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**2005 AIDS VACCINE INTERNATIONAL  
CONFERENCE, MONTREAL, CANADA,  
SEPTEMBER 6-9, 2005**

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**STAFF TRIP REPORT  
TO THE  
COMMITTEE ON FOREIGN RELATIONS  
UNITED STATES SENATE**

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## LETTER OF TRANSMITTAL

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*December 28, 2005*

HON. RICHARD G. LUGAR, *Chairman*,  
U.S. Senate Committee on Foreign Relations.

Dear Senator Lugar:

On behalf of the Senate Committee on Foreign Relations, I traveled to Montreal, Canada from September 6–9, 2005. The purpose of this trip was to attend the 2005 AIDS Vaccine International Conference.

The trip afforded me the opportunity to learn about the latest scientific progress in developing an AIDS vaccine, better understand the myriad social issues surrounding this work, and consult with key individuals working on this issue. Attached is a summary of the trip and a discussion of the impressions and conclusions developed throughout the trip. The conclusions in this report are my own and do not necessarily reflect the views of the Committee on Foreign Relations or its members.

Sincerely,

CHRIS ANN KEEHNER,  
*Counsel, Majority Staff*,  
*U.S. Senate Committee on Foreign Relations.*



## **2005 AIDS VACCINE INTERNATIONAL CONFERENCE, MONTREAL, CANADA, SEPTEMBER 6–9, 2005**

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### CONFERENCE OVERVIEW

Despite the dramatic increase in funding in the last few years for programs to prevent the spread of the human immunodeficiency virus (“HIV”) and to treat those living with the acquired immune deficiency syndrome (“AIDS”), the spread of the disease continues to outpace us. According to UNAIDS, there are an estimated 40.3 million people living with HIV today. Over three million people died of AIDS in 2005, and nearly 4.9 million people became infected with HIV this year. This means that every day around the globe, some 14,000 people are newly infected with HIV. In addition, experts are concerned about a possible “second wave” of countries with AIDS epidemics, including Russia, China, India, Nigeria, and Ethiopia.<sup>1</sup>

Getting ahead of this pandemic—through current prevention and treatment programs alone—will continue to be a challenge. An effective AIDS vaccine holds promise to be the world’s best chance to stop this pandemic. Historically, vaccines have led to some of the greatest achievements in public health and are among the most cost-effective health interventions. During the 20th century, global immunization efforts have successfully led to the eradication of smallpox and the elimination of polio from the Western Hemisphere, Europe, and most of Asia. Vaccines for diseases such as measles and tetanus have dramatically reduced childhood mortality worldwide, and vaccines for diseases such as influenza, pneumonia, and hepatitis now help prevent the sickness and death of adults, too.

The theme of the 2005 AIDS Vaccine International Conference was “Together, A Better Future for All,” and was held in Montreal, Canada. The Conference brought together scientists, policy makers, and activists from around the world with a special interest in the development of vaccines to prevent HIV and AIDS. The Conference provided a unique opportunity to learn about the most recent scientific progress in developing an AIDS vaccine and the social, ethical, and economic issues surrounding the pursuit of this goal.

### SCIENTIFIC CHALLENGES TO DEVELOPING AN EFFECTIVE HIV VACCINE

There are currently about 30 candidate AIDS vaccines in clinical testing around the world today. The immediate goal of AIDS vac-

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<sup>1</sup>For more information on the current state of the AIDS pandemic, see the *UNAIDS/WHO AIDS Epidemic Update: December 2005*, which can be found at <http://www.unaids.org>.

cine research is to design candidate vaccines that trigger responses from both the major arms of the body's immune system—humoral immunity and cellular immunity. Humoral immunity involves the creation of antibodies that recognize and attack a pathogen—like HIV—in the blood and prevent it from infecting the body's cells. Cellular immunity is triggered once the pathogen has infected some of the body's cells, and its role is to recognize and destroy infected cells to prevent further spread of the pathogen.<sup>2</sup>

The complicated nature of HIV, however, creates significant scientific challenges for researchers. One of these challenges is the way HIV interacts with the human immune system. Most vaccines work by triggering the body's immune system to produce antibodies against infection. The antibodies search out invaders in the bloodstream—like viruses or bacteria—and attack them. HIV, however, is extremely adept at evading the immune system, thus making this approach to an AIDS vaccine especially challenging. Determining how to design vaccines that stimulate an antibody-producing response is a priority for scientists. If a vaccine were able to produce this response, it would block HIV infection altogether. Although most researchers agree that solving this problem is essential to developing an AIDS vaccine, so far, trials have been unsuccessful in creating an antibody response.

Because of the difficulty in discovering a vaccine that triggers an antibody-producing effect, most of the current trials focus on cellular immunity, which if successful, might not prevent an individual from getting HIV, but would delay or prevent the progression of the disease and reduce transmission. Researchers are closely watching the clinical trials of Merck & Company, which has initiated a candidate aimed at stimulating cellular immunity. This ongoing study is testing the company's lead vaccine candidate known as "MRKA5" in approximately 3,000 volunteers. This trial will test the hypothesis that a vaccine based on portions of genetic material from HIV can stimulate cellular immunity to prevent HIV disease, and perhaps infection. This trial is being conducted in sites in the United States, Australia, the Caribbean, and Latin America. The results of this important trial are anticipated in 2007 at the earliest, and will likely shape the direction of future AIDS vaccine research.

Another complicating factor is HIV's diversity. There are several strains of HIV and the virus is constantly generating new ones. Globally, six different strains account for the majority of HIV infections. This means that scientists need to find vaccines that induce immunity against the broadest range of these HIV strains.

Given the scientific challenges of developing an effective HIV vaccine, researchers in the field are modifying the traditional vaccine development process. Normally, clinical trials are conducted in three phases. Phase I trials typically involve several dozen volunteers at low risk for HIV infection and test whether the vaccine triggers an immune response. Phase II trials involve several hundred volunteers, including some at high risk for HIV infection, and

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<sup>2</sup>For a more in-depth discussion of immunology and vaccine development with respect to an AIDS vaccine, see the AIDS Vaccine Advocacy Coalition's (AVAC) *AIDS Vaccine Handbook* (2d ed. 2005). The full text of the book is available online at <http://www.avac.org>.

gather both safety and immunogenicity<sup>3</sup> data. Phase III efficacy trials enroll thousands of participants and seek statistical determinations of whether a vaccine is effective. Very few of the vaccines tested will make it to Phase III testing. Although there have been dozens of different AIDS vaccines tested in Phase I trials, only three have made it into Phase III. Because of the high cost in taking a vaccine all the way to Phase III trials, AIDS vaccine developers have added a fourth phase to the process: Phase IIb or “proof of concept” trials. The goal behind this new phase is to look for preliminary evidence of efficacy in smaller, shorter, and far less expensive trials before engaging in a Phase III trial. (The Merck trial studying cellular immunity is a Phase IIb trial.)

#### EFFORTS TO COORDINATE AIDS VACCINE RESEARCH

Because of the complicated nature of AIDS vaccine research, most experts agree that there is a need for a much larger-scaled, better-coordinated, better-funded effort, consisting of researchers from different organizations working together to solve given scientific problems. Ideally, each of these organizations would contribute its special expertise and would share the information it discovers. Speakers at the Conference discussed how efforts to better coordinate AIDS vaccine initiatives have improved significantly over the past two years. For instance, the Global HIV Vaccine Enterprise (“Enterprise”), which was first proposed in *Science* magazine in June 2003 and established in 2004, is a “virtual consortium” of scientists, advocates, and other stakeholders organized to accelerate research efforts to develop an AIDS vaccine. In February 2005, the Enterprise published the Scientific Strategic Plan, a blueprint outlining the major scientific hurdles to be overcome in the development of an AIDS vaccine.<sup>4</sup> The Enterprise’s first Stakeholders’ Forum was held in London on May 23–24, 2005, organized by the U.K. Department for International Development and the Bill & Melinda Gates Foundation. In October, the Enterprise held its first Funders’ Forum. Currently, the Bill and Melinda Gates Foundation is acting as interim Secretariat, and the Enterprise is in the process of selecting an Executive Director.

On the domestic front, Dr. Anthony S. Fauci, Director of the National Institute of Allergy and Infectious Diseases at the National Institutes of Health, spoke at the Conference about the Partnership for AIDS Vaccine Evaluation (“PAVE”), the interagency group coordinating AIDS vaccine research among the Department of Defense, the Centers for Disease Control, the National Institute of Allergy and Infectious Diseases, and other agencies and offices. In addition, the Center for HIV/AIDS Vaccine Immunology (“CHAVI”) was established by President Bush last year, and is a consortium of universities and academic medical centers organized by the National Institute of Allergy and Infectious Diseases (NIAID) under Dr. Barton Haynes of Duke University. It is intended to solve major problems in AIDS vaccine development and to be a compo-

<sup>3</sup>When collecting data on immunogenicity, researchers are examining the strength and breadth of the immune response of a trial vaccine.

<sup>4</sup>For more information on the Global HIV Vaccine Enterprise, see <http://www.hivvaccineenterprise.org>.

ment of the Global HIV Vaccine Enterprise.<sup>5</sup> The CHAVI has received a seven-year grant of \$300 million for AIDS vaccine research and plans on holding its first clinical trials in 2007. In addition to federal funding for AIDS vaccine research, the Bill and Melinda Gates Foundation has allocated \$360 million for grants in the context of the scientific plan of the Global HIV Vaccine Enterprise.

#### OTHER CHALLENGES IN THE PURSUIT OF AN EFFECTIVE AIDS VACCINE

Apart from the scientific challenges researchers face in developing an effective AIDS vaccine, there are several other issues that create tremendous hurdles in this field.

#### *Increasing Private Sector Investment in AIDS Vaccine Research*

One of the biggest challenges is the lack of private sector investment in research and development of an AIDS vaccine. There are two main reasons for this. First, many pharmaceutical companies have ceased to invest in research and development of vaccines, due to the liability risks involved and the lower profit margin of vaccines compared to medicines taken to treat chronic illnesses. Representatives of the private sector spoke at the Conference about the tremendous costs involved in bringing a product to market, and explained that most medications are far more profitable than vaccines, which are typically administered only once. Second, when the target population for a new product, such as an AIDS vaccine, lives largely in the developing world, there is essentially no viable commercial market to entice research and development in the production of the product.<sup>6</sup>

In order to fill this economic gap, experts are developing various incentives to motivate the private sector to invest in research and development for vaccines to prevent diseases, like HIV, that are predominately found in the developing world. Among these incentives are tax credits, “wild card” patent extensions, and advanced market commitments. Public-private partnerships have also proved beneficial in the pursuit of vaccines for diseases of developing countries, and experts are seeking ways to increase these partnerships.<sup>7</sup>

#### *The Challenges of Conducting Vaccine Trials in Developing Countries*

Because the majority of people with HIV and AIDS live in developing countries, it is essential that vaccine trials be conducted in these countries to ensure an effective vaccine. Conducting vaccine trials in underdeveloped countries, however, is especially challenging for a variety of reasons. The biggest challenge to conducting trials in these countries is the lack of health care infrastructure and trained personnel. In addition, in order for trials to

<sup>5</sup> For more information on the CHAVI, see <http://www.chavi.org>.

<sup>6</sup> For a more thorough discussion of the challenges faced in encouraging increased private sector research and development for vaccines for diseases endemic to developing countries, see *Making Markets for Vaccines: Ideas to Action*, by Ruth Levine, Michael Kremer, and Alice Albright of the Center for Global Development. This report can be accessed at <http://www.cgdev.org>.

<sup>7</sup> In September, Senators John Kerry (D-MA) and Richard Lugar (R-IN) introduced the Vaccines for the New Millennium Act of 2005, a bill that seeks to accelerate efforts to develop vaccines for HIV/AIDS, tuberculosis, malaria and other diseases in developing countries. Representative Pete Visclosky (D-IN) introduced companion legislation in the House of Representatives. See S. 1698 and H.R. 3781.

be successfully carried out and understood by volunteers participating in them, there is a need for political leadership supporting the trials, and for countries to develop national AIDS vaccine plans. Finally, volunteers participating in vaccine trials need access to treatment and counseling programs, and to the extent possible, these trials should be coordinated with such programs funded by the President's Emergency Plan for AIDS Relief and the Global Fund.

One of the ethical issues raised at the Conference concerned informed consent among vaccine trial participants in developing countries. Generally, it is recommended that an individual have a sixth grade education level for all informed consent processes. This standard is inapplicable in much of Africa, where most of the population is illiterate. In addition, in countries where participants' beliefs about health and illness differ from those of scientists, it is critical that researchers be sensitive to local beliefs, values, and practices. It is important that researchers use local language and concepts in explaining vaccine trials and ensuring that participants truly understand how trials work. Some cultures are far less individualistic than Western cultures, and the needs of the community outweigh those of the individual. In these situations, researchers are developing methods to ensure that the decision to participate in a trial is made by an individual and not by a community leader or representative. Given the challenges of illiteracy and cultural differences, experts are continuing to explore the best methods to ethically obtain informed consent in developing countries.

*The Importance of Including Women, Adolescents, and Children in Clinical Trials*

To date, AIDS vaccine trials have focused almost exclusively on adults. However, given the alarmingly high HIV prevalence rates in adolescents—especially females—in Sub-Saharan Africa, some experts argue that the ideal AIDS vaccine would target adolescents, prior to their sexual debut.<sup>8</sup> In addition, a vaccine for infants could help prevent the transmission of HIV through breast milk, which is the primary source of nourishment for most newborns in the developing world. Many experts in the field agree that an AIDS vaccine must ultimately include children, but that conducting the necessary research raises a host of scientific and ethical concerns. Because women and girls constitute the fastest growing population in Sub-Saharan Africa to become infected with HIV, it is imperative that the scientific community ensure the inclusion of women in the pursuit of an AIDS vaccine.

Enrolling children and adolescents in such trials, however, is controversial because in many places, this would clash with cultural beliefs against discussing sex with young people and in acknowledging their sexual activity and risk of HIV infection. In addition, government officials may be hesitant to advocate for the involvement of children in trials as communities may be suspicious and fearful of allowing their children to serve as “guinea pigs.” The

<sup>8</sup>According to UNAIDS, in 2005 in Sub-Saharan Africa, among young people aged 15–24 years, an estimated 4.6% of women and 1.7% of men were living with HIV. See *UNAIDS/WHO AIDS Epidemic Update, December 2005*, p. 17.

issue of “informed consent,” already a challenge when dealing with adult participants in clinical trials, would be even more complicated when dealing with minors. The issue of including children and minors in clinical trials will require further debate by AIDS vaccine researchers, and the concerns of representatives from developing countries must be considered.

### *Regulatory Issues*

Finally, one of the issues raised by speakers at the Conference was the issue of regulating AIDS vaccines. Currently, there is no consensus as to what properties an AIDS vaccine will need in order to be granted a license. Given the variety of strains of HIV, it is also not clear whether countries will require a vaccine that has been proven effective in one or several regions to be tested again in local populations or against certain strains. Moreover, each country or region has its own licensing authority with its own requirements. Therefore, it will be impossible for vaccine producers to apply for a single license that is valid everywhere.

Regulatory agencies in developing countries often lack the capacity to review new products, such as an AIDS vaccine. Authorities in these countries will likely look to developed countries or the World Health Organization for guidance in licensing a particular AIDS vaccine but, as has been the case with the regulation of anti-retroviral drugs, each country will ultimately need to reach its own conclusions. AIDS vaccine researchers, activists, and policy makers need to begin to consider how to streamline the regulatory process for an AIDS vaccine so as to prevent the delay in distribution of a vaccine once one is developed.

### CONCLUDING THOUGHTS AND RECOMMENDATIONS

Given the rate at which the HIV/AIDS pandemic continues to spread around the world, and with growing concerns about “second wave” countries like Russia, India, China, Nigeria, and Ethiopia, it is critical that a way to prevent the spread of this disease is found. The best hope for such prevention is a vaccine. Although the biggest hurdles to the development of an effective AIDS vaccine are scientific, more needs to be done to accelerate the research behind this effort and to address the non-scientific hurdles to developing such a vaccine. Donors should collaborate so that AIDS treatment, counseling, and testing programs support on-going vaccine trials. Activists and policymakers need to work with the private sector to implement meaningful incentives that will create viable markets and encourage increased private sector activity in this area. Although experts agree that an effective AIDS vaccine is possible, it will take a greater commitment from a range of governments, organizations, scientists and committed individuals to create a vaccine to end the AIDS pandemic.