles. [FN49] To achieve this end, the Commission reviewed the existing HEW framework, recommended changes to the Secretary of HEW, and revised HEW's policy pertaining to clinical trials in the Belmont Report. [FN50] The Belmont Report was an outgrowth of the Commission's deliberations regarding ethical protections at

monthly meetings and a 1976 conference at the Smithsonian Institute's Belmont Conference Center. [FN51] In 1979, the Belmont Report was published in the Federal Register as the official policy statement of basic ethical principles and guidelines of HEW regarding research with human subjects. [FN52] In the Belmont Report, the Commission selected Justice as one of the three fundamental ethical principles [FN53] and defined Justice by first asking the question: "Who ought to receive the benefits of research and bear its burdens?" [FN54] To answer this question and establish the contours of Justice, the Commission defined what is just and what is unjust.

According to the Commission, an injustice occurs during clinical trials when a benefit is denied to a person without good reason or a burden is unduly imposed on a person, "whereas Justice requires that equals be treated equally." [FN55] In the context of clinical trials, the Belmont Report states:

Whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford *1135 them and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research. [FN56]

Thus, Justice prevents one population or group from being used for research without a benefit, while other populations or groups not used for research receive a benefit. The Commission's statement of Justice evolved from its view of the historical use of many vulnerable and disadvantaged populations for research that lead to the exploitation of these populations for the good of society. [FN57] Furthermore, the Commission specifically mentioned the need to apply the Justice principle to clinical trials to prevent other atrocities, such as those committed in the Tuskegee Syphilis Study and in the Nazi concentration camps. [FN58] Thereafter, the Commission applied this definition to evaluate who should bear the burden and receive the benefits of clinical research.

To protect human subjects in clinical trials, the Commission determined that when research subjects are selected, "the principle of justice gives rise to moral requirements that there be fair procedures and outcomes in the selection of research subjects." [FN59] Justice requires that the selection of human subjects for clinical trials be scrutinized to ensure that the population is not selected merely because research subjects are easily available, in a compromised position, or readily manipulated. [FN60] Moreover, in government-funded clinical trials to develop drugs and vaccines in the United States and abroad, Justice dictates that subjects from vulnerable populations receive a benefit from the results of the trials. [FN61]

The Belmont Report's iteration of the Justice principle was codified in 1986 in the Code of Federal Regulations. [FN62] Initially the principle was only applicable to research conducted and funded by HEW, but in June 1991, the Belmont Report was changed to govern all federally funded research. [FN63] Today, before U.S. scientists conduct government-funded clinical trials in the United States and abroad, the researcher must comply with the above-mentioned requirements of the Justice principle. [FN64] The problem with the Belmont Report is that it only applies*1136 to trials conducted or funded by the United States. [FN65] Trials funded by private industry do not have to comply with the Belmont Report's protections. These trials would be governed by international law, such as the Declaration of Helsinki, which includes some of the same ethical principles featured in the Belmont Report.

The Declaration of Helsinki, drafted and adopted in 1964 by the World Medical Association, is a statement of ethical standards that was 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. [FN66] In 2000, thirty-six years after the adoption of the document, [FN67] the World Medical Association amended the Declaration of Helsinki to include the Justice principle. [FN68] The impetus of this revision was a proposal submitted by the American Medical Association (AMA) in 1997, which significantly revised the Declaration of Helsinki. [FN69] The AMA's revisions were issued as a World

Medical Association document and discussed at the World Medical Council's 153rd Session in Santiago, Chile in April 1999. [FN70] The revisions submitted produced considerable debate and controversy because they addressed the use of placebos in research and the standard of care ethically required for subjects participating in clinical trials in developing countries. [FN71] After debating the revisions at conferences, symposiums, and workshops, the World Medical Association adopted the revisions on October 7, 2000, making it the first international***1137** ethical document to recognize the Belmont Report's Justice requirement. [FN72]

Comparable to the Belmont Report, the Declaration of Helsinki advises medical researchers that clinical trials are only just if the population used for research benefits. The Declaration of Helsinki states: “[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.” [FN73] 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. [FN74] If the population will not benefit from the results of the research, then the researcher must choose subjects from another population. [FN75] 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.

Nevertheless, Professors Francis Crawley and Joseph Hoet describe the Declaration of Helsinki as “the cornerstone of biomedical research for the last 30 years [and] the largely unquestioned anchor for ethical decision-making in clinical trials.” [FN76] Moreover, many medical journals, such as the *New England Journal of Medicine*, require that researchers publishing articles concerning clinical trials meet the ethical requirements of the Declaration of Helsinki. [FN77] In May 2002, the United Nations Programme on HIV and AIDS (UNAIDS) included the Justice principle from the Declaration of Helsinki in its guidance document, *Ethical Considerations in HIV Preventive Vaccine Research*, which is now being used by researchers and foreign governments in structuring clinical HIV vaccine trials in developing countries. [FN78] Although many researchers acknowledge the significance of the ethical protections in the Declaration of Helsinki and the Belmont Report, some researchers continue to disregard the Justice requirement discussed in these documents and use Africans to bear the burden and ***1138** risk of the research, while giving the benefit of the results of the research only to citizens of developed countries. [FN79] This was the case in the now defunct HIV drug trials conducted in Africa in the 1990s. [FN80]

III. HIV Drug Trials in Africa

A. Brief History of AZT Clinical Drug Trials in the United States and in Africa

In February 1994, the AIDS Clinical Trials Group Study 076 (Study 076) was concluded in the United States. [FN81] Study 076 showed that orally administering the drug Azidothymidine (AZT) to HIV-positive pregnant women in the second trimester of pregnancy, intravenously during labor, and orally to newborns upon birth reduced perinatal transmission of HIV by two-thirds. [FN82] This regimen of AZT cost \$800 per patient in U.S. dollars. [FN83] The expense of this regimen limited the accessibility of this treatment, so researchers began to search for a shorter, less expensive version of this AZT regimen, but they were uncertain about what research design method to use to test this new regimen. In June 1994, the World Health Organization [FN84] convened a group, which included no ethicists, in Geneva, and in an unpublished report, the group concluded that replicating Study 076 was neither economically nor structurally feasible in developing countries. [FN85] Instead, they concluded: “[P]lacebo-controlled trials offered the best option for a rapid and scientifically valid assessment of alternative antiretroviral drug regimens to prevent [perinatal] transmission of HIV [in

developing countries].” [FN86]

Documents from the Centers for Disease Control and Prevention (CDC) after the Geneva meeting show that eighteen clinical trials studying interventions to prevent perinatal HIV transmission were initiated. [FN87] These trials tested a variety of interventions to prevent perinatal*1139 transmissions of HIV, including giving a dose of AZT over a shorter length of time than used in Study 076. [FN88] Two of these studies were conducted in the United States, while sixteen trials were conducted in developing countries. [FN89] Ten of the sixteen studies were funded by the CDC or the National Institutes of Health (NIH), while other foreign governments funded five, and UNAIDS funded one. [FN90] The ten studies funded by the U.S. government were regulated by the Belmont Report, while the six other trials funded by foreign governments and UNAIDS were governed by the Declaration of Helsinki. [FN91] These studies involved more than 12,000 pregnant women. [FN92] The primary site of these trials was Africa. [FN93] Despite the identical purpose of the trials, the structure of the studies conducted in the United States and in Africa were vastly different.

All the subjects in the United States trials were provided access to AZT. [FN94] Some subjects were given the shorter length treatment of AZT, and others were given the longer treatment of AZT. [FN95] Thus, all the pregnant women who participated in the U.S. study were given some form of treatment to prevent their newborns from contracting HIV. Access to the longer treatment of AZT during the clinical trials, however, was not standard practice in the clinical trials conducted in developing countries. [FN96] In fact, only the researchers conducting the study in Thailand provided access to AZT for all the participants. [FN97] *1140 The researchers conducting trials in Africa failed to provide AZT to all the subjects. [FN98] Instead of giving African subjects the longer treatment of AZT that U.S. subjects were given, researchers gave pregnant African women participating in the study placebos, even though it is widely accepted that placebos cannot be used if a known treatment is available. [FN99] Because of the use of placebos, it was estimated that 1,000 babies contracted HIV. [FN100] In addition to this reprehensible act, the benefits of these clinical trials were not fairly or equitably distributed between the U.S. and African populations used for the clinical trials.

B. Who Benefited from the AZT Drug Trials Conducted in Africa?

The societal benefit from the AZT drug trials was gaining access to a shorter-length treatment of AZT that prevented perinatal HIV transmission. In this case, access to this drug was determined by the cost of the treatment. The CDC estimated that the cost of the shorter-length treatment of AZT was fifty dollars per patient, plus an additional ten dollars per patient charge for the initial HIV test to determine who was infected. [FN101] The cost of sixty dollars per patient for the short treatment of AZT made the drug accessible to most Americans with or without health insurance. [FN102] In the 1990s, the United States spent approximately \$3,000 per patient. [FN103] However, the shorter-length treatment of AZT tested in the clinical trials conducted in Africa was not financially feasible to the citizens of Africa and other developing countries. In the 1990s, when the majority of these trials were conducted, the amount spent on health-care per patient in U.S. dollars in each African country was well below sixty dollars per patient, as evidenced by Table 1.

*1141 Table 1 Health Care Expenditures of African Countries Involved in Perinatal HIV Transmission Prevention Trials [FN104]

Country (Year)	Amount spent per patient (U. S. dollars)
Burkina Faso (1992)	22

Cote d'Ivoire (1995)	22
Ethiopia (1990)	5
Kenya (1992)	13
Malawi (1990)	11
Tanzania (1990)	5
Uganda (1994)	10
Zimbabwe (1991)	86

The countries listed in Table 1 were sites of the clinical AZT drug trials. Based on the numbers in Table 1, seven out of eight of these countries would not have been able to afford the sixty dollars per patient necessary to purchase and provide the short-length AZT treatment to infected pregnant women, unless they significantly increased health care spending. [FN105] As a result of the short-length AZT trials conducted in Africa and other developing countries, these drugs were marketed and available to U.S. residents but not Africans. [FN106] Based on the amount spent per patient per year, clearly these African countries did not have access to the short-length treatment of AZT after the drug trials. Thus, the society that benefited most from the results of these trials only included populations from developed countries such as the United States. Many researchers and ethicists questioned whether these studies were just, because the African population did not benefit from the results of the African trials while the U.S. population did benefit.

C. Justice or Fair Access?: The Debate over AZT Drug Trials Conducted in Africa

Leading ethicists, physicians, and researchers on both sides of the debate wrote articles addressing the ramifications of applying different*1142 standards of Justice in AZT drug trials conducted in the United States and in Africa. [FN107] One critic of the trials, Dr. Marcia Angell, wrote in an editorial, "Human subjects in any part of the world should be protected by an irreducible set of ethical standards. . . ." [FN108] Otherwise, acceptance of this "ethical relativism" could result in widespread exploitation of vulnerable populations in developing countries participating in clinical trials. [FN109] Researchers who conducted the short-length AZT trials in Africa argued that the lack of money dedicated to paying for healthcare for Africans negated their duty to provide Africans access to the results of the trial: a shorter-length AZT treatment. [FN110] Therefore, because of cost limitations, researchers argued they should not be required to ensure that the populations used for the study actually benefited from the results. [FN111] However, these assertions show a patient misunderstanding of the Justice principle and its application.

The statement of Justice in the Belmont Report demands, not advises, that populations not be unduly burdened with research that is unlikely to benefit them without mention of cost. [FN112] According to the Belmont Report, Justice is used to evaluate what population should be used for research before the clinical trial is commenced to protect vulnerable populations from exploitation. [FN113] Before research is conducted, federal funding agencies, researchers, and drug companies must evaluate whether the population being used as subjects for the clinical trial will benefit, not when it conveniently becomes apparent after the conclusion of the research that the subjects will not be able to afford the treat-

ment. If the decision that Africans will benefit from the results of the research is not made prior to the selection of research subjects and countries, then what is the purpose for the research other than exploitation? [FN114]

Furthermore, in an article supportive of the AZT drug trials, the CDC and NIH, the institutions funding some of the drug trials conducted in Africa, responded to these ethical questions by stating that Justice does not simply require that populations participating in *1143 clinical trials benefit from the results but also that developing countries have “equitable access to clinical trials.” [FN115] According to the former Surgeon General and the former director of the NIH, Justice requires that vulnerable populations be allowed to participate in clinical trials without being barred by the unavailability of the resulting treatment. [FN116] Hence, it is unjust if researchers do not conduct clinical trials in developing countries because it limits the ability of Africans to benefit from the trials. [FN117]

This viewpoint alludes to the theory of fair opportunity espoused by Norman Daniels. That theory states that everyone should have a fair opportunity to resources, such as healthcare. [FN118] Fair opportunity is a precept of Justice; however, fair opportunity without fair or equal distribution of benefits is unjust. Mere access to clinical trials without providing access to trials that benefit developing countries undermines the very principle of Justice stated in the Belmont Report and the Declaration of Helsinki. The Belmont Report states that Justice demands that researchers conducting clinical trials do not “unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research”; otherwise, the groups will be exploited because they are easily accessible. [FN119] So, even if fairness requires equal access to clinical trials, these trials are not just unless a benefit is given to the population.

This statement regarding fair access to participation in clinical trials is further misguided because it focuses on the benefits of individual citizens, rather than on the benefits to the population, which the Justice principle addresses. Justice is defined in terms of protection of the population not just protection of the individual participating in the research trial. [FN120] In fact, the Belmont Report and the Declaration of Helsinki state that it is not enough for the participants of the clinical trials to be offered a benefit from the research; the population from which the subjects are a part must actually benefit. [FN121] Thus, Justice requires researchers to select populations to use as subjects in clinical trials based on the populations' ability to benefit from the research. If *1144 the population will not benefit from the results of the research then, according to the Belmont Report and Declaration of Helsinki, it is neither justifiable nor ethical to use it for the benefit of others. [FN122]

Many of the African HIV drug trials funded and conducted by the United States were abruptly halted because of pressures placed on researchers and funding agencies to conform to the ethical standards used in the United States. [FN123] Accordingly, these actions suggest that U.S. researchers from developed nations recognize the Justice principle's requirement in selecting research subjects from populations based on who will benefit from the results of the studies. To evaluate whether clinical researchers are currently abiding by the dictates of Justice, one can review the current HIV vaccine trials being conducted in Africa.

IV. HIV Vaccine Trials in Africa: Are the Trials Unjust?

A. The Structure of Clinical 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 in the case of the flu vaccine. [FN124] To develop an effective HIV vaccine through clinical trials, researchers must complete three phases. [FN125] Phase I is conducted using

a small number of subjects, usually less than fifty people, to obtain information regarding the safety and effect of the candidate vaccine on human subjects. [FN126] Information regarding the immune system's response to the vaccine, 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. [FN127] 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.*1145 [FN128] Under each phase of the trials, subjects are given a number of vaccine doses and then tested for HIV several months later. [FN129]

In 1987, the first Phase I clinical trial for the HIV vaccine was conducted in Zaire. [FN130] Since 1987, sixty Phase I and II trials have been conducted, testing more than thirty candidate HIV vaccines. [FN131] Most of the studies have been conducted in the United States and in Europe; and Phase III trials have only been conducted in the United States and Thailand, not in Africa. [FN132] This is important because only Phase III trials provide information concerning the effectiveness of the HIV vaccine to prevent HIV infection. [FN133] Currently, researchers are conducting three Phase I HIV vaccine trials in the African countries of Botswana, South Africa, and Uganda. [FN134] The U.S. government funded the Botswana and South Africa HIV vaccine trials, while the IAVI [FN135] funded the Uganda trials. [FN136] Because these trials commenced in 2003, it is hard to determine whether the results of the study will benefit Africans. A review of these three vaccine trials shows some improvements from the AZT clinical trials but still raises questions regarding what "society" will benefit from the trials. The main question is whether a successful HIV vaccine will be accessible to Africans.

B. Issues Concerning Current HIV Clinical Vaccine Trials [FN137]

The benefit to African society for participating in the three HIV vaccine trials is actual access to a vaccine that will prevent new HIV *1146 infections or decrease the number of deaths from AIDS. [FN138] Developing an effective vaccine for Africans is complicated because individual Africans are infected with different types and strains of HIV between themselves and a different type and strain of HIV than with which Americans are infected. [FN139] The discussion of the specific differences in types and strains of HIV is beyond the scope of this Article; however, it is because of this diversity in types and strains of infections that many researchers believe that a vaccine, which prevents one type of HIV infection, will not be efficacious in preventing infection by another strain. [FN140] Instead, researchers will probably need to develop a different HIV vaccine to prevent each of the major types and strains of HIV. [FN141] This problem has been addressed in each of the vaccine trials conducted in Africa. [FN142] In the Botswana trial, researchers are using a vaccine based on a combination of the infection most prevalent in the United States and in Africa. [FN143] In the trials in South Africa and Uganda, researchers are using an HIV vaccine based on the most prevalent type of infection in that region. [FN144] Yet, it is still questionable whether Africans will benefit from any of these studies because of the limited monetary resources available to pay for a vaccine. [FN145]

*1147 The Botswana trial is conducted by the HIV Vaccine Trial Network, [FN146] the medical schools of Harvard University in Boston and St. Louis University in St. Louis, and funded by the NIH. The HIV trials in Botswana are using the same vaccine currently being tested in trials in Boston and St. Louis. Because these trials are being conducted in the United States and in Africa, positive results from the trials promote the possibility that a multinational vaccine, which would benefit a broader society, would be developed. However, the possible benefits also create ethical dilemmas. There is no guarantee that the company manufacturing the vaccine will price it at a level affordable for the Botswana population. Instead, the company could simply decide to sell the vaccine to Botswana and the United States at a price affordable for the United States. Arguably, this would make the vaccine accessible to the population of Botswana. Notwithstanding this access, no one in Botswana would be able to afford to buy the vaccine, and therefore, the Botswana population

would not realize the benefits of the research trial.

To address this issue of access, the researchers from Harvard University are currently conducting studies in Botswana to create health infrastructures to treat HIV infection and a fellowship program to train scientists to conduct research in developing countries, such as Botswana. But, this neither addresses the issue of affordability of the vaccine nor guarantees that the citizens of Botswana will realize the benefits of the trial: access to the vaccine if it proves effective. The failure of Africans to realize the benefits of clinical trials is not an uncommon occurrence. This is what happened in the AZT drug trials conducted in the 1990s in the United States and Africa. Although the results of those trials, a shorter-length treatment of AZT, were offered to both the United States and Africa, only the United States could afford to provide the treatment to its citizens. [FN147] Thus, those trials violated the Justice principle, as espoused in the Belmont Report, because Africans bore the burden but failed to receive the benefit from the trials. As in the case of those trials, if the Botswana trial *1148 fails to provide an actual benefit to the population of Botswana, the trial would violate the Belmont Report's Justice principle, because the "society" bearing part of the burden, the Botswana population, would receive none of the benefits of the research. This is also a problem in the South African HIV vaccine trial.

The South African trial is being conducted by the HIV Vaccine Trial Network and funded by the NIH in conjunction with the Medical Research Council for South Africa (MRC). Testing has recently begun, but there is no mention in the literature whether the vaccine, if effective, will be accessible to the population of South Africa. [FN148] The MRC's guidelines on ethics in medical research state that any result from research supported by MRC vests rights in MRC to patent the product of the research. [FN149] However, the guidelines also allow financial sponsors to have full rights to the results of the research, making the HIV Vaccine Trial Network or NIH or both, the owners of the vaccine patent. [FN150] Without further information, it is impossible to determine whether the trials will provide a benefit to the South African population that it is testing. The past has shown, however, that after studies are concluded there is no guarantee that African society will have actual access to the treatment tested. Thus, the failure of the HIV Vaccine Trial Network or the NIH to pledge access to the vaccine if it proves effective in either the Botswana or South African trial leaves the door open for violations of the Justice principle that occurred in past AZT drug trials.

The Uganda trial conducted by IAVI, an international scientific, nonprofit organization founded in 1996, seems to be the one HIV vaccine trial most likely to produce a benefit for the African population. [FN151] Concerned with reports of vaccine researchers and manufacturers using clinical trials in poor countries to exploit weaker ethical protections for conducting biomedical research, the Ugandan government negotiated an agreement with IAVI that the vaccine, if effective, be accessible to the local population. [FN152] This agreement *1149 seemingly ensures that Ugandans will benefit from the results of the vaccine trials, but what is "accessible" ? Uganda does not have the intellectual property rights to the vaccine, the infrastructure to administer the vaccine, or the right to manufacture the vaccine. [FN153] Thus, the same problem that arose in Uganda in 1997 during the AZT drug trial studies could reoccur. In 1997, Uganda only spent ten dollars per patient per year on health care; thus, they could ill afford to provide the shorter length AZT treatment at sixty dollars per patient to pregnant women to prevent perinatal HIV transmission. [FN154] If the vaccine is more than what Uganda currently spends per patient per year, then Ugandans may not actually have access to a vaccine, and the trials will be unjust. [FN155]

C. Solution to Promote Justice in All International Clinical Trials

Both the South African and the Ugandan HIV vaccine trials pose a new quandary for ethicists: how to regulate clinical trials funded and conducted by different countries or private companies. Neither trial would exclusively fall under the realm of the Belmont Report because the U.S. government does not wholly fund the research. The Declaration of Hel-

sinki could be used to regulate the researchers conducting the trials, because each of the studies is conducted in part by foreign entities, thus triggering international law; however, the Declaration of Helsinki is only advisory. To rectify this problem, some scholars have suggested the use of prior agreements between foreign countries and researchers regarding the benefits of the research as the best way to address the ethical requirements of Justice; however, prior agreements pose the same problem as using the Declaration of Helsinki--there is no enforcement mechanism. [FN156]

As discussed above, IAVI and Uganda entered into a prior agreement regarding the accessibility of an effective HIV vaccine. Although the agreement between Uganda and IAVI purports to ensure that Ugandans have access to an effective vaccine, Uganda does not ***1150** have any more enforceable mechanism to challenge the manufacturer than it did under the Declaration of Helsinki. IAVI has implemented a number of legally enforceable contractual measures including transferring the rights to produce the vaccine to another manufacturer if the manufacturer is unwilling to provide the HIV vaccine at a price that Uganda can afford, but this legally enforceable remedy is not available to Uganda. [FN157] IAVI retains all rights and powers to the production of the vaccine. Therefore, IAVI, a private organization, can decide whether or not to enforce its contracts with private manufacturers for the benefit of Uganda. If IAVI decides not to enforce the provision, Ugandans will not receive any benefit from the results of the trials.

Another possible solution to prevent the continued exploitation of Africans and the perversion of the Justice requirement is the creation of an international compulsory standard of ethical protections of human subjects participating in clinical trials. The standards would be drafted, implemented, and enforced by one international body. The United Nations Programme on HIV and AIDS has become the premier international organization in terms of HIV and AIDS research and would be the best place for this newly formed international regulatory body. For the organization to be effective, the standards must have penalties if they are violated, and the organization must have some ability to enforce their decisions. The organization's ability to enforce this standard will be subject to the structure of its governing document and the membership of the organization. If the document mirrors some of the current standards already compulsory in the United States under the Belmont Report and already agreed to by many medical professionals under the Declaration of Helsinki, then more countries will opt to comply because it will not challenge the status quo. Furthermore, if the membership of the organization includes the United States and key members of the European Union, researchers from those countries will comply with the dictates of the organization.

However, membership to the organization must be balanced to include many of the developing countries being exploited. To be fair in combating ethical violations in developing countries, the membership of the organization must be proportionate to the amount of research conducted in a country by researchers from other countries. With the creation of this compulsory international statement of ethics and enforcement, researchers and private funders will be held accountable ***1151** for their ethical violations and deterred from committing the violation again, thus protecting vulnerable populations from exploitation. Private funders and pharmaceutical companies may try to argue that their research is private and not subject to the mandates of an international organization; however, researchers from member countries will be required to follow the dictates of the organization, and, thus, their funders must comply in order to conduct research in developing nations. This is the best way to ensure that Africans are not exploited for the benefit of other populations, because it empowers the exploited society to protect its own citizens through enforceable means, rather than leaving them to rely on the mercy of a private entity.

V. Conclusion

The large number of persons infected with HIV in Africa combined with the inadequate monetary resources for purchasing medications to treat HIV-infected persons makes Africa ideal for conducting HIV vaccine trials.

[FN158] However, in light of the recent history of the AZT drug trials in which Africans were exploited, [FN159] Africans were concerned about reports in the foreign media that manufacturers might choose to test vaccines in poor countries to reduce product liability in case of injury or to exploit weaker legal, ethical, or regulatory mechanisms for conducting biomedical research. [FN160] In fact, many Africans “asked whether the [HIV vaccine] trial was an example of ‘hit and run research’ by scientists from rich countries, in which a poor country was chosen as the setting because the study would be cheaper and fewer questions would be asked about safety and ethics.” [FN161] As clinical HIV vaccine trials commence, Africans wonder if they will receive any benefit as a society from the research or will simply be exploited. [FN162]

In the past, there has been much discussion regarding the requirement of providing a benefit to an African society after conducting an HIV clinical trial in Africa. [FN163] Some have lauded the research community***1152** for giving Africans equitable access to clinical trials, [FN164] but mere access to trials without any guarantee that the results of the trials will provide a benefit to Africans leaves them with the burden but no benefit. Both the Belmont Report and the Declaration of Helsinki require that the population studied receive a benefit to ensure that populations are not exploited or used in trials for the benefit of others. [FN165] In the current HIV vaccine trials, the very structure of clinical trials would negate any significant benefits individual Africans would receive from participating in clinical trials. Because these Phase I clinical trials are merely evaluating the safety of the vaccine versus the dangers and side effects of the vaccine, the net benefit from the trials is to the society that gains access to an effective vaccine after Phase III trials, not the participants in the clinical trials.

Therefore, rather than focusing on mere access to trials, there is a need for researchers to shift their thinking and perception of the benefits of clinical trials in Africa. The key to this shift is to focus on the fact that the benefit researchers are trying to obtain is for society. Society includes all countries but specifically the country researchers used for the research. Thus, as researchers choose research subjects for HIV vaccine trials in Africa, they should make the choice based on the view that research is conducted to save human lives, which includes the lives of the people in the country where clinical trials are conducted. Simply viewing these subjects as dispensable figures neglects not only the spirit of the research subject protocol rules but also violates the letter of the rule. The Belmont Report and the Declaration of Helsinki require that the population benefit from the research, not simply that the researchers offer the population a benefit; otherwise, the research is not justified. [FN166] Unfortunately, the Belmont Report and the Declaration of Helsinki do not protect all research subjects. The Belmont Report is only compulsory for research funded by the United States, while the Declaration of Helsinki is only a guide to researchers.

To prevent this gap in protection, some scholars have suggested promoting prior agreements between the researchers, funders, and the foreign country. [FN167] However, these agreements are not always enforceable and can lead to different outcomes for different countries based on the power base of the country negotiating the deal. A better ***1153** way to prevent the continued exploitation of Africans is to create an international compulsory standard of ethical protections of human subjects participating in clinical trials enforced by an international body whose membership includes representatives from developing countries. With the creation of this compulsory international statement of ethics and enforcement organization, researchers will be held accountable for their ethical violations in developing countries, which would deter them from committing the violations again and would protect vulnerable populations from exploitation.

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[FN1]. 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 The Ctr. for HIV Info., Univ. of Cal., San Francisco Sch. of Med., Sub-Saharan Africa Map (2003), at <http://hivinsite.ucsf.edu> (last visited Feb. 4, 2004).

[FN2]. See A Difference of 15 Years, Wash. Post, July 4, 2000, at <http://www.washingtonpost.com/wp-srv/world/daily/july00/aidsgraphic.htm> (last visited Feb. 4, 2004).

[FN3]. See Jose Esparza, An HIV Vaccine: How and When?, 79 Bull. World Health Org. 1133 (2001); Barney S. Graham, National Institutes of Health Vaccine Research Center Report, Clinical Trials of HIV Vaccines 2 (2001).

[FN4]. Tom Beauchamp & James Childress, Principles of Biomedical Ethics 441 (4th ed. 1994).

[FN5]. Id.

[FN6]. Id.

[FN7]. Id.

[FN8]. These three principles are found in the Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Biomedical and Behavioral Research. See The Belmont Report, 44 Fed. Reg. 23,192, 23,194 (Apr. 18, 1979). This document was drafted by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research in 1976 and published in the Federal Register. Id.

[FN9]. The doctrine of Respect of Persons includes two main ethical canons: autonomy and protection. Researchers must treat human research subjects as autonomous agents and provide protections for those with diminished autonomy. Id. at 23,193.

[FN10]. Beneficence requires researchers to “not only respect the autonomy of the research subjects but also make an effort to secure their well-being.” Id. at 23,194.

[FN11]. Id. This is important because most of the countries in which the United States is funding and conducting clinical trials do not have effective mechanisms available to review the ethical implications of the research. See UNAIDS Report: UNAIDS Sponsored Regional Workshops To Discuss Ethical Issues in Preventive HIV Vaccine Trials, U.N. Programme on HIV and AIDS (UNAIDS), at 8, UNAIDS Doc. 00.036 (2002).

[FN12]. 45 C.F.R. § 46.101 (2003).

[FN13]. In fact, the principle of Justice was found only in the Belmont Report until 2000, when the World Medical Association added the principle to the Declaration of Helsinki, a renowned document of bioethics for clinical trials. The Belmont Report, 44 Fed. Reg. at 23,192; see also World Med. Ass'n, The Declaration of Helsinki (2002), available at <http://www.wma.net/e/policy/b3.htm> (last visited Feb. 4, 2004).

[FN14]. The Belmont Report, 44 Fed. Reg. at 23,196; see also World Med. Ass'n, *supra* note 13.

[FN15]. The Belmont Report, 44 Fed. Reg. at 23,196; see also World Med. Ass'n, *supra* note 13.

[FN16]. Recently, many countries, such as the United Kingdom, Canada, Nepal, Uganda, and Brazil, have revised their ethical guidelines to address access to post-trial benefits. See Alice Page, *Prior Agreements in International Clinical Trials: Ensuring the Benefits of Research to Developing Countries*, 3 *Yale J. Health Pol'y, L. & Ethics* 35, 50 (2002). Nevertheless, many of the guidelines are not compulsory and have no enforcement mechanism. *Id.*

[FN17]. The Belmont Report, 44 Fed. Reg. at 23,194; see also World Med. Ass'n, *supra* note 13.

[FN18]. For example, researchers conducting AZT drug trials in Africa to prevent mother-to-child transmission offered some subjects placebos even though the same trials conducted in the United States provided each subject with drugs. *Id.* For more discussion, see *infra* subpart II(B).

[FN19]. David Studdert & Troyen Brennan, *Clinical Trials in Developing Countries: Scientific and Ethical Issues*, 169 *Med. J. Austral.* 545 (1998).

[FN20]. *Id.*

[FN21]. Ronald Bayer, *The Debate over Maternal-Fetal HIV Transmission Prevention Trials in Africa, Asia, and the Caribbean: Racist Exploitation or Exploitation of Racism?*, 88 *Am. J. Pub. Health* 567, 570 (1998).

[FN22]. *Id.*

[FN23]. George Annas & Michael Grodin, *Human Rights and Maternal-Fetal HIV Transmission Prevention Trials in Africa*, 88 *Am. J. Pub. Health* 560, 560-61 (1998); R.A. Crouch & J.D. Arras, *AZT Trials and Tribulations*, 28 *Hastings Center Rep.* 26, 29 (1998); L.H. Glantz, *Research in Developing Countries: Taking Benefit Seriously*, 28 *Hastings Center Rep.* 38, 40-42 (1998); Marcia Angell, *The Ethics of Clinical Research in the Third World*, 337 *New Eng. J. Med.* 847, 847-48 (1997).

[FN24]. See Peter Lurie & Sidney Wolfe, *Unethical Trials of Interventions To Reduce Perinatal Transmission of Human Immunodeficiency Virus in Developing Countries*, 337 *New Eng. J. Med.* 853, 854-55 (1997).

[FN25]. Harold Varmus & David Satcher, *Ethical Complexities of Conducting Research in Developing Countries*, 337 *New Eng. J. Med.* 1003, 1004 (1997).

[FN26]. Studdert & Brennan, *supra* note 19, at 545.

[FN27]. The Zairians tested were HIV-negative before receiving the vaccine. Nicholas A. Christakis, *The Ethical Design of an AIDS Vaccine Trial in Africa*, 18 *Hastings Center Rep.* 31, 31 (1988).

[FN28]. Zaire, *Ending Secrecy, Attacks AIDS Openly*, *N.Y. Times*, Feb. 18, 1987, at A1, cited in Christakis, *supra* note 27, at 31.

[FN29]. In an article published in the *Nature* journal, Dr. Daniel Zagury claims that he not only had the full support of the Zairian government but also worked with a group of Zairian scientists on the project. *Id.* Dr. Zagury used this to justify the vaccine trial; however, human research guidelines of the World Health Organization and the Council for International Organizations of Medical Sciences required that the ethical standards, which are applied to research studies conducted in the researcher's own country, must also be applied to research studies conducted in developing countries.

Christakis, *supra* note 27, at 31.

[FN30]. See Roy Mugerwa et al., First Trial of the HIV-1 Vaccine in Africa: Ugandan Experience, 324 *British Med. J.* 226, 228 (2003); Nat'l Inst. of Health, Safety of an HIV Vaccine (AVX101) in HIV Uninfected Volunteers in the United States and South Africa (2003), available at <http://www.clinicaltrials.gov> (last visited Feb. 4, 2004); Nat'l Inst. of Health, Safety of and Immune System Response to an HIV Vaccine (EP HIV-1090) in HIV Uninfected Adults (2003), available at <http://www.clinicaltrials.gov> (last visited Feb. 4, 2004).

[FN31]. Richard Rettig, The Industrialization of Clinical Research, *Health Aff.*, Apr.-May 2000, at 129, 131.

[FN32]. Mugerwa et al., *supra* note 30, at 228.

[FN33]. 45 C.F.R. § 46.101 (2003).

[FN34]. World Med. Ass'n, *supra* note 13.

[FN35]. Page, *supra* note 16, at 38-43.

[FN36]. The Belmont Report, 44 Fed. Reg. 23,192, 23,194 (Apr. 18, 1979).

[FN37]. Norman Daniels, *Just Health Care* 34-58 (1985).

[FN38]. Beauchamp & Childress, *supra* note 4, at 328.

[FN39]. Jean-Jacques Rousseau, *The Social Contract* 4 (Maurice Cranston trans., Penguin Books 1968) (1762).

[FN40]. Edward Cahn, *The Sense of Justice* 14-15 (1949).

[FN41]. The precursor to international ethical protections of human subjects participating in clinical trials was the Nuremberg Code (Code) in 1947, which was developed in response to the Trials of War Criminals before the Nuremberg Military Tribunals. See Nuremberg Code (1947), available at <http://ohsr.od.nih.gov/nuremberg.php3> (last visited Feb. 4, 2004). The Code does not explicitly discuss the equal distribution of burdens and benefits from the results of clinical trials; however, the Code notes that experiments should yield fruitful results for the good of society. Although this statement does not directly address who is included in society, it served as the building block of the Justice principle defined in the Belmont Report. See The Belmont Report, 44 Fed. Reg. at 23,192.

[FN42]. The Belmont Report, 44 Fed. Reg. at 23,192.

[FN43]. *Id.*

[FN44]. See generally James H. Jones, *Bad Blood: The Tuskegee Syphilis Experiment* (1981).

[FN45]. The U.S. Department of Health, Education, and Welfare was renamed the U.S. Department of Health and Human Services in 1980. See Department of Education Organization Act, Pub. L. No. 96-88, § 509(e), 93 Stat. 695 (1979) (codified at 20 U.S.C. § 3508 (2000)).

[FN46]. See National Research Act of 1974, 42 U.S.C. § 2891 (2000).

[FN47]. The Commission was composed of eleven members appointed by the Secretary of HEW. The National Research

Act advised the Secretary of HEW to choose the members of the Commission from distinguished individuals from the fields of medicine, law, ethics, theology, philosophy, humanities, health administration, government, public affairs, and the biological, physical, behavioral, and social sciences. *Id.* Five of the members of the Commission had to be individuals engaged in biomedical or behavioral research involving human subjects. *Id.* Members of the Commission included Dorothy I. Height, President of the National Council of Negro Women, Inc., Dr. Albert R. Jonsen, Professor Emeritus of Medical History and Ethics at the University of Washington, and Patricia King, the Carmack Waterhouse Professor of Law, Medicine, Ethics, and Public Policy at Georgetown University Law Center. See *The Belmont Report*, 44 Fed. Reg. at 23,192.

[FN48]. 42 U.S.C. § 2891.

[FN49]. *Id.*

[FN50]. The Commission issued several reports that addressed the need for ethical protections and a summary of their monthly meetings; however, the Belmont Report was their final statement of ethical principles that govern medical and behavioral research. See Nat'l Inst. of Health, *Guidelines for the Conduct of Research Involving Human Subjects at the National Institutes of Health* (1995), available at <http://ohsr.od.nih.gov/guidelines.php3> (last visited Feb. 4, 2004). After drafting the Belmont Report, the Commission was dissolved in 1978. *Id.*

[FN51]. *Id.*

[FN52]. In 1979, HEW began revising its policies regarding clinical trials. The revisions became final in 1981. See *The Belmont Report*, 44 Fed. Reg. at 23,192.

[FN53]. The two other principles were Respect for Persons and Beneficence. For a definition of each of these ethical principles, see *supra* notes 9 and 10.

[FN54]. *Id.* at 23,194.

[FN55]. *Id.*

[FN56]. *Id.* (emphasis added).

[FN57]. The Commission noted the relevance of Justice because of the egregious ethical violations committed in the Tuskegee Syphilis Study and in the Nazi concentration camps. *Id.*

[FN58]. Nat'l Inst. of Health, *supra* note 50.

[FN59]. *The Belmont Report*, 44 Fed. Reg. at 23,192.

[FN60]. *Id.* at 23,194.

[FN61]. *Id.* at 23,197.

[FN62]. Nat'l Inst. of Health, *supra* note 50.

[FN63]. 56 Fed. Reg. 28,003, 28,003 (June 18, 1991).

[FN64]. Before U.S. researchers begin clinical trials, they must submit a written assurance to the appropriate Institutional

Review Board (IRB). 45 C.F.R. § 46.101(a)(2) (2002). A complete written assurance includes a statement of the ethical principles protecting the rights and welfare of human research subjects based on the ethical principles of the Belmont Report. 45 C.F.R. § 46.103(b)(1) (2002). An IRB, a board found in all federal agencies and universities that conduct biomedical research, reviews all written assurances in application for clinical trials. See 10 C.F.R. § 745.101 (1991); 28 C.F.R. § 46.101 (1991); 45 C.F.R. § 46.109 (2002). The IRB reviews the proposal to ensure that the proposed trials are ethical and has the authority to “approve, require modifications in (to secure approval), or disapprove” any application. 45 C.F.R. § 46.109(a).

[FN65]. 45 C.F.R. § 46.101.

[FN66]. Research governed by the Declaration of Helsinki includes research involving identifiable human material or data. See World Med. Ass'n, *supra* note 13.

[FN67]. The 2000 revision of the Declaration of Helsinki was the fifth revision to the document. *Id.* The document was revised in 1975, 1983, 1989, 1996, 2000, and 2002. *Id.*

[FN68]. The latest version of the Declaration of Helsinki was published in 2002; however, the principle of Justice first appeared in the Declaration of Helsinki in 2000. The World Medical Association amended the Declaration of Helsinki at the 52nd World Medical Association General Assembly Meeting in Edinburgh, Scotland in October 2000. The World Medical Association in Washington added a note of clarification in 2002, but this revision did not affect the statement of the Justice principle. *Id.*

[FN69]. Delon Human & Sev S. Fluss, *The World Medical Association's Declaration of Helsinki: Historical and Contemporary Perspective* 1, 13-15 (2001), at <http://www.wma.net/e/ethicsunit/helsinki.htm> (last visited Nov. 17, 2003).

[FN70]. *Id.* at 13.

[FN71]. *Id.* at 15.

[FN72]. *Id.* at 16.

[FN73]. World Med. Ass'n, *supra* note 13.

[FN74]. *Id.*; see also *The Belmont Report*, 44 Fed. Reg. 23,192, 23,197 (Apr. 18, 1979).

[FN75]. *The Belmont Report*, 44 Fed. Reg. at 23,196.

[FN76]. Francis Crawley & Joseph Hoet, *Ethics and Law: The Declaration of Helsinki Under Discussion*, 150 *Bull. Med. Ethics* 9, 10 (1999).

[FN77]. Marcia Angell, *Ethical Imperialism? Ethics in International Collaborative Clinical Research*, 319 *New Eng. J. Med.* 1081, 1082-83 (1988).

[FN78]. UNAIDS, *Ethical Considerations in HIV Preventive Vaccine Research* (2002), at <http://www.unaids.org> (last visited Feb. 4, 2004).

[FN79]. Varmus & Satcher, *supra* note 25, at 1004. Studdert & Brennan, *supra* note 19, at 546-48.

[FN80]. Annas & Grodin, *supra* note 23, at 560-61.

[FN81]. *Id.*; Bayer, *supra* note 21, at 567.

[FN82]. Perinatal transmission of HIV is when an HIV-positive pregnant woman gives the disease to her newborn child. Annas & Grodin, *supra* note 23, at 560-61.

[FN83]. Bayer, *supra* note 21, at 570; Varmus & Satcher, *supra* note 25, at 1004.

[FN84]. The World Health Organization (WHO) is the health organization of the United Nations. See <http://www.who.int/country/en> (last visited Feb. 4, 2004). All countries that are members of the United Nations may become members of WHO by accepting its constitution. *Id.* The United States is a member of WHO. *Id.*

[FN85]. Bayer, *supra* note 21, at 570; see also Lurie & Wolfe, *supra* note 24, at 854.

[FN86]. Researchers used this unpublished document to justify their use of placebos in subsequent AZT drug trials in developing countries instead of providing the long treatment of AZT that was given to American research subjects. Lurie & Wolfe, *supra* note 24, at 854.

[FN87]. *Id.*

[FN88]. *Id.*

[FN89]. *Id.* Actually, there were sixteen trials conducted in developing countries, but there is so little information in the medical literature regarding the sixteenth trial, other than that it was conducted in Thailand and the participants of this trial were given access to both the shorter and the longer treatment of AZT. *Id.* Because of the lack of substantive information regarding this trial, a detailed discussion of this trial has been omitted from this Article.

[FN90]. *Id.*

[FN91]. There is little information in the medical literature regarding the outcome of the six other clinical trials funded by the foreign government and the UNAIDS, so a discussion regarding the arguments to support those studies based on international law has been omitted. If the arguments centered on the requirements of the Declaration of Helsinki, the discussion would be similar to the arguments raised under the Belmont Report.

[FN92]. Jay Dyckman, *The Myth of Informed Consent: An Analysis of the Doctrine of Informed Consent and Its (Mis)Application in HIV Experiments on Pregnant Women in Developing Countries*, 9 *Colum. J. Gender & L.* 91, 92 (1999).

[FN93]. Nine of the sixteen studies were conducted in Africa. Lurie & Wolfe, *supra* note 24, at 853.

[FN94]. *Id.*

[FN95]. *Id.* at 854.

[FN96]. *Id.* at 854-55.

[FN97]. Marc Lallemand, a researcher at the Harvard School of Public Health, conducted the only study that provided drugs to all participants in the developing country in Thailand. *Id.* Although the National Institutes of Health finally funded the study, Lallemand and the Harvard School of Public Health were initially pressured by the NIH to conduct a placebo-controlled trial. *Id.* at 853-54.

[FN98]. *Id.*

[FN99]. See Beauchamp & Childress, *supra* note 4, at 451; Lurie & Wolfe, *supra* note 24, at 854-55; Angell, *supra* note 77, at 1082. The withholding of AZT was especially egregious because the manufacturer of AZT usually made the drug available free of charge for use in clinical trials. Lurie & Wolfe, *supra* note 24, at 855.

[FN100]. Dyckman, *supra* note 92, at 93.

[FN101]. Annas & Grodin, *supra* note 23, at 563.

[FN102]. *Id.*

[FN103]. The amount spent per patient in the United States jumped to \$4,178 in 1998. See Office of the Actuary, Ctrs. for Medicare & Medicaid Servs., Table 1: National Health Expenditures and Selected Economic Indicators, Levels and Average Annual Percent Change: Selected Calendar Years 1980-2012 (2003), available at <http://cms.hhs.gov/statistics/nhe/projections-2002/t1> (last visited Feb. 4, 2004).

[FN104]. Table reprinted from Annas & Grodin, *supra* note 23, at 564.

[FN105]. Many researchers could argue that any African country could decide to spend more per patient each year to purchase the drug. This discussion is important because it addresses the need of countries to prioritize the use of their resources for the good of their citizens. However, the decisions of African countries to spend an amount of money on other things besides health spending is beyond the scope of this Article and still does not preclude researchers' responsibility to use a population that will benefit from the results of the research. If a drug is estimated to cost more than what is normally spent per year per patient the question is: Without a change in spending, will the population benefit from the research?

[FN106]. Lurie & Wolfe, *supra* note 24, at 854-55.

[FN107]. Full issues of the *New England Journal of Medicine*, the *American Journal of Public Health*, and the *Hastings Center Report* were devoted to this topic. See generally 337 *New Eng. J. Med.* 1 (1997); 88 *Am. J. Pub. Health* 1 (1998); 28 *Hastings Center Rep.* 1 (1998).

[FN108]. Angell, *supra* note 77, at 1083.

[FN109]. *Id.*; Angell, *supra* note 23, at 847-48.

[FN110]. Bayer, *supra* note 21, at 570.

[FN111]. *Id.*

[FN112]. The Belmont Report, 44 *Fed. Reg.* 23,192, 23,197 (Apr. 18, 1979).

[FN113]. *Id.* at 23,196-97.

[FN114]. Lurie & Wolfe, *supra* note 24, at 854-55; Annas & Grodin, *supra* note 23 at 560-61; Angell, *supra* note 23, at 847-48.

[FN115]. Varmus & Satcher, *supra* note 25, at 1003.

www.clinicaltrials.gov/ct/show/NCT00063778?order=q (last visited Feb. 4, 2004) [hereinafter Nat'l Inst. of Health, AVX101]; Nat'l Inst. of Health, Safety of and Immune System Response to an HIV Vaccine (EP HIV-1090) in HIV Uninfected Adults (2003), at <http://www.clinicaltrials.gov/ct/show/NCT00054866?order=2> (last visited Feb. 4, 2004) [hereinafter Nat'l Inst. of Health, EP HIV-1090].

[FN135]. IAVI is an international nonprofit organization that is headquartered in the United States. For more information, see *supra* subpart III(B).

[FN136]. See sources cited *supra* note 134.

[FN137]. There is some dispute when, and in what country, the first HIV vaccine trial was conducted based on the most prevalent types found in Africa. There are two sources that suggest that the first trial started in Kenya in 2001. See Int'l AIDS Vaccine Initiative, *supra* note 134; AIDS.Org, First Vaccine for Africa Begins Trials (Jan. 26, 2001), at <http://www.aids.org/atn/a-359-02.html> (last visited Nov. 5, 2003). Susan Mayor, AIDS Vaccine Trial Begins in Uganda, 326 *British Med. J.* 414 (2003). The literature is also unclear on whether the Kenya study has been concluded. See Int'l AIDS Vaccine Initiative, *supra* note 134. Thus, this trial will not be discussed in further detail in this Article.

[FN138]. The difference in benefit depends on what type of HIV vaccine is being tested. If a prophylactic vaccine is effective, it would prevent HIV infection after exposure, while a therapeutic vaccine would only slow the progression of HIV to AIDS. See Lurie & Wolfe, *supra* note 24, at 854-55. Further discussion of the consequence of developing different types of vaccines for use in the United States is beyond the scope of this Article; however, the author is in the process of drafting an article to discuss the burdens and benefits of the different types of vaccines in respect to the Justice principle.

[FN139]. Esparza, *supra* note 3, at 1133.

[FN140]. *Id.*; Lurie et al., *supra* note 124, at 297.

[FN141]. *Id.*

[FN142]. See Press Release, First HIV Vaccine Trial Commences in South Africa (Nov. 3, 2003), available at <http://www.mrc.ac.za/pressreleases/2003/37pres2003.htm> (last visited Feb. 4, 2004); see also Mugerwa et al., *supra* note 30, at 228.

[FN143]. See Jenny Badner, Botswana & Harvard: Teaming Up To Find an AIDS Vaccine, *Voice of America*, available at 2003 WL 59719040.

[FN144]. *Id.*

[FN145]. Even before HIV vaccine trials were launched in Africa, there was speculation from many U.S. physicians and ethicists regarding the lack of HIV vaccine trials based on the types of infection most prevalent to Africa. Dr. Peter Lurie, an American researcher and ethicist, stated that it was important that vaccine trials included strains from Africa because the majority of HIV infections were located in Africa. See Lurie et al., *supra* note 124, at 297. Additionally, Dr. Lurie suggested that trial sites of HIV vaccine clinical trials be located in different developing nations such as in Africa, otherwise the vaccine will disproportionately benefit one population while shouldering the burdens with others. *Id.*

[FN146]. In 1999, the HIV Vaccine Trial Network was formed by the Division of AIDS of the National Institute of Allergy and Infectious Diseases (NIAID), a component of the National Institutes of Health (NIH), when the federal govern-

ment reorganized. See About the HIV Vaccine Trial Network (2003), at <http://www.hvtn.org/about> (last visited Feb. 4, 2004). Since that time the HIV Vaccine Trial Network has blossomed into an international organization dedicated to conducting international HIV vaccine trials composed of twenty-seven research institutions worldwide and headquartered at the Fred Hutchinson Cancer Research Center. *Id.*

[FN147]. Lurie & Wolfe, *supra* note 24, at 854-55.

[FN148]. See Press Release, First HIV Vaccine Trial, *supra* note 142.

[FN149]. Guidelines on Ethics for Medical Research, Ownership of Results: Patent Rights, Copyright, and Confidentiality (1993), available at <http://www.mrc.ac.za/ethics/ownership.htm> (last visited Feb. 4, 2004).

[FN150]. Med. Research Council, Guidelines on Ethics for Medical Research, Ownership of Results of Research (1993), available at <http://www.mrc.ac.za/ethics/ownership.htm> (last visited Feb. 4, 2004) (discussing ownership rights of financial sponsors).

[FN151]. The main purpose of IAVI is to accelerate the development of safe, effective, and accessible HIV vaccines globally. Page, *supra* note 16, at 57. To achieve this end, IAVI provides money for private industry to develop and test HIV vaccines and then links the industry to foreign countries for testing. *Id.*

[FN152]. Mugerwa et al., *supra* note 30, at 228.

[FN153]. *Id.*

[FN154]. Annas & Grodin, *supra* note 23, at 564. Currently, Uganda only spends \$6 per year per patient, while the United States spends approximately \$5,775 per patient. See Mugerwa et al., *supra* note 30, at 228; see also Office of the Actuary, *supra* note 103.

[FN155]. Uganda does have its own ethical requirements, but the requirements relating to the Justice principle are advisory. The Uganda National Consensus Conference Guidelines for the Conduct of Health Research Involving Human Subjects in Uganda requires a researcher only make a reasonable effort to secure the product's availability to the local community in which the research occurred. See National Conference, Guidelines for the Conduct of Health Research Involving Human Subjects in Uganda § V(D)(4) (1997), cited in Page, *supra* note 16, at 51 n.58.

[FN156]. Page, *supra* note 16.

[FN157]. *Id.* at 59.

[FN158]. *Id.*

[FN159]. An example of exploitation of Africans used in clinical trials was the 1990 AZT drug trials. For more information, see *supra* subpart II(B).

[FN160]. *Id.*

[FN161]. See Mugerwa et al., *supra* note 30, at 228.

[FN162]. *Id.*

[FN163]. See generally *id.*; David Orentlicher, *Universality and Its Limits: When Research Ethics Can Reflect Local Circumstances*, 30 *J.L. Med. & Ethics* 403 (2002); Joanne Roman, *Note, U.S. Medical Research in the Developing World: Ignoring Nuremberg*, 11 *Cornell J.L. & Pub. Pol'y* 441 (2002).

[FN164]. Varmus & Satcher, *supra* note 25, at 1004.

[FN165]. *The Belmont Report*, 44 *Fed. Reg.* 23,192, 23,196-97 (Apr. 18, 1979); see also *World Med. Ass'n*, *supra* note 13.

[FN166]. *The Belmont Report*, 44 *Fed. Reg.* at 23,194.

[FN167]. Page, *supra* note 16.
53 DePaul L. Rev. 1127

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