Eight Years and Counting: What Will Speed Development of an AIDS Vaccine?

Executive Summary and Agenda for Action
AIDS Vaccine Advocacy Coalition, May 1999

Executive Summary

In May 1997, President Clinton set a national goal of developing an HIV vaccine within the next decade. This goal is laudable, but there is evidence that it may not be met. The development and testing process will be long, and the number of vaccine candidates in early clinical trials is falling, not rising. So far, only one product has entered large-scale efficacy testing. Although some promising new ideas are percolating in laboratories around the world, it might be years before these will be tested in humans.

We urge government, industry, and community to dedicate themselves to the development of a safe and effective HIV vaccine. If the goal for 2007 cannot be achieved, then we need to know what *will* be accomplished over the next eight years toward a vaccine that could bring the HIV pandemic under control. With 16,000 new HIV infections each day, the world can afford no delay. This report describes what each of these sectors has accomplished during the past year and outlines what each can do to speed the search for a preventive vaccine.

Government is funding the basic research needed for a vaccine, and it is developing a structure to advance promising concepts and products. But US government agencies should expand their capability to research and develop new vaccines rapidly.

- Government must be bolder in coordinating its agencies' agendas and must demonstrate farsighted, results-oriented leadership and research plans.

- Government must increase the pace of research, by moving outside its basic science focus to strengthen product development and clinical research efforts.
- Government must facilitate community participation in research through more active support of trial site community advisory boards.

Industry has the expertise and infrastructure to bring a vaccine to the public. Some companies are investing more now than in years past. But too many companies are failing to treat this as their responsibility, largely because of scientific risk and uncertain profits.

- The world's largest vaccine pharmaceutical companies must shoulder more of the risk involved in HIV vaccine discovery and development and must commit more dollars and expertise to the effort.

- Industry must take greater advantage of government funding initiatives and smaller company ventures to leverage vaccine development.

Not-for-profit organizations and community advocates are finally stepping up to the plate in the drive for an HIV vaccine, and they are beginning to realize their potential for public education and support of innovative research.

- Funders and advocates should do all they can to support not-for-profit organizations such as the International AIDS Vaccine Initiative, the American Foundation for AIDS Research, and the Elizabeth Glaser Pediatric AIDS Foundation that directly fund HIV vaccine research and development.

- The public can support initiatives such as the tax credit for vaccine research recently introduced in the US Congress (House Resolution 1274).

- HIV treatment and prevention advocates must integrate support for HIV vaccine research and development into the AIDS research advocacy agenda.

- Not-for-profit AIDS organizations, public health organizations, and HIV prevention planning groups must seize responsibility and opportunities to mobilize the public about the priorities and potential results of biomedical research on vaccines.

- Trial site community advisory boards increasingly have a place at the table in planning research, but must live up to this responsibility with sustained, well-informed involvement.

Recommendations

Last year's report of the AIDS Vaccine Advocacy Coalition (AVAC) opened with a photo of humankind's first giant footsteps on the moon. This year, the AIDS vaccine program looks less like the soaring Apollo adventure than like the static orbit of Sputnik.

The missing element in the search for an HIV vaccine is urgency. Everything takes too long. As we said a year ago, without explicit goals and greater accountability, an effective HIV vaccine will not be available by 2007.

To boost the vaccine endeavor into higher orbit, AVAC has the following recommendations.

US Government

Request Adequate Funding Increases

For FY 2000, President Clinton requested a meager 2.1% increase for the National Institutes of Health, a 1% increase for the Centers for Disease Control, and level funding, after a 40% decrease in FY 1999, for the Department of Defense AIDS research program. These funding requests from the White House reflect crass political budget maneuvering and belittle the hard work done by these three US government agencies. The White House must request adequate funding increases for the US government agencies that conduct biomedical research.

Coordinate Efforts

The time has come for the National Institutes of Health, the Walter Reed Army Institute of Research, the Centers for Disease

Control and Prevention, and the US Agency for International Development to formulate compatible plans and make them clear

to the rest of the world. There is mid-level communication among these US government agencies; what's needed is leadership strong enough to harness the abilities of all four agencies. These agencies should present a coordinated effort wherever they are supporting clinical trials.

Set and Adhere to Interim Goals

In last year's report, we said, "Agencies funded to conduct HIV vaccine research and development should establish clearer plans and goals to expand the HIV vaccine pipeline," and "the US government must be clear about who should take responsibility and accountability to achieve these goals." We listed five interim goals that would indicate a widening of the product pipeline; this year we have added a sixth:

- increase the annual number of targeted research projects that are applicable to new and improved vaccine concepts;

- increase the annual number of vaccine concepts evaluated in primate models;

- increase the annual number of vaccine products evaluated in phase 1 trials;

- increase the number of industry partners involved in developing HIV vaccines;

- increase the annual number of products developed that can move into phase 2, proof-of-concept, or phase 3 efficacy trials; and

- *(added interim goal)*: increase the number of domestic and international trial sites with the capacity to participate in phase 3 testing of HIV vaccines.

We challenge the government agencies involved in HIV vaccine research and development to set clear, measurable goals for each of these six areas. These goals should be stated, and progress toward them reported, by May 2000 – when the countdown reaches "seven years and counting."

National Institutes of Health

Move Faster

In 1996, in our *Agenda for Action for an HIV Vaccine*, AVAC's first key recommendation was that "NIH leadership must be accountable for effectively advancing efforts in AIDS vaccine research." We recommended that, "If NIH does not take up this critically important responsibility within a fixed period of time, authority and funds for the task should be placed elsewhere."

Since 1996, we have witnessed a great deal more attention and government money in the vaccine effort as well as well-qualified committed leaders finally in place. During the past year, of the NIH $1.8 billion dedicated to AIDS research, $194 million (11%) was allocated for HIV vaccine research. During the past year, NIH veteran Peggy Johnston was appointed as Assistant Director for AIDS Vaccines at NIAID and Associate Director of Vaccines within the Division of AIDS (DAIDS), National Institute of Allergy and Infectious Diseases (NIAID). Virologist and AIDS Vaccine Research Committee member Neal Nathanson was appointed as Office of AIDS Research Director, and gene therapy researcher Gary Nabel as Director of the NIH Vaccine Research Center.

These individuals have taken on important new responsibilities, in many cases they have been provided with additional funds, and obviously they will need time to have an impact. Opportunities for accelerating the pace of vaccine development can be seized now, as shown by the examples below.

- In 1997, NIAID created a new Innovation Grants program with minimal red tape and got it up and running in just a few months, which is record time. Now, two years later, that program has begun to look like any other: it is reviewed by sound standing study sections along with other grants, and more awards are going to the same kinds of basic immunology and pathogenesis projects that older programs also fund. The number of applications is declining, and more and more awards are going to the same researchers who have always received NIAID support, rather than expanding the research pool. Johnston, Nathanson, Nabel, and members of the AIDS Vaccine Research Committee should publicize this program and actively seek new applicants.

- One large-scale comparative primate study of HIV vaccines is beginning soon. This will be the second large primate study of HIV vaccines conducted by NIH; the first has yet to publish data. NIAID and the National Center for Research Resources should move these studies forward and initiate additional comparative development work in primates immediately. To that end, NIAID should increase product development funding to generate vaccine candidates that are optimized for comparative primate studies.

- The HIV Vaccine Design and Development Program has not yet accepted applications or funded a single team. DAIDS management has been presenting and describing this program as a key element of its vaccine program for the past two years. NIAID staff should take the opportunity to ensure that this program attracts appropriate interest and moves the development process forward in ways that the old programs could not.

- NIH has finally hired the University of Michigan's Gary Nabel as director of the much-touted Vaccine Research Center (VRC). The building cornerstone will be laid any day, and the next challenge is to make VRC a true center of excellence for HIV vaccine research and development. NIH should, as promised, provide Nabel with the authority and resources needed to staff the center with the best and brightest vaccine scientists, whether they are selected from within NIH or brought in from outside NIH.

- NIAID should increase the number of clinical trials and ensure that the new clinical trial networks are adequate to evaluate candidate vaccines at all stages, from initial safety studies through large-scale trials needed for licensure. So far, countless hours of investigator time and attention have been consumed by replacing a phase 1 and 2 network for vaccines (AIDS Vaccine Evaluation Group) and a phase 3 trials network for vaccines and prevention (HIV Network for Prevention Trials), with the new HIV Vaccine Trials Network and HIV Prevention Trials Network. This has distracted NIAID staff and extramural scientists from the real task at hand – conducting trials that will move an array of vaccine candidates forward. Another cause for concern is the capability of the new HIV Vaccine Trials Network to launch a phase 3 vaccine trial in 2000.

Link Vaccines With Other Prevention Research

NIAID's Division of AIDS should be very careful as it separates vaccine research from research on other prevention interventions and hands responsibility of clinical testing to independent investigators. In principle, this reorganization and delegation could increase the focus and scientific viability of each program. However, giving more control to outside researchers will not by itself improve the pipeline of vaccine development. In addition, the reorganization threatens important and hard-won gains, such

as community involvement and education. Coordination and synergy between vaccine and prevention research will be needed. This is more likely if some trial sites participate in both networks and if they have the flexibility to test the most scientifically promising strategies – whether these are vaccines or other interventions. Johnston and her team should be active in their management of these networks, mandating coordination of infrastructure and research as well as making sure that research findings are promptly reported and shared.

Support Community Input

Clinical trial sites, whether funded by government or industry, have an obligation to develop guidelines for local community input into the planning and conduct of research. Community must be involved before, not after, research plans are set. Community advisory boards (CABs) should be supported more actively as one way to facilitate community involvement.

US Department of Defense

Adequately Fund WRAIR

The HIV vaccine program of the Walter Reed Army Institute of Research (WRAIR) has considerable strengths in applied research, relationships with companies and countries, and coherent long-term strategizing for product development. Unfortunately, this year WRAIR suffered two setbacks: a drop in funding, and the prospect of having a larger-than-expected efficacy trial in Thailand due to the laudable success of prevention programs among potential vaccine cohorts. Even well-made battle plans do not always succeed. WRAIR needs alternate locations for its research as well as sufficient funds to prepare and support them; yet, it has consistently been under-budgeted, depending on congressional whim for adequate support.

The US Department of Defense must budget and support the WRAIR AIDS research program at realistic, progressive levels that are flexible enough to accommodate unforeseen developments. The few million dollars this would require are minuscule compared to the damage inflicted by AIDS in locations where the United States has defense interests or in relation to the total defense budget.

The WRAIR HIV vaccine program has an advantage over other US government agencies in that it is targeted in its approach and is not hindered by multiple oversight and review committees. Still, WRAIR could increase public input and scientific review by researchers in industry and outside the Department of Defense.

Centers for Disease Control and Prevention

Further Define and Expand the CDC Vaccine Unit

In 1998, the Centers for Disease Control and Prevention (CDC) established an HIV Vaccine Unit within its National Center for HIV, STD, and TB Prevention. Its budget is small: $2.6 million out of the agency's $2.5 billion total (0.1%). Yet CDC has longstanding international and US contacts and capability to conduct virology studies and preparedness studies in several potential trial sites. The agency can also bring expertise to risk reduction and informed consent procedures in phase 3 trials.
We challenge CDC to fulfill its potential by defining its plans and setting clear and measurable goals for coordinating its activities with better funded domestic and international players, especially NIH, WRAIR, and companies whose products may be suitable for testing in sites prepared by CDC. Funding should be increased as needed to implement these plans.

International Funding

Expand the UNAIDS Effort

Designing and testing vaccines will have to be a cooperative international effort. In African, Asian, Latin American, and Caribbean countries where HIV vaccine trials might be held, vaccine manufacturers and sponsoring companies need to work with local governments, researchers, and community advocates to prepare for useful, ethical, and cost-effective research. The Joint UN Programme on HIV/AIDS (UNAIDS) has played a valuable role in supporting countries in building capacity to evaluate the scientific and ethical merits of potential HIV vaccine trials. Unlike the pharmaceutical companies and Western governments seeking to sponsor HIV vaccine trials, UNAIDS can have a neutral advisory role regarding HIV vaccine research.

Governments should increase funding for UNAIDS vaccine efforts. UNAIDS should leverage additional resources and expertise from partner agencies and countries to expand technical assistance to countries preparing for HIV vaccine trials.

Private Industry

Invest in a Big Way

Industry's investment in preventive HIV vaccine development remains inadequate. Most companies that have performed significant vaccine work have benefitted from direct or indirect government support. Although government-industry partnerships are valuable and should be encouraged, more reciprocity should be involved. Companies can shoulder more of the risk involved in HIV vaccine research and development, and most should be willing to invest more of their own resources in an endeavor of such public health significance.

Leverage Private Investment

Attempts to "leverage" private investment have taken several forms. Government agencies such as NIH have provided research resources, including viral isolates, access to primate centers, and infrastructure for clinical trials. More recently, NIH and the not-for-profit International AIDS Vaccine Initiative (IAVI) have established programs that provide direct financial support for private companies conducting HIV vaccine research. IAVI has chosen two teams, and NIAID plans to choose teams this summer. On the legislative side, US Representatives Nancy Pelosi and Charles Rangel recently introduced legislation (House Resolution 1274) to provide a tax credit for new research on HIV, malaria, and tuberculosis vaccines. These initiatives should be supported by advocates and industry more aggressively.

The US government and foundations have come forward with a variety of measures to address the financial costs, risks, and "opportunity costs" of researching and developing HIV vaccines. Large and small pharmaceutical companies should stop making excuses, take advantage of the incentives, and pitch in to conquer this problem.

Industry must take advantage of initial investment by private foundations or government to determine feasibility of new approaches to HIV vaccines at minimal risk and cost to companies. Whereas investment by large pharmaceutical companies such as Pasteur Merieux Connaught and Merck is laudable, corporate management should appreciate the magnitude of this project and its potential contribution. Additional industry investment could shave years off the vaccine development process, save many lives, and accelerate research progress and profits.

Not-for-Profit Organizations and Community Advocates

Mobilize Support for Research and Industry Involvement

Advocates for HIV treatment and prevention must integrate HIV vaccine research into the AIDS agenda. Not-for-profit AIDS and public health organizations should seize responsibility and opportunities to mobilize the public about the priorities and potential results of biomedical research. All should support direct funding of HIV vaccine research and development by the International AIDS Vaccine Initiative, the American Foundation for AIDS Research, and the Elizabeth Glaser Pediatric AIDS Foundation. All should support initiatives such as vaccine research tax incentive legislation recently introduced in the US Congress (House Resolution 1274) and a vaccine purchase fund currently under consideration at the World Bank.

Unite and Organize

Advocates for AIDS research, women's health, health and rights of vulnerable communities, and international health should also unite to advocate for HIV vaccine research. The major AIDS organizations, AIDS media, and CDC-sponsored prevention planning groups ought to integrate support for vaccine research into their policy analysis, education, and communications.

Institutionalize CAB and Community Involvement

Local and national community advisory boards (CABs) can secure more support and resources from trial sites and from the new vaccine and prevention trial leadership. Local CABs, assisted by program staff and researchers, should develop standards and expectations for local activity. On a national level, clearer processes for CAB dialogue and decision-making would benefit CABs and the government agencies and private companies that work with them.

Work for Access

An HIV vaccine cannot save lives unless people have access to it. Advocates can mobilize in advance to make preventive vaccines for HIV and other diseases widely available to economically disadvantaged populations and individuals. Advocates can work to understand and address access issues, such as tiered pricing, product liability, intellectual property rights, and international product licensing laws.

AIDS Vaccine Advocacy Coalition. *Eight Years and Counting: What Will Speed Development of an AIDS Vaccine?* Washington, DC: AVAC, 1999.