
VACCINE TRIALS: LEAVING COMMUNITIES BETTER OFF

What will poor communities in developing countries get out of agreeing to take part in AIDS vaccine clinical trials? The question is vexing, especially since the road to an effective vaccine is looking longer than once anticipated and the prospect of a vaccine that prevents HIV infection, as opposed to HIV disease progression, is not on the immediate horizon.

Given the long haul ahead, AIDS vaccine scientists, who are rushing to line up international vaccine trial sites in developing countries, need to focus on a key issue: How they can leave poor communities better off for having taken part in a trial even if the particular vaccine being tested turns out not to work or to be only partially effective.

As Seth Berkley, President of the International AIDS Vaccine Initiative (IAVI), puts it: “Communities participating in AIDS prevention and treatment trials, whatever the results, are contributing knowledge that is a global public good and should benefit in return.”¹

No more safari research

Fortunately, the world has moved a long way from the “safari research” that used to be conducted by Western scientists in poor countries. It is no longer considered ethical for researchers to parachute into impoverished communities, collect their data, and then leave without the community reaping any tangible benefits for having taken part in the study. Such an approach would violate international ethical guidelines,² and politically savvy communities in the developing world would no longer accept it anyway.

But how, exactly, can AIDS vaccine researchers contribute to the health and welfare of poor communities where vaccine trials will be conducted?

Much attention over the past year has focused on the provision of antiretroviral drugs (ARVs) to trial participants who become infected during the course of a trial. This is a critical issue—and a difficult one—since these drugs can dramatically reduce mortality rates from HIV, but they are not yet widely available in the developing countries where vaccine trials will be conducted. However, the major trial networks—including the US government’s HIV Vaccine Trials Network (HVTN) and the former US Army-sponsored network, IAVI, and the South African AIDS Vaccine Initiative (SAAVI)—have now all committed to making ARVs available as needed to trial volunteers. And they have laid plans for funding mechanisms (typically, an insurance fund) to pay for the drugs.

Important details—such as how long the drugs will be provided, whether infected family members will also qualify, and whether there will be an effort to provide ARVs to entire communities—remain to be worked out. But there is consensus among the trial sponsors that these life-extending medicines will at least be offered for free to trial participants who have breakthrough infections. That is an important



advance—and one that is not likely to break the bank. Only a small percentage of trial volunteers are expected to become infected during a trial and ARVs likely won't be needed until people develop symptoms, which could take as long as 10 years. By then, ARVs are expected to be much more widely available in the developing world.

ARVs are just one benefit

Providing access to antiretroviral drugs for trial participants, however, is just one way that AIDS vaccine researchers can leave poor communities better off. There are myriad benefits that AIDS vaccine trials can bring to host countries and to specific communities within those countries.

Ideally, specific benefits will be determined at the grassroots level as AIDS vaccine researchers engage with national and community leaders and with members of the community advisory boards (CABs), which advise local trial units. Each community may want and need something different.

To stimulate the dialogue, AVAC offers this checklist of ways that vaccine trials can leave communities better off:

- **Voluntary HIV testing and counseling.** Since vaccine trials involve HIV negative volunteers, people have to be tested for HIV before they can participate in a trial. As many AIDS vaccine researchers are now doing, the screening process should be used as an opportunity to introduce rapid HIV-testing kits to the community, and to teach local people how to administer tests and how to counsel those who test positive.
- **Support groups for those who are HIV positive.** In much of the developing world, AIDS carries more social stigma than it does in the industrialized world. By helping set up support groups for people who test HIV positive in trial screenings or turn positive during a trial, AIDS vaccine researchers can provide emotional support to people with HIV while helping to break the silence and prejudice surrounding the disease. While no substitute for broad educational programs, access to ARVs and treatment for opportunistic infections, group support can provide a pathway to testing and treatment not sought for fear of societal penalty.
- **Prevention of mother-to-child transmission (MTCT).** Short-course nevirapine helps prevent the transmission of HIV from infected mothers to their newborns. AIDS vaccine researchers can partner

with local health officials to provide this simple and inexpensive regimen and educate HIV positive pregnant mothers about its life-saving potential. Health care should extend beyond that to include provision of ARVs for these mothers on an on-going basis. Mothers must also be counseled about the complex issues surrounding the risks and benefits of breastfeeding in resource-poor settings.

- **Antibiotics and medicines to combat malaria and TB.** Quite apart from antiretroviral drugs, many communities in the developing world have little access to standard antibiotics and medicines to fight two leading killers—malaria and tuberculosis. As many research groups are now doing, AIDS vaccine trial units in developing countries should provide these medicines to trial participants. Vaccine trial units should also make treatments available for other sexually transmitted disease (STD) infections, which, if left untreated, can greatly increase the risk of people contracting HIV.
- **HIV prevention programs.** AIDS vaccine researchers are ethically required to educate clinical trial volunteers about what HIV is and how to keep themselves from becoming infected. Vaccine trials offer the opportunity to expand HIV prevention efforts into the larger community. Community advisory boards play an important role in this effort. If male and female condoms are not widely available in the community, vaccine researchers can use their leverage with public health officials and international aid agencies to provide them at no cost.
- **Professional training.** Vaccine trials can be an opportunity to expand the number of medical professionals—doctors, nurses, technicians, social workers and others—in short supply in many developing countries. Trials cannot proceed without trained professionals—and the people best able to understand and respond to the needs of a community will come from the community. Trials can offer not only on-the-job training, but also the chance for classroom and laboratory training at associated academic institutions in the host country or abroad.
- **Shared laboratory facilities.** Many AIDS vaccine trials research teams will be setting up laboratories to conduct tests on blood samples drawn from trial volunteers. Depending on what's being measured, these labs may use sophisticated equipment and a wide range of assays. In poor communities without access to advanced testing facilities, these labs might also provide services such as antibody tests, T-cell counts and viral loads to help public health officials treat HIV-infected people and track the epidemic in the local area.

AIDS vaccine researchers can provide certain benefits directly or they can link up with others who can provide them. Most importantly, scientists need to make certain that whatever is put in place to improve public health infrastructure can be sustained after the trials end.

A chilling example of what can happen without that commitment comes from an HIV prevention study in Zambia by researchers from the University of Alabama, Birmingham. During a temporary hiatus in the program due to a funding glitch, mortality rates among trial participants doubled. The reason was not diminished access to ARVs; none were provided to trial volunteers as part of the study. Rather, scientists attribute the jump in death rates to the fact that participants no longer had access to the TB and malaria medicines provided at the site.³

Some ethicists argue that providing these benefits offers an unfair inducement for people in poor communities to take part in AIDS vaccine clinical trials. If so, that would be a violation of international ethical guidelines. However, as Ruth Macklin, biomedical ethicist at Albert Einstein College of Medicine in New York, points out, the unfair inducement argument is relevant only when benefits offered during a trial provide an incentive for an individual to take risks that he or she would otherwise not take.⁴

In the case of AIDS vaccines, however, the medical risk of participating in an AIDS vaccine trial appears to be minimal. No product in the research and development pipeline is made with whole HIV so the vaccine cannot give someone HIV.

The larger issue is more related to social risk rather than medical: Will participation in a vaccine trial, for instance, stigmatize trial participants? For women in particular—who have little power in many traditional cultures—participation could mean ostracism from the family, loss of financial support and even physical abuse. That risk scenario is even more reason for AIDS vaccine researchers to ensure that trial sites have effective community-wide HIV education programs.

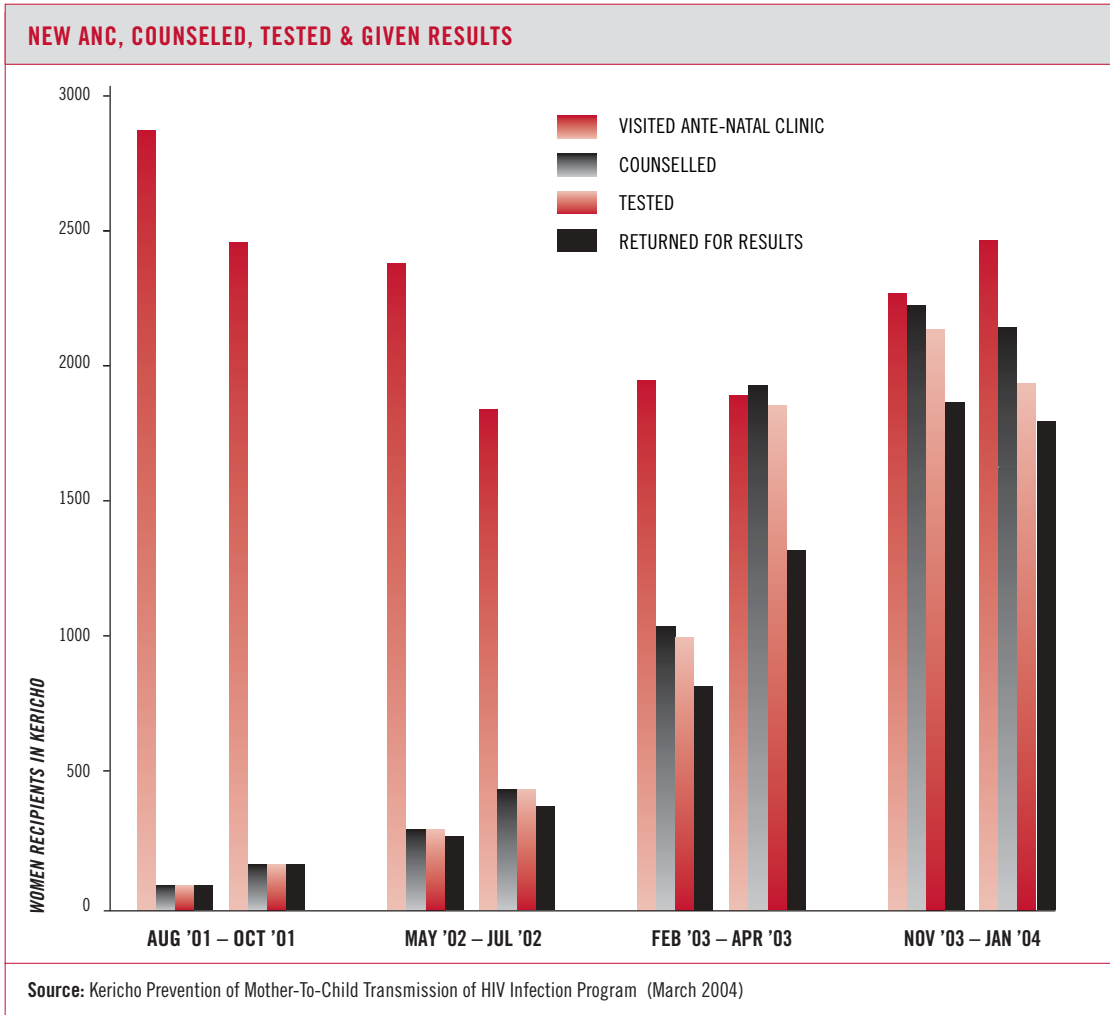
Kericho: A model program

While AIDS vaccine sponsors have launched a number of initiatives to improve public health at various trial sites in the developing world, a particularly outstanding effort is underway on the highlands of western Kenya. In a district known as Kericho, the United States Army Medical Research Unit (USAMRU) is



engaged in a comprehensive effort to prepare for a large-scale trial of the US government's DNA vaccine against clades A, B and C of HIV.

The trial site is a large tea plantation owned by the British-based James Finlay & Co. Ltd., a global tea conglomerate. About 18,000 Kenyans work at the company, either as pickers or tea processors. Virtually all live in company housing and receive medical care at the company hospital. An average picker makes the equivalent of \$1.65 a day based on the weight of tea picked. An estimated fifteen percent of all the workers are infected with HIV.⁵



Under the leadership of Merlin Robb, of the Henry M. Jackson Foundation, and Col. Deborah Birx, director of the US Army’s AIDS vaccine research program, scientists from the US and Kenya have teamed up to enlist senior management of Finlay and residents of Kericho in preparation for a trial of the Vaccine Research Center’s multi-clade DNA vaccine. If the vaccine works, it could reduce the incidence of HIV disease among tea workers while also boosting worker productivity.

The site team—which launched its effort nearly four years ago before any particular vaccine candidate had been selected for testing—views improvements in public health for the entire Kericho community as integral to the trial itself. “Our effort is to get a handle on this disease—whether we do vaccine research,



primary prevention or treat disease,” said Fredrick Sawe, a Kenyan obstetrician and gynecologist on the research team. “The end is the same. We are trying to stop this disease in its tracks.”

To that end, the vaccine researchers have conducted a community-wide education program to teach people about behaviors that put them at risk of HIV infection. The message has gone out not only in conventional brochures, but also in rap performances and condom distributions at pre-game soccer shows, and at “barazas” or traditional community meetings, where research staffers perform dramas about HIV prevention in both Kiswahili and English.

Until the research team came along, nobody had a handle on the prevalence and incidence of HIV infection in the area. Last year, the team recruited 3,000 volunteers and tested them for HIV. After six months, volunteers were tested again to determine the incidence of new infections.

With funding from the Elizabeth Glaser Pediatric AIDS Foundation, the team also brought the first program to prevent mother-to-child transmission (MTCT) to Kericho. As part of that effort, it built the community’s first ante-natal clinic on the grounds of the Kericho District Hospital. The clinic now offers short-course nevirapine to HIV positive mothers—and the same regimen is provided at twenty-two other centers upgraded as part of the program.

In setting up the MTCT program, researchers trained fifty-six nurses and counselors to implement the program, which includes post-test counseling for mothers who test positive or negative for HIV. Another thirty-six people were trained to do rapid HIV antibody testing.

So far, the team has not been able to provide ARVs at the site beyond the short-course nevirapine provided for HIV positive mothers and their newborns. By 2008, however, it hopes to have the capacity to offer ARVs to approximately 30,000 people in the Kericho district and in a neighboring district where workers have family members.

Who pays?

How ARV therapy for vaccine trial volunteers will be paid for has not yet been determined. Under federal regulations, the National Institutes of Health, which now oversees the Army’s AIDS vaccine research program, cannot use federal research dollars to fund treatment unless it is the focus of a particular study. A logical funder would be the President’s Emergency Plan for AIDS Relief (PEPFAR), the State Department bilateral program that will pump some \$9 billion of new US funding into AIDS treatment, prevention and care in twelve African countries, including Kenya, over the next five years. The program has agreed to provide an initial \$2.9 million to the site, but additional dollars are needed if drugs are to be provided more widely in the community as Army researchers have proposed.

The advent of generic ARVs opens an opportunity for the Bush administration's new program to provide treatment for large numbers of people. However, the administration has balked at providing generics—a decision that needs to be reconsidered as the program rolls out.

The Finlay Co., which stands to achieve productivity gains from a healthier workforce, is currently underwriting the cost of upgrading health-care infrastructure on the plantation and adding nurses and other medical personnel. If the Army can demonstrate the benefit of providing ARVs to the HIV-positive workforce, Finlay will likely pay for the medicines, says Col. Birx. Such an approach has been adopted by gold-mining conglomerates in South Africa.

In order to extend the ARV program to all in the Kericho area who need them, however, additional funds need to come from PEPFAR. The site might also qualify for treatment dollars from the Global Fund to Fight AIDS, Malaria and Tuberculosis. However, the Global Fund is struggling to finance projects already approved and may be reluctant to pay for ARVs when the much-better financed PEPFAR program has already targeted Kenya for stepped-up treatment dollars.

Such Catch-22 situations are likely to arise at other trial sites. They speak to the need for more flexibility from both US and international agencies dealing with the AIDS pandemic, as well as closer collaboration among all players—trial networks for both prevention and treatment trials; bilateral/multilateral AIDS relief programs; and the public/private sector, particularly the Bill & Melinda Gates Foundation whose Global HIV Vaccine Enterprise initiative might set aside funding of ARV provision to entire communities where vaccine trials will be conducted.

Success in using AIDS vaccine trials to leave poor communities better off, however, is not just a matter of money. Fundamentally, it's attitude. Instead of doing research *on* communities, scientists need to do research *with* communities. Instead of narrowly focusing on trial outcomes only, scientists need to care about the overall health of individuals and their communities.

In Botswana, Harvard scientists have it right—testing an AIDS vaccine in the context of a national ARV program, largely funded by philanthropies. As Richard Marlink, executive director of the Harvard AIDS Institute puts it, “We commit to the health of Africa, not to a single project or proposal.”⁶

While not even Harvard is rich enough to provide health care for all of Africa, the intent is on the mark.

As AIDS vaccine trials roll out around the world over the next five to ten years, that's exactly the mindset the AIDS vaccine field as a whole needs to adopt—in Africa as well as in impoverished communities of eastern Europe, Asia, the Caribbean and Latin America. Without volunteers from these communities willing to roll up their sleeves and be inoculated, no effective AIDS vaccine will ever be developed for anyone.