Abstract

The protection of human rights will be critical to the success of HIV vaccine trials throughout the world. A vaccine for HIV remains our best hope to control the global epidemic. In order to launch and sustain useful and successful human trials of HIV vaccines, a partnership between scientists, governments, pharmaceutical companies, and affected communities is essential. This article provides a review of some of the key issues relevant to human rights in the design, testing, and dissemination of HIV vaccines. The article gives specific examples from three countries—Brazil, Thailand, and the United States—which may initiate large-scale trials in the near future.

La protection des droits de la personne sera primordiale pour le succès des essais de vaccins contre le VIH à travers le monde. Un vaccin contre le VIH demeure notre meilleur espoir pour juguler l'épidémie mondiale. Un partenariat entre les scientifiques, les gouvernements, les entreprises pharmaceutiques et les communautés affectées est essentiel pour la mise en oeuvre durable, l'utilité et le succès des essais humains de vaccins contre le VIH. Cet article passe en revue certains des problèmes clé concernant les droits de la personne associés à la conception, au test et à la dissémination de vaccins contre le VIH. L'article présente des exemples spécifiques en provenance de trois pays—Brésil, Thaïlande et Etats-Unis—qui pourraient être utilisés pour entre prendre des essais à grande échelle dans un futur proche.

La protección de los derechos humanos será primordial para el éxito de los ensayos de la vacuna contra el VIH a través del mundo. La vacuna contra el VIH continua siendo nuestra mayor esperanza para controlar la epidemia mundial. Es esencial establecer un partenariazgo entre científicos/as, gobiernos, compañías farmacéuticas, y comunidades afectadas para iniciar y sostener ensayos humanos de las vacunas contra el VIH que sean útiles y con éxito. Este artículo revisa algunos de los asuntos clave sobre derechos humanos relacionados con el diseño, los ensayos, y la diseminación de las vacunas contra el VIH. El artículo presenta ejemplos específicos de tres países (Brasil, Tailandia, y Estados Unidos) que pueden iniciar ensayos de gran escala en un futuro inmediato.

HIV Vaccine Research and Human Rights: Examples from Three Countries Planning Efficacy Trials

Jorge Beloqui, Vichai Chokevivat, and Chris Collins

The official slogan of the 1996 International AIDS Conference in Vancouver offered an inspiring image, "One World, One Hope." But at the opening ceremony an AIDS activist stood at the podium and turned that slogan into a difficult question, "Whose World, Whose Hope?" A major theme of the week-long event had been born: now that new therapies are showing promise in the treatment of AIDS, access to these drugs must be extended to those who cannot afford the more than US$18,000 annual price tag.

In the months since July 1996, it has become clear that the good wishes in Vancouver will not translate into widespread international access to protease inhibitors and other new drugs. For the vast majority of people in the world, improved prevention is likely to remain for a long time the only available strategy to control AIDS. Public health officials know there are few more valuable prevention tools than an effective, widely distributed vaccine. But the same question applies: whose vaccine?

Many behavioral interventions have proven effective at reducing risky behaviors and will remain essential even if a vaccine becomes available. Yet an inexpensive preventive

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vaccine for HIV has the potential to overcome many of the complex obstacles which have limited the effectiveness of other prevention methods: the challenge of delivering culturally appropriate and persuasive HIV education to all populations; political limitations on prevention messages; personal difficulties in consistently practicing safer sex; lack of power and control in sexual situations; a premium on unprotected sex in sex-for-money exchanges; limited access to condoms and clean needles; and physiological factors contributing to infection such as untreated sexually transmitted diseases (STDs).

If human rights are understood to incorporate adequate health care and prevention resources, then an accessible, easy-to-administer HIV vaccine would be an enormous victory for human rights, particularly in poorer countries hit hard by the epidemic. But even in rich countries, a vaccine could extend effective prevention to populations that are especially hard to reach with behavior-based prevention interventions, including individuals without access to health care or prevention services and those who fail to consistently practice safer sex because they do not perceive themselves to be at risk for HIV infection.

Respect for human rights has been considered a linchpin of successful HIV vaccine research and testing. The potential for discrimination and physical harm to vaccine trial participants, as well as the possibility of limited access to an HIV vaccine when one is developed, raise legitimate human rights concerns. Without respect for the rights of participants in trials, there will be few willing volunteers. Without public confidence in the ethics of trials, there will be little support for research. Without widespread and equitable access, a vaccine will protect a few lucky individuals rather than contribute to the control of the epidemic.

The human rights issues involved in HIV vaccine research are potentially as challenging and important as the other hurdles that must be overcome to achieve a vaccine: the daunting scientific obstacles, the cost of research and trials, and the disincentives for private investment in HIV vaccine research. Though progress on HIV vaccine research has not proceeded as rapidly as originally predicted, more than 25 experimental preventive HIV vaccines have been evalu-

ated in small clinical trials worldwide, and candidate vaccines are now being readied for large scale Phase III trials in the coming years.[1,2]

HIV vaccine-related human rights issues can be considered in two primary areas: rights and protections for participants in human trials of HIV vaccines, and broader issues of equity and access affecting whole populations.

Human Trials of HIV Vaccines

Large-scale human trials of HIV vaccines will fundamentally be an exercise in trust—in the safety of products, the intentions of trial sponsors and researchers, and the worthiness of experimental vaccines. Inevitably, public controversy and scientific disagreement about particular vaccine candidates will surround any trials. Without adequate safeguards, participants may find themselves treated as experimental subjects by researchers and foreign pharmaceutical companies. Vaccine trial participants may be asked to put themselves at some risk of harm as well as of potential discrimination in insurance, travel, and other areas of life. In some countries, trial participants may again be recruited from vulnerable communities—those that have experienced past abuses in biomedical research or have been denied the benefits of research in which their members have participated.

Human rights advocates have long acknowledged the fundamental importance of confidentiality and non-discrimination for people with HIV and AIDS. And though only HIV-negative individuals will be enrolled in preventive HIV vaccine trials, guarantees of protection of confidentiality and assistance to address potential discrimination are essential. Participants in vaccine trials should be assured an adequate informed consent process, compensation for medical treatment for any harm caused by the trial vaccine, quality behavioral interventions, the ability to participate in a trial without coercion, and continuous involvement of community-based organizations in trial design and monitoring.

Each of these issues is complex and requires the involvement of locally-based community members, scientists, and ethicists, among others. The potential for discrimination clearly exists: early testing of HIV vaccines in the United States has demonstrated that trial volunteers risk putting

themselves at social, as well as physiological, risk. Because current vaccine candidates make some vaccinees test positive on the standard Elisa HIV antibody test, a few uninfected trial volunteers allege that they have experienced difficulty with international travel, government employment, and acquisition of life and health insurance—all areas in which discrimination against people with true HIV infection remains legal in many countries, including the United States.

Whether or not they test positive on HIV antibody tests, trial participants may be subjected to discrimination simply because, as trial enrollees, they are perceived to be in a particular "high risk" group, such as gay men, drug users, or sex workers. A comprehensive article on ethical issues in international HIV vaccine trials noted that "...the very activities...that place potential subjects at risk for HIV, and thus make them desirable research subjects in a phase III trial, may place them at risk for social and legal sanctions."[3] It is also possible that employers, landlords, and others may misunderstand the purpose of the vaccine trial and assume participants have HIV or AIDS. Participants in HIV vaccine trials therefore need ongoing legal assistance and social support to help them address any instances of trial-related discrimination that may occur.

Another necessary protection for participants is provision of medical care (or compensation for medical care) to individuals injured as a result of their participation. Relevant here is the wealth of medical ethics literature which argues that participants in clinical trials should be compensated for any injuries related to their participation. For example, guideline 13 of the *International Ethical Guidelines for Biomedical Research Involving Human Subjects* states that "research subjects who suffer physical injury as a result of their [trial] participation are entitled to such financial or other assistance as would compensate them equitably for any temporary or permanent impairment or disability."[4]

Behavioral effects of trial participation must also be anticipated and thoroughly addressed. There is always the danger that participants in a vaccine trial will be more likely to put themselves at risk of infection, having assumed that the unproven vaccine is providing them with full protection. It is therefore essential that, throughout the trial, participants

have access to information and receive ongoing behavioral interventions and condoms to help them protect themselves from infection.

The avoidance of coercion in the recruitment of participants is another critical precept in the conduct of HIV vaccine trials. Yet there is a delicate balance to be struck between adequate reimbursement to compensate trial participants for expenses related to trial participation, and the absence of financial and other enticements designed to encourage participation. Community members should be engaged in order to help researchers think through this and other complex issues. Individuals from populations affected by the epidemic where the trial takes place must participate in the development of trial protocols and informed consent procedures, and be involved in addressing all matters relevant to the assurance of safe and respectful treatment of those who volunteer for trials.

Equity and Access Issues

HIV vaccine research raises many broad equity issues that concern whole populations. Attention to these issues requires working not just with governments and international organizations, but engaging private industry as well.[5] Several questions are important to consider. Is the vaccine product being tested suitable for use in the population participating in the trial? Is the vaccine's delivery mechanism and suggested regimen appropriate for the local population? Has the product been tested in the country in which it was developed? And the issue with the widest reach: will there be broad public access to the vaccine in the country of testing if the vaccine proves to be effective at preventing HIV? Only when these questions are addressed can prospective trial participants judge for themselves whether they are pioneers taking calculated risks in order to end the epidemic in their own communities, or merely testing a product for use primarily among individuals with access to preventive health care in rich countries.

International access to whatever vaccine is eventually proven effective is a crucial issue and one that has thus far received relatively limited attention. Pharmaceutical companies, government, researchers, and members of affected

communities must begin to address strategies to extend widespread international access to whatever vaccine is eventually licensed. Today, HIV vaccine pricing and access issues may seem like distant concerns, but the limited availability of protease inhibitors in poorer countries demonstrates the importance of advance planning for access. Absent an international plan for subsidized access to vaccines, there are few compelling reasons for individuals in poorer countries to participate in trials.

Options for increasing access include use of a two-tiered pricing system, patent donation by manufacturers, direct purchase by international organizations, and a patent "exchange" in which the country donating a vaccine patent for international distribution is provided with a patent extension on another product.[6] Organizations such as the International AIDS Vaccine Initiative, which finance targeted vaccine research, may partially begin to address access issues by retaining limited patent ownership on research it helps finance.

But access issues are also pressing in richer countries such as the United States. HIV vaccine trials in the United States are likely to draw many volunteers from younger, lower-income populations, as they have become the main focus of the U.S. epidemic. It is likely that many of these individuals will not have health insurance coverage which would include access to new vaccines.

Recent action by international organizations and individual governments to increase their focus on HIV vaccine research and improve coordination of research efforts are encouraging. In addition, volunteers in the first large-scale HIV vaccine trials are likely to make more sense of their participation if, through increased media attention, they believe they are working in concert with dedicated researchers and industry scientists.

Efforts to secure the rights and assurances outlined above may be seriously complicated in cases where large-scale human trials of HIV vaccines are sponsored by private industry, rather than governments or international health organizations. In the United States, activists have worked closely and cooperatively with staff at the National Institute of Allergy and Infectious Disease (NIAID) and other public research institutions in order to assure community involvement and

address the concerns of trial participants. It remains to be seen whether affected communities in all countries where trials occur will have the same level of access and influence with trial sponsors, particularly if those sponsors are not affiliated with public sector institutions. It is incumbent upon scientific researchers and trial planners to insist upon adequate community involvement in HIV vaccine trials that are sponsored by private sector companies.

Finally, recent controversy over clinical trials of short course AZT in Africa foretells similar debates for vaccine trials. As Barry Bloom has pointed out, the increasing use of antiretroviral therapy early in the treatment of HIV infection in the U.S. has important implications for vaccine trials.[7] It is likely that, in the United States, vaccine trial participants will be offered antiretroviral therapy if they become infected with HIV through unsafe sex or drug use practices. But what about individuals in poorer countries who become infected while in an HIV vaccine trial? Would they be offered therapy that is not widely available to others in the country? Is it appropriate to use different standards of care for HIV vaccine trials in different parts of the world? The Joint United Nations Programme on HIV/AIDS (UNAIDS) is in the process of conducting regional consultations on ethical and human rights issues involved in HIV vaccine trials, and it is hoped some consensus on this and other related dilemmas will emerge from these meetings.

Perspectives on HIV Vaccine Testing

In 1991, the World Health Organization's Global Programme on AIDS (GPA) visited 14 developing countries to determine sites for evaluation and development of potential HIV vaccine efficacy trials. GPA identified four priority countries having high incidence of HIV infection: Thailand, Brazil, Rwanda, and Uganda. Large-scale vaccine trials were also planned in several industrialized countries, in particular the United States.

Given the complexity of issues encountered in designing and implementing HIV vaccine trials, there is a need for best practice to emerge as trials proceed. The process of collective learning requires that a dialogue is assured between those involved in vaccine design and production, the intended

beneficiaries of these new products, communities participating in trials, and policy makers. To describe the current status and progress achieved in opening and sustaining this dialogue, below are perspectives from three countries, each with plans to conduct HIV vaccine tests in large-scale population-based trials in the near future.

In Brazil, the conjunction of activities surrounding preparations for an HIV vaccine trial with public debate concerning the ethical aspects of an ongoing clinical trial resulted in increased attention towards the involvement of affected communities in vaccine research programs. In Thailand, concurrent with intense HIV prevention efforts, the government has taken gradual steps towards the development and implementation of procedures to verify the compliance of planned HIV vaccine trials with international scientific and ethical standards. In the United States, at a time when past abuses in medical research are coming under increasing scrutiny, community advisory boards are being created to work closely with government and private sector interests in large-scale HIV vaccine trials.

The Involvement of Brazilian Nongovernmental Organizations with HIV Vaccine Trials

In 1991, Brazilian nongovernmental organizations (NGOs) welcomed the meeting of the World Health Organization (WHO) with Brazilian authorities to discuss the initiation of a protocol for HIV vaccine trials in Brazil. Now, seven years later, important progress has been made. A National Committee on HIV Vaccines has been created within the Ministry of Health, with five positions for NGO representatives. Three research centers for HIV vaccines have been created in the cities of Belo Horizonte, Rio de Janeiro, and São Paulo, and several documents have been produced by the National Committee, including a "National Plan on Anti-HIV Vaccines," and a "Position of the Ministry of Health on Anti-HIV Vaccines."[8]

Current research and NGO activities in Brazil

Stimulated by this initiative, some important studies have been completed or are on course. These include behavioral and seroincidence studies on four cohorts of men who

have sex with men (MSM): one in Belo Horizonte, one in São Paulo, and two in Rio; and two Phase I clinical trials, involving 15 volunteers each. Both clinical trials, which tested the peptide V-108, produced by United Biomedical, were recently completed. The laboratories involved have also performed HIV subtyping, in collaboration with a global network of laboratories. As a result, the predominance (80 percent) of a special kind of the B subtype has been determined, together with the presence of subtypes C, F, and D. In addition, some surprising cases of coinfection have been reported and published. It is hoped that the predominance of subtype B, the same subtype as in some industrialized countries, may mean that vaccines effective for these countries can also be effective for Brazil.

In 1994, the informed consent procedures for prospective trial participants, developed in collaboration with NGOs, were presented and discussed at several national workshops. NGOs organized two national meetings on vaccines (1994 and 1996) and have published three bulletins with up-to-date information on HIV vaccines. These activities have been sponsored by the Ministry of Health. During the First Brazilian National Meeting on Anti-HIV Vaccines in 1994, a global Community Vaccine Network was formed by 150 NGOs from 40 countries.[9]

On the whole, there are unequivocal advantages to Brazil's taking part in all of these efforts. Light has been shed on the ethical and human rights dimensions of several issues until recently ignored: behavioral and seroincidence studies, HIV subtyping, and research ethics within the AIDS community. Discussion of this last topic has been of great value in the pursuit of ethical drug trials for treatment of persons with AIDS (PWAs). Although drug researchers have not followed the same steps as vaccine researchers, NGOs have used their experience with vaccine research to understand and question drug trials.

The discussions on vaccine trials have helped establish an understanding of the importance of including human rights concepts in trial research design. The participation of NGOs from the first moments in these discussions, and community commitment to participation in all phases of the trial, has obliged some NGO members to deepen their knowledge

of the issues involved. This attitude, and the willingness to share with their communities both problems and the knowledge necessary to follow up and draw conclusions, has resulted in the conduct of several NGO workshops on vaccines.

Initial feelings among NGOs about the trials included both suspicion and hope. Fears that foreign companies were using Brazilian citizens for their own research interests were calmed by recognition that trials with local volunteers were also being held in the country that produced the candidate vaccine.[10] However, fears were exacerbated by the conduct of trial 028, which concerned a new protease inhibitor (indinavir). Trial 028 compared the clinical outcome of three treatment regimens: indinavir, AZT, and AZT and indinavir combined. At the beginning of 1995, physicians from São Paulo had consulted with NGOs about these planned protease inhibitor trials. Some members of these NGOs even joined the trials as volunteers.

The main concerns about the conduct of the 028 trial included: 1) delays in adding a second drug to the AZT regimen; 2) refusal to add drugs to the indinavir monotherapy; 3) refusal to provide the results of the viral load assays to the volunteers; and 4) refusal to change therapy, even after the appearance of AIDS-defining clinical symptoms, such as persistent diarrhea, weight loss, or declining CD4 counts.

All of these concerns were brought to the attention of the Ethics Committees of the five health institutions involved, and the Physicians Regional Council (CRM). The Ethics Committees were cooperative, and the Data and Safety Monitoring Board (DSMB) also supported the investigation.

São Paulo state NGOs, through the Community Advisory Board, publicly denounced the trial on November 18, 1996. The story was covered by Brazilian television and other media, and also received a great deal of media attention in the United States. By March 1997, the National Ethics Committee declared that drugs should be added to the monotherapy arms of the study, and that the results of the assays must be provided. The CRM is still investigating the trial.

This controversy unfortunately reinforced suspicions that volunteers in developing countries are exploited by pharmaceutical companies from the industrialized world.

Discrimination against volunteers in their personal life

As the design of trial 028 was being debated, Phase I vaccine trials were being completed and preparations progressed towards large-scale HIV vaccine trials, including the selection of volunteers. In the Phase I trials, some of the initial group of 15 volunteers experienced stigmatization when they acknowledged to families and friends that they were trial volunteers.[11] It is widely believed that these individuals were paying a price because they were the first to volunteer. Some decided to publicly acknowledge their participation, considering their volunteerism a question of citizenship and collaboration with society. The concerns of the volunteers were addressed through interactions with a multidisciplinary trial team. All those who experienced stigmatization were able to resolve their problems, except for one, who remained in the trial but decided not to ask for further aid from the team. He is a widower who lost the guardianship of his child to his mother-in-law, and is currently appealing this decision.[12]

Releasing news on incidence within stigmatized communities

Epidemiological and behavioral researchers, especially in the Bela Vista Project (São Paulo), developed several activities for volunteers enrolled in the large-scale vaccine trial in order to provide a sense of group and community. For instance, at the Bela Vista Project, gay films are exhibited every other Thursday, and workshops on current gay issues are held regularly (such as gay couples recognition, gay pride day, etc.). It seems likely that as a consequence, there was great compliance within the cohort.

Stigmatization of trial participants has largely been the result of irresponsible media attention. For example, when incidence data about the MSM cohorts were released, some newspapers reported infection and condom use rates without contextualizing them. For example, one article was entitled "49% Of Homosexuals Do Not Use Condoms Regularly," ignoring the fact that the heterosexual population has a far lower rate of condom usage.[13] Another article referred to volunteers in the cohort who did not use condoms consistently as playing "Russian roulette."[14] Perhaps the press's motivation for this kind of statement lies in the papers' interest

in attracting more readers via sensational headlines. Are these data used to stigmatize gay men more than others? It would certainly appear that these data could be presented more responsibly.

Vaccine trials in Brazil have come far, but there is still much room for improvement. The participation of NGOs in trials and the independence of trial monitoring boards are essential components in any vaccine trials. Possible dangers—including the stigmatization of minority populations, the reinforcement of prejudice by a sensationalistic press, and the questionable practices of foreign researchers working in developing countries—remain of great concern.

Preparation for HIV Vaccine Trial in Thailand

The first reported AIDS case in Thailand was a student who became ill while he was studying in the United States. He returned in 1984 to die in Thailand. The epidemic began to grow in Thailand in 1987 among homosexual men and intravenous drug users. Later, HIV/AIDS rapidly spread among female sex workers (FSWs), their male clients, and, finally, to families.[15] Thailand has put a clear policy into place to deal with the AIDS crisis. Top-level authorities give high priority to the problem, demonstrated by the fact that the Prime Minister serves as the Chairman of the National AIDS Prevention and Control Committee (NAPCC). During the decade since the start of the epidemic, there has been an extensive education campaign, and every six months since 1989, a sentinel seroprevalence survey has been conducted in various groups of the population. Thailand was one of two developing countries to receive recognition from UNAIDS at the 1996 International AIDS Conference in Vancouver for its successful national HIV/AIDS prevention and control program. The country's openness in policy, concern across all sectors, and successful nationwide condom promotion program have been the keys of that success.

There is increasing evidence of the success of these efforts. HIV prevalence is decreasing in Thailand, especially among male military conscripts. The rate of condom use among FSWs has increased remarkably, from 14 percent in early 1989 to more than 90 percent in 1996.[16] The number of reported STD cases for both men and women has declined

incredibly, from 365,525 in 1987 to 29,362 in 1996. By 1996, it was estimated that a 100 percent condom usage program among FSWs had already prevented 2 million HIV infections.[17] Nevertheless, projections from sentinel surveillance data estimate that the cumulative number of HIV-infected persons may have reached 850,000 by mid-1996, with infections among pregnant women, including some FSWs, continuing to rise. More recent data indicates a decline in the national HIV prevalence, but the infection rate is still high in many provinces. It is clear that an HIV vaccine would be an important prevention tool for the Thai population.

Measures taken

Thailand, with GPA support, created a "National Plan for HIV/AIDS Vaccine Development and Evaluation." The National Plan was inaugurated in 1993, with one of its main objectives being to protect trial volunteers.

The Plan's guidelines included ethical provisions; the volunteers would have to be well-informed about the study, informed about the risks involved in participation, and able to decide voluntarily whether or not to participate, based upon proper education and counseling. Further, the National Plan stated that the vaccine candidate(s) must be safe, as determined by sufficient data from animal and Phase I studies from the country of the vaccine's origin. In addition, in case of health problems resulting from the trial, participants would have to receive appropriate care and compensation with at least five years of long-term follow-up care for side effects.

Other important measures in the National Plan involve safeguarding the confidentiality of volunteer information, and providing access to testing that differentiates between natural infection and vaccine-induced immune response. Procedures were developed to assist trial volunteers in the event of problems resulting from a vaccine-induced positive serology tests, such as seeking life insurance, applying for a job, or traveling internationally.

In order to monitor the above standards as well as to lend support to research on HIV vaccines, the NAPCC and the Ministry of Public Health assigned the National Plan two sub-committees. The Technical Sub-Committee is responsible for reviewing proposals and protocols pertaining to con-

duct of HIV/AIDS vaccine-related research, and ensuring that vaccine protocols meet appropriate regulatory requirements and are followed rigorously. The Ethical Review Committee of the Ministry of Public Health is responsible for ensuring the safety and rights of individuals participating in research studies, and using internationally approved guidelines for research, including those developed by WHO and the Council for International Organizations on Medical Sciences (CIOMS), on human subjects.

Thai researchers have taken several additional steps to ensure the ethical treatment of participants in HIV vaccine trials. First, the NAPCC mandated that any AIDS vaccine research protocol must receive approval by both the Scientific Committee and the Ethical Review Committee. This has become the mechanism for ensuring that all submitted projects conform to scientific as well as ethical standards. Second, every AIDS vaccine research project in Thailand must be guided by a DSMB or oversight committee. Third, at the beginning of volunteer vaccination, ethical review committee members are invited to observe the procedures to ensure proper conduct. The Ministry of Public Health is also trying to improve the system by paying more attention to infrastructure and data management.

Collaboration with institutions in industrialized countries, such as the U.S. Centers for Disease Control and Prevention (CDC) and National Institutes of Health (NIH), or international authorities, such as WHO and UNAIDS, is greatly needed. State-of-the-art information is key to the ability of the Ethical Review Committee to fully address its responsibilities.

In addition to scientific issues, AIDS vaccine research has a social component, especially the possibility of the volunteers feeling exploited for the purpose of scientific research. The Ethical Committee keeps track of ethical issues and approaches taken in other countries to help guide its own decision-making. For example, it is widely known that the science behind the first purported AIDS vaccine was unsound, and was merely a device for boosting the stock market value of the company in question. This episode has served as an object lesson for the Ethical Committee's plans for the future.

The Ethical Review Committee has developed criteria to be used specifically for AIDS vaccine trials. Submitted research proposals should be supported with documented evidence showing approval for clinical studies in Phase I, Phase II, or Phase III issued by the national authorities dealing with vaccine trials in the country in which the vaccine originated. In the United States, for example, approval would be required in the form of an Investigational New Drug (IND) approval, or other approval from agencies such as the Food and Drug Administration (FDA), or the National Institute of Health (NIH).

The first AIDS vaccine research began in 1993 with Synthetic Peptide V3 Loop, BMN strain produced by UBI, Inc., USA. This was followed by two projects, in 1994 and 1995, respectively: Recombinant gp120 MN of Genentech, USA, and Recombinant gp120 SF2 of Biocine, USA. All three studies were in Phase I. Currently, Thailand is preparing cohorts in three groups (cohorts of army conscripts, recovering IDUs, and STD clinic clients) for Phase III vaccine efficacy trial.

The AIDS vaccine development plan has been revised. In 1988, Thailand allocated a budget of US$185,000 for an HIV/AIDS prevention and control program. This was the first year funds were allocated specifically for HIV. The budget increased to US$87,875,400 in 1996, 72 percent of which was allocated for clinical care, 11 percent for prevention campaigns, 4 percent for social support, 3 percent for research, and 10 percent for training and administrative work.

With no history of a designated budget for AIDS vaccine development, in 1996, the government established the Vaccine Sub-Committee under the National AIDS Committee, to replace the former Technical Sub-Committee on AIDS Vaccines with broader responsibilities for AIDS vaccine development and scientific review of protocols for vaccine study. The Ministry of Public Health established the HIV/AIDS Vaccine Development and Evaluation Collaborating Center to serve as a secretariat for this Committee, with UNAIDS funding the early phase. Ethical reviews, however, remain the responsibility of The Ethical Review Committee of the Ministry of Public Health.

In the past, most non-HIV vaccines were developed and tested through Phase III trials in industrialized countries.

However, it appears that it is difficult to establish an appropriate cohort to use for Phase III AIDS vaccine efficacy trials in these countries because the incidence of HIV infection is low. Collaboration with developing countries that have high incidence rates is therefore necessary. However, protection of volunteers must be based on the same principles and practices used in industrialized countries. Through appropriate public relations, the public should understand that the study is important and that the researchers have no intention of abusing volunteers. All volunteers should receive proper education and counseling to prevent HIV infection.

The magnitude and widespread occurrence of HIV disease in most all countries means there is an urgent need for efficacious vaccines. The governments of countries where vaccine trials are being considered must be prepared and have the power to bargain with vaccine-producing companies to assure fair and equitable access, in case the vaccine is proven effective. To achieve these objectives, international organizations such as UNAIDS, well-known research institutions such as the NIH, Pasteur Institute, or the CDC can serve as coordinators and work with the vaccine companies and institutions in developing countries. Finally, the governments of the countries with good potential for funding support, such as Thailand, should consider investing in AIDS vaccine development to reduce the time it will take to develop an effective product for everyone.

Securing Participant Rights in the United States

Despite major advances in the ethical conduct of biomedical researchers in the United States, and recognition of the human rights dimensions of research involving human subjects, the potential for government abuse of individuals is a matter of record, and vivid in the minds of many potential HIV-vaccine trial participants. It is over two decades since the end of the infamous Tuskegee experiments, during which penicillin was withheld from African-American syphilis study participants. It is only several months since a series of conflicting reports raised concerns about exposure of American soldiers to toxic substances during the Gulf War, and about the government's apparent lack of openness regarding these

potential exposures. Differential access to health care is a reality in the United States.

With large-scale human trials of HIV vaccines on the horizon in the United States, there has been an initial tendency among both researchers and community representatives to emphasize the need for "trust-building" and "community education." But a solitary emphasis on trust building implies that trial participant concerns represent more a problem of perception, rather than legitimate fears. Alongside trust building, there must be tangible actions to address ethical issues and protect human rights in the conduct of biomedical research.

Fortunately, the U.S. National Institute of Allergy and Infectious Diseases (NIAID) has actively involved community members in preparations for trials and has worked closely with these representatives to address specific issues of concern. This is the first step in a human rights approach to the conduct of clinical trials. AIDS treatment activists set the standard for community representation in clinical trials research in the United States, and U.S.-based HIV vaccine trial sites have incorporated many of these standards. Each trial site has its own community advisory board (CAB) and CAB members are full members of key national trial planning and protocol committees. In addition to representing community perspectives and concerns on these committees, CAB members have secured additional protections for individual trial participants in three chief areas.

- *Compensation for trial-related injuries.* In 1995, soon after HIVNET (the NIAID-sponsored network of vaccine trial sites) was established, CAB members asked for a guarantee that trial participants would be compensated for trial-related injuries. Two years later, after continued pressure from CAB representatives, NIAID stated that the two manufacturers of vaccines slated for Phase II testing had agreed to a trial protocol stating that compensation for medical expenses necessitated by serious trial-related injury will be paid by vaccine manufacturers.[18]
- *Ongoing efforts to alleviate social harm.* So far, NIAID has been effective in working with insurers,

government agencies, and others to restrain most instances of discrimination against Phase I and II vaccine trial participants. CAB representatives and members of the community-based group, Vaccine Advocates, requested a guarantee that services addressing incidents of discrimination would be provided as long as needed after conclusion of a specific trial. Such ongoing assistance is necessary since trial participants may test positive on standard HIV antibody tests and be subject to other forms of discrimination after completion of the trial.[19] In response to these requests, NIAID noted that the agency "plan[s] to continue these services to our participants as long as needed, well past the conclusion of our trials."[20]

- *Provision of HIV prevention counseling to volunteers and the community.* Other tangible results of CAB activity have been the incorporation of extensive HIV prevention counseling protocols, collaborative work between trial study sites and community-based prevention agencies, creation of support groups for trial volunteers, and community-wide information sessions. These efforts have been critical to address community mistrust of federal research programs and to ensure the success of research activities.

In the United States, vaccines are becoming an increasingly visible issue on the AIDS activist agenda. Two community based groups, the AIDS Vaccine Advocacy Coalition and Vaccine Advocates, have formed to press for increased investment in HIV vaccine research, adequate protection for trial participants, and broad access to an HIV vaccine when licensed.[21]

Conclusion

Respect for human rights and attention to ethical issues is key to the development and distribution of HIV vaccines—our best hope to control the global HIV epidemic. It would be a dangerous mistake to identify good science, trial participant rights, and community involvement as competing interests in the HIV vaccine trial process. Building and maintaining trust in the HIV vaccine research enterprise is neces-

sary to launch and sustain a series of large-scale human trials over many years in several countries. Attention to the multiple issues involved in HIV vaccine research is essential in order to ensure trials are ethically grounded in human rights principles. This will maximize the chances that scientists will eventually develop a widely useful and accessible vaccine to fight HIV.

References

1. In 1983, then Secretary of the U.S. Department of Health and Human Services, Margaret Heckler, predicted development of a vaccine for AIDS within a few years.

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4. The Council for International Organizations of Medical Sciences in collaboration with the World Health Organization, *International Ethical Guidelines for Biomedical Research Involving Human Subjects* (Geneva, 1993), p. 36.

5. For further discussion on the status of private industry investment in HIV vaccines and governmental options to increase investment see: AIDS Vaccine Advocacy Coalition, *Industry Investment in HIV Vaccine Research* (San Francisco: AVAC, 1996) (also viewable on the World Wide Web at http://www.vaccineadvocates.org).

6. For further discussion on access issues see note 3, p. 300.

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10. This concern was the subject of a long article entitled "The Guinea Pig" in an important weekly magazine, *Veja* 1329 (March 22, 1995).

11. Panel on Clinical trials. II National Meeting on Anti-HIV Vaccines, Rio de Janeiro, Brazil, October 10, 1996.

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14. *Folha de São Paulo,* December 1, 1996.

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17. N.J. Robinson, J. Noah, N. Silarug, A.B. Surasiengsunk, R. Hanenbeg,

et al., "Two Million HIV Infections Prevented in Thailand: Estimate of the Impact of Increased Condom Use," Program Supplement, XI International Conference on AIDS, Vancouver, July 7 – 12, 1996, p. 16.

18. Letter from Pat Fast, MD, PhD, Associate Director for Vaccine and Prevention Research, Division of AIDS, National Institute of Allergy and Infectious Disease, National Institutes of Health, to Tom Gibson, dated June 5, 1997.

19. The San Francisco-based AIDS Legal Referral Panel has noted that U.S. law may protect individuals from discrimination based on perceived HIV status resulting from HIV vaccine trial participation. This protection comes, in part, under the Americans with Disabilities Act, 42 U.S.C. 12102(2).

20. Letter from Pat Fast, MD, PhD, Associate Director for Vaccine and Prevention Research, Division of AIDS, National Institute of Allergy and Infectious Disease, National Institutes of Health, to VACT UP, dated May 29, 1997.

21. More information on these organizations is available on the World Wide Web at http://www.vaccineadvocates.org.