

**When Progress is Incremental:  
Implications of a Partial Efficacy HIV Vaccine for U.S. Foreign Policy**  
*Council on Foreign Relations*

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“Today, let us commit ourselves to developing an AIDS vaccine within the next decade. There are no guarantees. I will take energy and focus and demand great efforts from our greatest minds.”

- U.S. President Bill Clinton, Remarks at Morgan State University, May 18, 1997

Over a decade has elapsed since President Clinton announced this bold commitment to the development of a vaccine to end the AIDS pandemic. Yet still today we find ourselves entrenched in the same battle with no end in sight, without a vaccine to curtail the rising rate of new HIV infections. Over 40 million people are currently infected with HIV and approximately 11,000 people are newly infected each day despite massive increases in global funding and political will to respond to the disease. How can this battle be won? Could an HIV vaccine be the panacea? Why has the development of an HIV vaccine taken so long?

In 2009 preliminary results will be released from trials of two HIV vaccine candidates that do not prevent infection, but rather, may boost the immune response against HIV, allowing infected individuals to live AIDS-free lives, or delay the onset of full blown AIDS, and eventual death. It is also possible that by bolstering the immune response against HIV, a vaccine would radically decrease the levels of viral contamination in blood and semen, thereby decreasing person-to-person transmission. If the 2009 clinical trial results indicate one of the vaccines offers a 50-65% efficacy, U.S. agencies and private American philanthropies will face tough decisions regarding when, where and under what circumstances to use the product overseas.

On July 11, 2007 the Global Health Program at the Council on Foreign Relations brought together leading experts in advocacy, research, and development of the HIV vaccine for a discussion moderated by Laurie Garrett, CFR Senior Fellow for Global Health and organized by Council members Michelle Forrest, Laura Efos and Betsy Williams. Seth Berkley, President and Founder of the International AIDS Vaccine Initiative (IAVI); Michael Robertson, Director of Clinical Research at Merck; and Mitchell Warren, Executive Director of the AIDS Vaccine Advocacy Coalition (AVAC) discussed the daunting challenges posed by HIV, the evolution of HIV vaccine research, the role a partial efficacy vaccine may play in quelling the infection, and the challenges the global community faces in implementing an HIV Vaccine program. The session was the fourth in the global health roundtable series “Can U.S. Foreign Aid Support What Works for Global Health?” developed with the Global Public Health Practice at McKinsey and Company.

Despite massive advocacy efforts, reenergized political will, and significant increases in financial support, our response to the AIDS epidemic has been sorely inadequate, focusing more on treatment and crisis management than attention to the prevention of new infections. Earlier this month the United Nations AIDS Programme (UNAIDS) released

data revealing that for each patient that started HIV treatment in 2006, six other individuals became infected with the virus.<sup>1</sup> The world's focus on treatment will become increasingly costly as people develop resistances to first line drugs and have to be moved to more expensive second and third line medications. The only way to curb the rate of infection and bottomless pit of spending is through the development and implementation of new prevention technologies, such as microbicides, male circumcision, post-exposure prophylaxis, and HIV vaccines. Beyond a humanitarian imperative, better prevention technologies are critical to capping costs, Berkley commented. A safe, effective, globally accessible, inexpensive HIV vaccine remains our best hope to control, and ultimately end the pandemic

Why has an HIV Vaccine taken so long to develop?

HIV could be the most formidable virus ever encountered by scientists. HIV is the ultimate chameleon; it reproduces at a rate of 10 billion copies per day, mutates rapidly as it reproduces, and there are multiple strains of HIV globally, within countries, and even within an individual, Robertson explained. Within days of infection, HIV begins to destroy critical immune cells rendering the body powerless to fight off infection. Finally, HIV inserts itself into the DNA of human cells where it can remain undetected indefinitely by the body's immune system. Even with extended drug therapy that reduces viral loads (measured as the quantity of viruses found in a milliliter of blood) to undetectable levels, HIV is never completely eradicated from the body:-

Vaccines typically work by mimicking the effects of natural exposure to a specific virus. After an initial exposure to a virus, the immune system develops the ability to recognize the specific microbe and can protect the body if it reappears. But in the case of HIV there is no beneficial "natural" immune response to mimic, as no human being has ever managed to clear the virus from their body. There are no human beings who carry effective antibodies that can neutralize and destroy HIV. In this, HIV stands as a radically greater challenge than those diseases – measles, polio, diphtheria, HPV, hepatitis B – for which vaccinologists have made successful products: In all of these cases significant percentages of people who are naturally exposed to the virus develop powerful antibodies that destroy the microbe. HIV, however, has thwarted scientists' attempts thus far to develop a classical preventative vaccine against the virus because of its ability to integrate into target cells and evade both detection and attack by the immune system.

"As far as we know, once you get the infection, you stay infected. No one is known to have fully recovered from or been 'cured' of HIV infection...at this time, we don't really even know what it would take to cure it," Robertson said.

None of the top HIV vaccine candidates currently in research and development holds promise of stimulating effective antibody responses, Robertson explained. Rather, if successful, the first HIV vaccines will boost a different arm of the immune system – the cellular or T-cell response – and thereby may reduce HIV levels in the body, delaying a progression to AIDS and the need to start antiretroviral drugs.

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<sup>1</sup> UNICEF, WHO, UNAIDS (2007). Towards universal access: scaling up priority HIV/AIDS interventions in the health sector: Progress Report, 2007.

## Current Status of HIV Vaccine Development

More than 30 candidates are currently in clinical trials in testing sites around the world. The expansion of testing sites to developing countries hard hit by AIDS is quite an achievement, commented Warren. In 1997 all trials were conducted in the US, UK, and Europe with as small fraction in Latin America and the Caribbean. Today, over 50% of trial sites are in countries where the epidemic is occurring in prevalence rates exceeding 5 percent of the general population. This is the best ingredient for success when the vaccine is available, because people will be familiar with the vaccine and be prepared for its introduction, Warren said. In HIV vaccines trials, volunteers are provided with the current state-of-the-art forms of protection technologies and behavior change education. While such general prevention campaigns are ethically prudent, they make it difficult to attribute incremental improvements solely to vaccine usage.

“Efficacy trials are not testing AIDS vaccines, they are testing the maximum forms of existing HIV prevention with an HIV vaccine candidate, versus maximum forms of existing prevention without a vaccine candidate”, Berkley explained.

In 2009, the preliminary results from two leading AIDS vaccine trials will be released. Both trials, one by Sanofi Pastuer and the other by Merck in collaboration with the National Institutes of Health (NIH) aim to boost T-cell immune responses. If the results from the Sanofi and Merck trials reveal that the HIV vaccine is only partially effective, and cannot significantly slow the spread of HIV within vaccinated communities, it begs the question “how good is good enough”, Warren commented.

An HIV vaccine with 50% efficacy, if administered to only 30% of the target population could still avert up to a third of new infections from occurring and therefore save tens of millions of lives, Berkley insisted, citing modeling studies done by IAVI.

“Even vaccines that don’t totally prevent infections and don’t work 100% of the time can be extremely useful vaccines,” Robertson said.

## Policy Challenges

Policymakers face many tough questions Robertson said: Should the FDA and other intentional licensing bureaus approve a partial efficacy vaccine for widespread use? How much will a vaccine cost and who will pay for it? How will we deliver the vaccine to those who need it most, including women and adolescents?

“We need to talk amongst ourselves, with policy makers, and with communities about this. There are a lot of very complicated results that will be much grayer than they are black or white,” Warren said.

A number of actions must be taken now in order to lay the foundation for the successful roll out of an HIV Vaccine, be that in 5 years, or in 20 years:

- *Fast track licensing and registration*

If a partial efficacy HIV vaccine leads to a licensable product, the U.S. government must find a way to facilitate fast track FDA approval and work with the G8 and leading developing countries to develop fast track approval and registration processes worldwide, Berkley said.

- *Clinical Guidelines*

The U.S must develop clinical guidelines for use of the vaccine to determine what settings are most appropriate, and which populations to target. The U.S. must also assist early adopter countries in the development of vaccine introductory plans that are customized to address the specific features of the epidemic in each country, Berkley said. All HIV vaccine roll-out strategies must be executed in tandem with existing prevention technologies.

“This I not as simple as eureka, we have a vaccine and lets just get it out to as many people we can. If you get an efficacy result, it’s not the vaccine alone. How do we roll these vaccines out, while still keeping the prevention strategies going?” Berkley asked.

“We should never seek to put the HIV vaccine in isolation from the rest – from other public health interventions in general or other HIV prevention strategies.” Warren cautioned. If the vaccine was used in isolation, without the accompaniment of other prevention strategies, the beneficial effects of the vaccine could be nullified by high-risk behaviors executed by individuals who falsely believe themselves to be immune to HIV infection.

“The vaccine alone is not the answer, it is part of the answer, but needs to be introduced in a larger prevention program,” Warren added.

- *Manufacture*

It is extremely hard for manufacturers to estimate the demand for a vaccine that is still in trials, Robertson said. Demand is likely to be dependent on clinical trial outcomes. It is also difficult to ensure that manufacturers will have the capacity to meet vaccine demand. Berkeley said. Incentives, financing and infrastructure should be forecast now, and manufacturers’ incentives are needed to spur innovations and discovery of new candidates, Berkley added.

- *Distribution and health systems strengthening*

There is currently no model for the delivery of vaccinations to adolescent and adults, and the delivery of available pediatric vaccines continues to be difficult in many parts of the world, Robertson commented. Much work needs to be put into strengthening health systems infrastructure, expanding cold chain capacity and investing in human resources, Berkley said.

“We know how to prevent babies from getting infected from their HIV positive mothers (PMTCT), we have this approach, but we cannot get it to people. This is what the world looks like today, so for all the work we are putting into developing a vaccine, we need to think about what we are going to do to move it forward,” Warren said.

- *Financing*

There is currently no funding mechanism for implementing an AIDS vaccination program, even if the vaccine is made available at no-profit prices. Berkley discussed some option for

financing including GAVI, AMC, and GFATM, but agreed there is currently no appropriate funding mechanism. A broad commitment from the G8 and leading developing countries for a vaccine purchasing scheme is critical. Equally critical is a sustained political commitment to continued vaccine research and development regardless of the outcome of the current clinical trials. Lack of sustainable political will and financial commitment has inhibited efforts in the past, and will do so in the future if AIDS vaccine research is not integrated into general AIDS and public health priorities, Berkley explained.

“Its amazing to me that I still have to argue for AIDS vaccines in political forums when we are spending tens of billions of dollars now and forever because people continue to get infected and you have to continue treatment for life - and people are still not talking about new prevention technologies - the fact that we have to advocate for this is a failure on the policy side, not the science side,” Berkley added.

### The Way Forward

Regardless of the immediate outcomes of the HIV vaccine candidate trials, commitment to the development of a policy framework that enables conditions for innovation is required for further research and development of prevention technologies to curtail the pandemic. “It is of critical importance that all partners dedicated to AIDS vaccine development and implementation work together to ensure the trial results are handled effectively – be they positive or negative,” Robertson reiterated.

#### - *Scientific Innovation and Prioritization*

There is a need to expand the pipeline for potential vaccine candidates. The only hypothesis currently being tested is based on cell-mediated immunity. These attempts need to be complemented by strategic efforts to find ways to elicit neutralizing antibodies and control HIV infection, Berkley said. Robertson noted that many of the bottlenecks in pipeline development could be solved by creating a system to prioritize which candidates will be tested, by whom, and with what expected result. “We’ve struggled for a long time to figure out what are we going to test here,” Robertson continued. “We’ve been testing the same sort of general concept...we don’t need to test 30 vaccines that are doing the same thing. No one has wanted to give up their pet project. We need to get out priority schemes – not pursue vaccines based on who gets their first.”

The U.S. research and pharmaceutical communities must continue to build partnerships in developing countries where the pandemic is taking its biggest toll, not just for testing, but to support local research and innovation. “We need to be pulling science and new ideas from wherever it can come”, Berkley said.

#### - *Commitment to Equitable Access*

The best example of inequitable access to new medical technologies is the HPV vaccine Berkley insisted, describing it as “an incredibly safe, effective fabulous vaccine and here it is being rolled out in the North with no roll out plans in the South. This is a global disgrace.”

A critical challenge for all current and future U.S. foreign policy makers is to establish policies and fund programs that enable the benefits of new and existing medical technologies to be shared by all.

Although the American research and development community failed to meet Clinton's deadline for the discovery of an HIV vaccine, we can hopefully meet his objective. Until then, U.S. efforts must be focused on facilitating equitable access to existing prevention technologies and paving the way for new developments. "It's not what we do today until we have a vaccine, its what do we continue to do as we hopefully soon prepare to integrate a vaccine into all of the other prevention pieces we have and will have going forward", Warren concluded.