

**The United States Agency for International Development (USAID) Report  
to Congress:  
International AIDS Vaccine Initiative (IAVI)**

Background

In Section 112 of P.L. 106-264, Congress requested a report on the effectiveness of the International AIDS Vaccine Initiative (IAVI) in meeting the goals of:

1. improving access to sustainable immunization services;
2. expanding the use of all existing, safe, and cost-effective vaccines where they address a public health problem;
3. accelerating the development and introduction of new vaccines and technologies;
4. accelerating research and development efforts for vaccine needed primarily in developing countries;
5. making immunization coverage a centerpiece in international development efforts.

The International AIDS Vaccine Initiative (IAVI) is an international, scientific non-governmental organization dedicated to ensuring the development of safe, effective, accessible, preventive AIDS vaccines for use throughout the world. IAVI is pursuing this mission through four complementary strategies:

- building worldwide demand for AIDS vaccines by mobilizing growing public and government support for accelerated vaccine development;
- accelerating development of new and innovative AIDS vaccine designs, and prioritizing the best candidate vaccines for large-scale efficacy testing where the epidemic is spreading fastest in the developing world;
- fostering an environment for successful AIDS vaccine development by expanding public/private collaboration and investment in a global vaccine effort; and
- confronting the challenges of making AIDS vaccines available to all who need them as soon as feasible.

IAVI plans over the next five to seven years to accelerate AIDS vaccine product development and testing to: develop new and innovative AIDS vaccine designs applicable for use in the developing world, prioritize candidate AIDS vaccines for accelerated progression to Phase III efficacy trials through head-to-head comparisons, and shorten timelines in all facets of the AIDS vaccine development process.

The goal of this accelerated scientific agenda would be to have six to eight of the most promising AIDS vaccines in large-scale efficacy trials in the developing world where the epidemic is most severe within the next five to seven years.

Several other governmental and non-governmental organizations (e.g. U.S. National Institutes for Health (NIH), the Centers for Disease Control and Prevention (CDC), and the VaxGen and Merck companies) are involved in AIDS vaccine research and development. Therefore, it is important to note that IAVI itself does not propose to shoulder the entire workload for this global commitment. Rather, they aim to complement ongoing national, transnational, and industrial efforts.

IAVI collaborates with other federal agencies as well, particularly the NIH working toward the common goal of a safe and effective vaccine for the developing world. Specifically, IAVI, as a leader in the HIV vaccine field, is regularly represented at key NIH meetings that discuss scientific issues confronting the HIV vaccine field. This is illustrated by IAVI's launch of the IAVI-NIH Neutralizing Antibody Consortium to address a major issue confronting HIV vaccine development. Another example of inter-organizational collaboration is with the AlphaVax Vaccine Development Partnership (VDP) described below. IAVI is working with NIH and private industry to develop this particular HIV vaccine candidate. The vaccine will undergo clinical trials at national and international sites of the NIH's HIV Vaccine Trial Network (HVTN).

With prevention efforts as the cornerstone of USAID's HIV/AIDS strategy, it is most logical that USAID be associated with the development of the world's best and only long-term prevention for ending this global epidemic. Although USAID provided a small amount of funds to IAVI in fiscal years 1999 and 2000, the formal relationship between USAID and IAVI began when a two-year grant was awarded to IAVI on September 26, 2001 for \$16 million.

### Accomplishments

IAVI's efforts have focused on accelerating the development and introduction of new vaccines and technologies, specifically an AIDS vaccine needed primarily in developing countries, and on putting the AIDS vaccine on the global policy agenda. This report outlines the many significant accomplishments they have achieved toward these goals.

IAVI's research and development strategy has four principal elements:

- identifying and addressing the primary scientific, design, manufacturing, and clinical trials challenges currently impeding AIDS vaccine development;
- expanding the pipeline of AIDS vaccine candidates in clinical trials that are applicable for use in the developing world;
- accelerating the most promising first-generation candidate vaccines into large-scale efficacy trials; and
- ensuring that second generation AIDS vaccines provide improvement over first generation candidates from the perspectives of safety, efficacy, and applicability for use in the developing world.

### Vaccine Development Partnerships

These elements have been accomplished primarily through the work of IAVI's Vaccine Development Partnerships (VDP) that link vaccine designers with manufacturers (when necessary) and with developing country sites suitable for testing promising AIDS vaccine candidates. IAVI spent nearly 70% of their 2001 expenses on vaccine research and development with financial support to these VDP's ranging from a portion of their funding to nearly 100 percent of the VDP's work. However, more important than their financial contribution are their efforts to bring the various partners together to facilitate interactions as well as represent the common interests of the vaccine developers, often small biotech companies, to raise and address issues with the global community. To further aid this effort and ensure vaccines would be readily available in developing countries, IAVI has negotiated groundbreaking intellectual property agreements for these VDP's. IAVI currently has developed seven VDP's, summarized below:

- The Oxford-Kenya VDP links vaccine designers in the United Kingdom with Kenyan clinical research scientists for vaccine trials in the U.K. and East Africa. The team has generated a combination vaccine, called a prime-boost, that combines two vaccine technologies. The candidate vaccine is derived from HIV-1 subtype A – a major strain of HIV circulating in Africa. Components of the vaccine have completed early phase safety testing in human trials. The Kenyan trials were a landmark event, representing the first time that human trials in Africa were conducted using a candidate AIDS vaccine specifically designed for a primary strain of HIV circulating in Africa. Expanded human clinical trials are planned for this year and next to determine whether the vaccine candidate should be moved forward to the larger field efficacy trials.
- The AlphaVax-South Africa VDP is a consortium that includes: AlphaVax, Inc, North Carolina; NIH's HIV Vaccine Trials Network; National Institute of Allergy and Infectious Disease, Division of AIDS, NIH; South Africa Medical Research Council; University of Capetown, South Africa; University of North Carolina; Walter Reed Army Institute of Research, and IAVI. Early human

clinical trials are planned for later in 2002 to assess the safety of this recombinant technology vaccine delivery system.

- The Targeted Genetics-Children's Research Institute-South Africa VDP teams researchers in Seattle, Washington and Columbus, Ohio. This vaccine candidate is based on genes from HIV subtype C, the most prevalent strain in South Africa. IAVI has supported the clinical research unit at the Chris Hani Bagaranwath Hospital, Soweto, South Africa, in advance of early human clinical trials. These are more than one year away as animal safety studies are being conducted.
- The Institute of Human Virology-Uganda Virus Research Institute VDP links the Institute at the University of Maryland and the Uganda Institute for the development and testing of a potential orally administered AIDS vaccine. This vaccine candidate is still in pre-clinical development, e.g. vaccine characterization, animal studies. IAVI's plan includes a human vaccine trial in Uganda with the Oxford-Kenya vaccine candidate.
- The Indian Council of Medical Research-Therion Biologics Corporation VDP is a collaboration between the Indian Council and the Corporation from Cambridge, Massachusetts. This program is unique in that it will represent the first instance of technology transfer from an American biotech company to an Indian vaccine manufacturer. This vaccine candidate is still in pre-clinical development, but will utilize genes from the HIV subtype C that circulates in India.
- The Aaron Diamond AIDS Research Center-Government of China VDP is a partnership between the Center in New York, New York and the Chinese Academy of Medical Sciences. This vaccine candidate is also in pre-clinical development.
- The Bioption-IAVI VDP is a partnership between the Swedish biotech company and IAVI to develop and test a new approach for vaccines built from a proprietary technology pioneered at the Karolinska Institute in Sweden. Phase I trials will likely take place in Asia and sub-Saharan Africa. This vaccine candidate also is still in pre-clinical development.

While a vaccine candidate is in early stages, IAVI is strategically ensuring that information gleaned from the leading candidates is used in the development of later vaccines candidates. Additionally, the later approaches work to improve upon and enhance the effectiveness of the earlier approaches.

### Applied Vaccine Projects

IAVI is also supporting a number of applied vaccine research projects aimed at filling critical gaps in scientific knowledge directly related to accelerating the development of safe and effective AIDS vaccines. They are

designed to complement the VDPs and to aid in prioritizing the most promising vaccine candidates. They are summarized below:

- The IAVI-NIH Neutralizing Antibody Consortium is a collaboration with the NIH Vaccine Research Center that is bringing together a number of the leading laboratories in the world to accelerate progress toward the development of vaccines able to induce broadly cross-reactive neutralizing antibody responses against the many types of HIV viruses found in the developing world.
- The Non-Human Primate Immunogenicity Studies is a project to help prioritize the most promising AIDS vaccines and minimize the number of non-human primates used in AIDS vaccine development efforts.
- The Core Immunology Laboratories have been established to accelerate development by undertaking standardized, head-to-head comparisons of samples from human vaccine trials and non-human primate studies. The Human Core Immunology Lab is located in London, United Kingdom. The non-human primate laboratory is planned to be located in Becton, Dickinson and Company – PharMingen, San Diego, California. Becton, Dickinson and Company also provides equipment, reagents, and training.

IAVI also hosts a variety of international meetings addressing AIDS vaccine research and development. Recent examples include: T-Cell Assays and Reagents, Optimization of DNA Vaccines, and the Latin American NGO Meeting on HIV Vaccine Development.

IAVI also established the first periodical devoted to chronicling HIV vaccine research, IAVI Report, which has more than 8500 readers in 140 countries. It is also available on the IAVI web site ([www.iavi.org](http://www.iavi.org)).

### Communications, Policy and Advocacy

As AIDS vaccine research and development advances, so too does the need to engage and educate a wide range of constituencies in each country where clinical trials will occur, including national and local government officials, media, scientists, health professionals, civic and religious groups, people living with HIV/AIDS and other community members. The focus of IAVI's Vaccine Preparedness program is to create a supporting environment in the host country for AIDS vaccine trials. To date, that has involved activities in Kenya, Uganda, and India, including: providing information to government officials, supporting national AIDS efforts and non-governmental organizations (NGOs), and preparing local communities for clinical trials. The IAVI Communications unit works closely with the Vaccine Preparedness group, and works to educate and motivate local and international press, focusing on Kenya, Uganda, and South Africa. To date, in Kenya and Uganda, they have used a three-part approach: meeting with media leadership (e.g. editors), conducting training

program in Nairobi for reporters, and plans to hold additional training for local media outside the capital where trials will occur.

IAVI works to expand policy and advocacy efforts to increase global support for the development and eventual distribution of AIDS vaccines. IAVI's focus is on policy issues and global, regional and country programs. With regards to the former, IAVI worked to increase attention to AIDS vaccine issues and build support through a range of strategies including specifically in 2001:

- proposing to the Global Fund to Fight AIDS, Tuberculosis, and Malaria the creation of a mechanism within the Global fund for the purchase of AIDS vaccine,
- participating with the Global Alliance for Vaccines and Immunization (GAVI) in creating innovative approaches to accelerate investment in vaccines against diseases prevalent in developing countries, and
- participating at the first Organization of African Unity Summit on AIDS and at the UN General Assembly Special Session on HIV/AIDS where IAVI worked to increase the focus on AIDS vaccines.

The result of these efforts was to put AIDS vaccines onto the global policy agenda and win significant increases in government funding for AIDS vaccine research and development.

To address the issue of swift global access to AIDS vaccines, IAVI published in 2001 a white paper entitled "A New Access Paradigm: Public Sector Actions to Assure Swift, Global Access to AIDS Vaccines." Today, developing countries usually wait an average of 20 years after new vaccines are licensed in industrialized countries before they are introduced to their own populations. Action is needed now to assure access in developing countries to the AIDS vaccines that are being developed today. Key components of the paper include:

- Commitments to provide adequate future financing for the purchase and delivery of AIDS vaccines, and support for tiered pricing and joint procurement and/or negotiation mechanisms for developing countries.
- Provision of additional resources for research and development of AIDS vaccines appropriate for use in developing countries.
- Focused efforts to coordinate regulatory requirements and expedite submission and review processes for AIDS vaccine candidates.
- Support for activities to ensure that sufficient manufacturing capacity is available to meet global health needs.

- Creation of delivery systems to assure adolescents, injecting drug users, commercial sex workers, and other high-risk individuals will be served.

IAVI initiated efforts in 2001 to spur the public sector to action on the above points contained in the white paper. (IAVI previously helped establish a World Bank task force in 1998 to study new financial mechanisms to spur the development, and eventual purchase, of AIDS vaccines for developing countries.) IAVI staff and other partners worked to increase support for vaccine tax credit proposals where large vaccine developers and manufacturers are located, i.e. U.S., U.K., and Belgium. IAVI provided technical, financial, and political support to the UNAIDS, WHO, and the World Bank for efforts to better understand and predict future demand for AIDS vaccines. IAVI began exploring the possibility of working with other agencies to initiate a pilot program that would distribute an existing vaccine to adults and adolescents in a country where IAVI already has an AIDS vaccine research effort underway. IAVI also began reviewing strategies for promoting regulatory reforms to ensure the efficient review of applications to conduct AIDS vaccine clinical trials and obtain licensing approval, without compromising safety.

### Conclusion

Clearly, IAVI has made significant steps toward accelerating the development and introduction of new vaccines and technologies, specifically an AIDS vaccine needed primarily in developing countries, and is strategically positioned for further advancements in the development and eventual fielding of a global AIDS vaccine. USAID's involvement will be critical once vaccine candidates are identified for large-scale clinical trials to demonstrate vaccine efficacy in countries with high HIV prevalence. USAID's established efforts in HIV monitoring and evaluation will aid HIV vaccine trial site preparation by providing useful information on community HIV prevalence rates and sexual behavior. USAID has a long history in HIV communication strategies, community mobilization, and efforts to involve people living with AIDS. This extensive experience will enable USAID to contribute to efforts to educate and gain support from the community, the media, and government officials in advance of field trials of HIV vaccines which have met safety and regulatory requirements.