IAVI’S WORLDWIDE PARTNERS AND PROGRAMS

Countries where IAVI has scientific collaborators

Belgium
Canada
China
Denmark
Germany
Ireland
India
Netherlands
Kenya
Norway
Netherlands
Rwanda
South Africa
Sweden
Switzerland
Uganda
UK
US

Governments that are financial donors to IAVI

Belgium
Brazil
Canada
Denmark
Finland
France
Germany
India
Ireland
Japan
Kenya
Netherlands
Norway
Rwanda
South Africa
Spain
Sweden
Switzerland
Uganda
UK
US

Countries in which IAVI has advocacy or policy programs

Belgium
Brazil
Canada
Denmark
Finland
France
Germany
India
Ireland
Japan
Kenya
Netherlands
Norway
Rwanda
South Africa
Spain
Sweden
Switzerland
Uganda
UK
US

Cover: (Top) The Kenya AIDS Vaccine Initiative and IAVI sponsored an advocacy walk in Nairobi to raise awareness about the search for an AIDS vaccine and trials underway in Kenya (Photo Gilbert Otieno). (Middle) South Africa launched its first-ever AIDS vaccine trials, including a trial with IAVI (Photo Greg Reynolds). (Bottom) The Uganda Virus Research Institute (UVRI) and IAVI have completed enrollment of a trial in Entebbe; the UVRI laboratory is analyzing the immune responses elicited by the vaccine candidates (Photo Vanessa Vick).
IAVI 2003 Annual Progress Report

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IAVI’s mission is to ensure the development of safe, effective, accessible, preventive HIV vaccines for use throughout the world.
According to figures released by UNAIDS in late 2003, the number of new HIV infections worldwide continues to increase, with more than 5 million men, women and children infected last year alone. As the virus spreads in every corner of the globe, it has never been clearer that a preventive AIDS vaccine is absolutely necessary to end this epidemic.

Many challenges face us in this work but we are heartened by the significant progress made throughout the field in 2003. This past year saw more new vaccine research and development partnerships underway than ever before, a record number of vaccine candidates in trials and major steps taken to solve the complicated scientific questions still surrounding HIV. This past year also marked a historic milestone: the completion of the first large-scale efficacy trials of an AIDS vaccine candidate. Although VaxGen's vaccine candidate, AIDSVAX, did not prove to be effective in Phase III studies, the completion of these trials clearly demonstrated that it is possible to recruit and retain thousands of volunteers in different countries and to safely and ethically complete a large-scale HIV vaccine efficacy trial.

While this progress is most welcome, it urgently needs to be built upon. AIDSVAX is still the only candidate to complete Phase III testing, more than 20 years after the start of the epidemic. In 2003 the journal *Science* published a paper, authored by Dr. Richard Klausner of the Bill & Melinda Gates Foundation and co-signed by IAVI and leading AIDS experts, that called for increased resources and collaborative efforts to address key scientific challenges and move more AIDS vaccine candidates into clinical trials. IAVI is working with the paper's authors to determine the next steps to achieving these critical goals.

IAVI is pleased to have made several contributions in 2003 to the global effort to develop an AIDS vaccine. As this report details, the IAVI-sponsored Neutralizing Antibody Consortium made advances in unlocking scientific challenges, and we are proud to have sponsored five of the vaccine candidates currently in trials. In addition, our first ever independent, external evaluation completed in 2003 highlighted IAVI’s extraordinary contribution to the global AIDS vaccine effort.

As we enter 2004, human trials of IAVI-sponsored vaccine candidates are currently underway in eight countries, including Kenya, South Africa, Uganda, Belgium, Germany, Switzerland, the United Kingdom and the United States. And we are providing support for the first AIDS vaccine trials now planned in India and Rwanda. IAVI also continues to build vital public support for AIDS vaccine development and to educate and engage the communities in which we work about the importance of AIDS vaccine research and trials.

Ending the AIDS epidemic must be made a global priority. With your dedication and commitment, the world is closer to reaching that goal. At IAVI we are deeply grateful for the generous and continued support provided by all our donors. Looking ahead, IAVI will build on the momentum of 2003 and work with you toward realizing our shared vision: a world without AIDS.

Sincerely,

Seth F. Berkley, MD
President and Chief Executive Officer
EXECUTIVE SUMMARY OF 2003
ACTIVITIES AND KEY MILESTONES

AIDS VACCINE RESEARCH & DEVELOPMENT (R&D)

In 2003, IAVI continued to make significant progress in advancing and clinically evaluating four of its leading AIDS vaccine candidates. These include the DNA.HIVA and MVA.HIVA vaccines, the tgAAC09 (rAAV-HIV) vaccine and the ADVAX (multigenic DNA) vaccine.

Throughout the year, IAVI continued to pursue the development of these vaccines in Phase I/II clinical trials in seven countries:

- **DNA.HIVA and MVA.HIVA AIDS vaccines.** Achieved important milestones in testing these two vaccines:
  - Completed a small study at the Kenya AIDS Vaccine Initiative (KAVI) at the University of Nairobi to evaluate the MVA.HIVA vaccine as a 'boost' in volunteers who had completed the Phase I trial of the DNA.HIVA vaccine;
  - Fully enrolled the first expanded DNA.HIVA+MVA.HIVA prime-boost Phase I/II trial at sites in Oxford and London;
  - Fully enrolled the Phase I study at sites in Nairobi and London to evaluate different routes and doses of MVA.HIVA as a boost for DNA.HIVA;
  - Fully enrolled the Phase I vaccine study at the Uganda Virus Research Institute (UVRI) in Entebbe comparing one versus two doses of DNA.HIVA followed by MVA.HIVA; and
  - Initiated a Phase I/II study in South Africa and Switzerland to evaluate different routes and doses of MVA.HIVA without DNA priming.

- **tgAAC09 (rAAV-HIV) vaccine.** In December, IAVI initiated the multicenter Phase I trial of this vaccine at its first site in Belgium. This represented the first clinical use of the rAAV as a vaccine platform. In addition, approval was obtained from the Committee for Somatic Gene Therapy (KSG) and the Ethics Committee for the Bonn site in Germany. Trials are expected to start at additional sites in Belgium and Germany in the first quarter of 2004.

- **ADVAX (multigenic DNA) vaccine.** In collaboration with the Aaron Diamond AIDS Research Center, initiated Phase I trials of the ADVAX vaccine at sites in the US. Preparation of the MVA vaccine (ADMVA2) was also completed and is undergoing characterization.

Semliki Forest Virus (SFV) Replicon DNA and Replicon Particle Vaccines. In addition to the candidates discussed above, production of the SFV DNA.HIVA was completed and it is being evaluated preclinically in anticipation of human studies. In parallel, multigenic SFV DNA and SFV particle vaccines are being designed.

Additional Vaccine Product Research. IAVI also continued its preclinical study and assessment of additional vaccine candidates.

- **Multigenic MVA Vaccine.** Vaccine materials were produced and released by Therion Biologics Corporation. These are undergoing preclinical characterization and evaluation.

- **Orally-Administered Bacterial Vector.** The Salmonella and Shigella bacterial strains were further studied as potential vaccine vector delivery systems.

IAVI’s Human Core Immunology Laboratory (the Core Lab). IAVI’s Core Lab at the Imperial College of Science, Technology, and Medicine in London continues to test blood samples from all IAVI-sponsored clinical trial sites. Provision of standardized reagents, equipment, protocols, training and technical assistance to IAVI-sponsored trial laboratories also continued.

Members of the Core Lab staff oversaw the start of new trials in Uganda and the US. Onsite training for these trials and also trials testing another candidate, rAAV, in Belgium, and a new trial of the MVA.HIVA in South Africa/Switzerland was provided by Core Lab staff. Personnel from the South Africa trial and from one of the US sites visited the Core Lab to receive training in various SOPs, and qualifying test runs were completed in Belgium, South Africa and the US.

The Vaccine Trial Units of the Kenya AIDS Vaccine Initiative (KAVI) at the University of Nairobi and the Uganda Virus Research Institute
Executive Summary

(UVRI) in Entebbe are measuring immune responses using ELISPOT and Flow Cytometry assays. Parallel testing of the vaccine trial samples is also being done at the Core Lab in London to validate results and ensure consistency. The Core Lab also provided Quality Control evaluation for these sites in Uganda and Kenya.

Site assessments in anticipation of future Phase I trials were conducted by the Core Lab team in Rwanda, India, China and at multiple sites throughout Europe.

As part of an ongoing effort to enhance and broaden immune response measurement capabilities, the Core Lab evaluated and implemented new standardized ELISPOT readers, completed validation of the Cytokine Flow Cytometry (CFC) assay, expanded on the current CFC assay by examining the production of additional cytokines, and also evaluated a new in-vitro test for ‘immune memory’.

Preparations for Large-Scale Trials. IAVI staff and expert consultants are working with potential sites in eastern Africa that may be suitable for participation in large-scale efficacy trials of HIV vaccines. The team has completed planning for feasibility studies to prepare the sites and demonstrate readiness for efficacy trials. One of the fundamental tenets for IAVI’s site preparation efforts is to partner with existing programs, building upon the requisite expertise rather than establishing new sites.

- In Kenya, feasibility studies are being initiated at Kangemi (a district of Nairobi) and Kilifi. The Kilifi site preparation is being conducted in partnership with the Kenya Medical Research Institute (KEMRI) and Oxford University, building on the programs in malaria epidemiology and vaccines supported by The Wellcome Trust.

- In Uganda, two sites were identified at Masaka and Kakira respectively, and feasibility studies will begin soon. The Masaka site preparation is planned in partnership with the MRC-UK, building upon years of cohort development by the MRC. The Kakira site preparation is planned in conjunction with the Uganda Joint Clinical Research Centre (JCRC), which undertook the first AIDS vaccine trials in Uganda.

- In Rwanda, clinical safety and immunology laboratories are being established. Courses on GCP and GLP have been conducted and staff are receiving added training. A Phase I trial to evaluate a higher dose of DNA.HIVA is expected to start at this site in the first quarter of 2004, which will give staff the opportunity to develop practical skills in conducting a vaccine trial. The Kigali, Rwanda site preparation builds upon years of experience in HIV epidemiology studies from Project San Francisco in association with the University of Alabama.

- In Southern Africa, detailed site assessments have been performed in Zambia and South Africa.

The Neutralizing Antibody Consortium (NAC). In collaboration with the National Institutes of Health Vaccine Research Center, IAVI formed a consortium of scientists in 2002 from leading laboratories working on designing vaccine candidates that will elicit broadly effective neutralizing antibodies. The Consortium has designed several new candidate envelope proteins and screened them for HIV neutralization. It has preliminary evidence that a number of engineered candidates elicit more effective levels of HIV neutralizing antibodies than standard preparations of gp120. Iterative studies are ongoing to generate improved candidates, and to optimize the immunogenicity of such candidates with vaccine adjuvants.

Non-Human Primate Studies. As part of its program to evaluate and prioritize AIDS vaccine candidates, IAVI is conducting non-human primate studies to generate supporting data for IAVI-sponsored candidate vaccines.

The University of Pittsburgh Primate Research Center is now fully operational as IAVI’s lead primate facility, and a partnership with Becton Dickinson’s Biosciences PharMingen subsidiary serves as a central immunology laboratory for the non-human primate studies. Preliminary studies were completed in 2003 for the DNA+MVA and rAAV candidates, and new studies will be undertaken in 2004 to lay the groundwork for a comprehensive analysis of vaccine antigens required for protection.
Educating and Engaging Communities in AIDS Vaccine Research

With IAVI-sponsored trials now underway in South Africa, Kenya and Uganda, and approval obtained for a new study in Rwanda, as well as the launch of several feasibility studies to prepare countries for efficacy trials, IAVI has concurrently expanded its efforts to educate and prepare countries and communities for participation in AIDS vaccine research. During this year, progress was made on several fronts:

- Established a Country and Regional Programs initiative, including a new regional office for Africa based in Nairobi, to strengthen coordination and communication among field offices and staff, and to facilitate exchange among various countries and regions.
- Developed a framework for the creation of a network of community-based partners and NGOs to guide the development of training and outreach materials; the establishment of a resource centre to facilitate dissemination of materials; and the documentation and dissemination of lessons learned/best practices with community outreach in vaccine trials.
- Undertook efforts to understand and address the barriers to women’s participation in trials through in-country and global consultations.
- After consultation with numerous partners and stakeholders, developed a baseline guidance document on the treatment and care of trial participants, including those who become HIV-infected during the course of a trial.
- Worked with the media to promote accuracy and expand reporting of vaccine research, including a workshop co-sponsored with the WHO/UNAIDS African AIDS Vaccine Programme (AAVP) for 25 African journalists from 12 countries, media briefings in Uganda and Brazil, and a communications and media workshop in South Africa to prepare for the start of trials.
- Strengthened collaboration with AAVP by providing technical assistance to their Community Preparedness Working Group; involvement in AAVP’s annual meeting that brought together over 130 researchers, policy makers and community representatives engaged in AIDS vaccine research and development in Africa; and participating in an AAVP workshop for the development of a template for national AIDS vaccine plans throughout Africa.
- Continued efforts to establish and maintain networks to engage government and civil society in AIDS vaccine efforts, including:
  - Presenting on vaccines to a new Brazil Parliamentarian working group on HIV/AIDS, working with NGO’s, and collaborating with the National AIDS Program to prepare a briefing paper for the Foro 2003 Latin American AIDS Conference.
  - Holding a meeting in China to introduce vaccine preparedness to government officials and to examine ways of involving various stakeholders in the vaccine research process.
  - Working in India with parliamentarians, holding interactive public meetings in six states with high HIV prevalence, engaging the corporate sector, and developing an NGO network.
  - Sponsoring briefings for health professionals and collaborating on the national vaccine plan and the expanded role of the Community Advisory Board (CAB) in Uganda.
  - Meeting with the new government in Kenya to secure support; introducing a new recruitment strategy to accelerate volunteer enrolment in current and future trials; and assessing the information needs among Kenyan NGOs in areas where trials are planned.
  - Meeting in Rwanda with the Minister of Health, the Minister of State for HIV/AIDS, other key Ministry officials, religious leaders and members of the media to present IAVI’s Phase 1 vaccine trial protocol and broader goals for local efficacy trials in that country.
  - Participating in strategic planning with the South African AIDS Vaccine Initiative (SAAVI) and the SAAVI Community Preparedness Program to focus on community education activities in South Africa.

To increase country-level support for AIDS vaccines and clinical trials, a set of materials
and basic curriculum are being developed to translate complex technical information for lay audiences in a form that can be adapted to the individual needs of countries and communities.

Working with the International Conference on AIDS and STDs in Africa (ICASA) Secretariat and various partners, IAVI developed a set of vaccine activities for the September conference in Kenya that included a scientific round table, a community satellite meeting, a Ugandan Parliamentarians meeting, and a skills-building workshop.

**POLICY AND ADVOCACY FOR AIDS VACCINES**

In 2003, IAVI’s public policy program supported activities to build political support for AIDS vaccine R&D, increase funding to accelerate vaccine development and use, and develop strategies to ensure swift access throughout the world once an AIDS vaccine is developed.

- Worked with other NGOs to highlight in the 2003 G8 Communiqué the need for increased research and development on diseases primarily affecting the poor.
- Participated in European Commission discussions exploring incentives to encourage private sector investment in R&D for diseases impacting the developing world.
- Co-convened an ad-hoc coalition to develop a legislative proposal to facilitate accelerated development of new prevention technologies against HIV, TB and malaria.
- Supported and participated in an international workshop of treatment, microbicide, and vaccine advocates to identify areas for collaboration and joint advocacy.
- Co-sponsored a roundtable discussion between Indian parliamentarians and US Congressional representatives.
- Presented preliminary results from an internal research project looking at global expenditures on AIDS vaccine research and development at the AIDS Vaccine 2003 Conference held in New York City.
- Initiated a study in partnership with the Institute of Public Health at Makerere University in Kampala exploring Uganda’s experience approving and adopting new health technologies.

**INDEPENDENT EVALUATION**

IAVI’s first independent evaluation—begun in 2002 in accordance with the organization’s grants from the World Bank, Development Cooperation Ireland and the Rockefeller Foundation—was completed and published in April 2003. The evaluation panel’s final report said in part: “The panel believes that IAVI has met or exceeded most of its key goals and has been a very positive and effective force in the development of an AIDS vaccine and the likelihood that such a vaccine will be used in a timely manner where it is most needed.”

**RESOURCE DEVELOPMENT**

New grants and contributions in 2003 brought IAVI’s total cumulative funding to date to nearly US$340 million. Significant new commitments included:

- $26 million earmarked for IAVI by the US Congress for 2004-2005 in the wake of President Bush’s January 2003 announcement that the US Government has committed to spending $15 billion over the next five years on global AIDS programs.
- First-ever funding from the European Union as the European Commission’s Directorate General for Development announced that it would provide €3 million in matching funds for IAVI’s vaccine preparedness activities in east Africa for 2004-2006.
- Renewed support from four OECD government donors—Denmark, Ireland, Norway and the Netherlands.
- Renewed and increased support of US $5 million over two years by The Starr Foundation, one of IAVI’s founding donors.
- A partnership initiated with DHL, the world’s leading express delivery and logistics company, providing free essential courier service to and from IAVI’s Core Lab in London.

Even with these commitments, and broad support from other donors including the governments of Canada, the United Kingdom, and Sweden, as well as private funders such as the Bill & Melinda Gates Foundation, IAVI is actively working to raise more than US $250 million in new grants that are needed to continue funding IAVI’s programs through 2008.
INTRODUCTION

In the two decades since HIV was identified as the cause of AIDS, only one preventive vaccine candidate has completed Phase III trials to test efficacy. The long-anticipated results of these trials—conducted in two different studies, one in North America and Europe and the other in Thailand—were announced by the vaccine’s developer, VaxGen, Inc., this year and the vaccine (known as AIDSVAX) did not demonstrate protection against infection with HIV. A second HIV vaccine approach—combining a canarypox-vectored vaccine designed to induce cell-mediated immunity boosted by gp120—has now begun efficacy testing in Thailand. However, data from this trial are not expected before 2008. Many other vaccines have not advanced beyond conceptual development in the laboratory.

A landmark paper published in June in the journal Science, which IAVI co-signed with Dr. Richard Klausner of the Bill & Melinda Gates Foundation and many of the leading AIDS vaccine development agencies, argues: “Almost everyone involved in HIV vaccine research agrees that there is an urgent need to create and evaluate systematically more candidate vaccines. Despite the wide variety of conceptual approaches to HIV vaccine design, the pace of development of new HIV vaccine candidates needs to be accelerated.”

Accelerating Promising AIDS Vaccine Candidates toward Efficacy Testing

The centerpiece of IAVI’s research and development agenda for the next five years is to accelerate the development of up to half a dozen promising preventive AIDS vaccine candidates, evaluating them in small Phase I and Phase II clinical trials for safety and immunogenicity, with the ultimate goal of advancing the most promising of these to large-scale efficacy testing in the developing world.

In small trials currently underway and others slated to begin in the next few years, IAVI plans to identify which are the most promising and should be prioritized for efficacy testing. The relative advantages of these candidates will be judged from the perspectives of safety and immunogenicity, as well as manufacturing feasibility and applicability for use in developing countries.

One IAVI-sponsored candidate, a DNA.HIVA and MVA.HIVA combination AIDS vaccine, designed by Drs. Andrew McMichael and Tomas Hanke of Oxford University and based on subtype A, the most common subtype in east Africa, is being studied in partnership with the UK Medical Research Council and the University of Nairobi. The original design of this product included two DNA vaccine components to be followed by two MVA components. To date, the first DNA and the first MVA have entered clinical trials, which are currently underway in the UK, Kenya, Uganda, Switzerland and South Africa. The immunogenicity data from these trials are anticipated by early 2005.

In December 2003, two other IAVI-sponsored candidates entered clinical trials:

The ADVAX DNA vaccine (planned as part of a DNA+MVA boost) that is being developed in partnership with the Aaron Diamond AIDS Research Center (ADARC) is being tested at two centers: Rockefeller University and Rochester University in New York (US). This vaccine incorporates modified versions of six HIV genes based on subtype C, the most common subtype in Asia and Africa.

The tgAAC09 (rAAV-HIV) vaccine, also based on subtype C, entered trials in Belgium. A similar experimental vaccine has induced long-lasting T cell and antibody responses in animal models.

Because IAVI’s mission is to ensure the development of an AIDS vaccine, rather than promoting any one particular candidate, IAVI will ensure that the best and most promising candidates, regardless of the developer, reach the appropriate stages of clinical evaluation. To this end, IAVI is closely monitoring the progress of other candidates—including those now in clinical testing by Merck & Co., Aventis Pasteur and the US National Institutes of Health’s (NIH) Vaccine Research Center—and is prepared to provide assistance or to partner with if appropriate.
IAVI WELCOMES DR. EMILIO EMINI

In 2004, IAVI welcomes a distinguished new member to help lead its R&D effort. In March, Dr. Emilio A. Emini joins the IAVI senior management team as Senior Vice President and Chief of Vaccine Development.

Dr. Emini comes to IAVI after 20 years at Merck & Co., Inc., where he gained recognition as one of the world’s preeminent AIDS vaccine scientists (please see page 41 for more on Dr. Emini’s background). At IAVI, Dr. Emini will work alongside Wayne Koff, Ph.D., who has been appointed Senior Vice President and Chief of Vaccine Research. Dr. Koff will lead IAVI’s efforts to address major scientific challenges in AIDS vaccine development, and will oversee IAVI’s research to identify the next generation of promising vaccine concepts. Dr. Emini will focus on developing these concepts into vaccine candidates that are tested in human trials, and accelerating the most promising to large-scale efficacy trials and eventual licensure. Since 1999, Dr. Koff has led all of IAVI’s research and development programs.

IAVI-Sponsored AIDS Vaccine Candidates Currently In Clinical Trials

DNA+MVA (MODIFIED VACCINIA ANKARA) VACCINE

Project Background Summary

Launched at the end of 1998, the DNA+MVA (Modified Vaccinia virus Ankara) Vaccine Development Partnership (VDP) links vaccine designers in the UK with clinical research scientists in Kenya. Led by Dr. Andrew McMichael of the University of Oxford and the UK Medical Research Council (MRC) and Dr. J.J. Bwayo of the University of Nairobi and the Kenya AIDS Vaccine Initiative (KAVI), the project has generated a vaccine designed to stimulate HIV-specific cellular immune responses. Clinical trials of this vaccine are underway in the UK, Kenya, Uganda (UVRI in Entebbe), Switzerland and South Africa (Chris Hani Baragwanath Hospital, University of Witswatersrand, Johannesburg, and Medical Research Council, Durban). It is also planned to be tested in the Netherlands and Rwanda.

This vaccine candidate is planned to potentially consist of a mixture of two DNA plasmid vaccines and two MVA vectors containing genes of HIV-1 subtype A—a clade circulating in east Africa. It utilizes a “prime-boost” strategy: first, the naked DNA is injected into the body to prime the immune system, followed a few weeks to months later by the injection of MVA to boost the response.

Two Vaccine Constructs—HIVA and RENTA.

The first component, termed HIVA, consists of the gag gene of HIV-1 subtype A p24, p17, and a series of mini-genes representing CTL epitopes from HIV-1 env, gag, pol and nef. Preclinical studies with an analogous vaccine candidate in non-human primates generated high levels of CD8+ effector cell responses, as measured by cytotoxic T cell assays, ELISPOT and flow-based assays.

The second component, termed RENTA, consists of HIV clade A reverse transcriptase gene (RT) split to inactivate biologic activity, tat and nef genes that have been mutated for inactivation of biologic activities, and the two most immunogenic regions of env.

Thus the final candidate may consist of a two-part DNA prime (HIVA+RENTA) plus a two-part MVA boost (HIVA+RENTA). The DNA.HIVA and MVA.HIVA are currently undergoing clinical testing to determine the optimal dosing, route of injection and interval between DNA and MVA inoculations.

Progress in 2003

Manufacturing. Clinical Good Manufacturing Practice (cGMP) contracts were signed in 2001 with Cobra Biomanufacturing plc (UK) for the DNA.HIVA and DNA.RENTA, and with Impfstoffwerk Dessau-Tornau GmbH (IDT) (Germany) for the MVA.HIVA and MVA.RENTA, in order to secure a supply of the test vaccines for the trials in the UK, Kenya, Uganda, South Africa, Rwanda, Switzerland and the Netherlands.

The plasmid DNA.RENTA vaccine has been manufactured and released according to cGMP standards and is currently undergoing immuno-potency testing. Preclinical studies of the
DNA.RENTA and combined HIVA+RENTA DNA constructs will be finalized in the first quarter of 2004. The MVA.RENTA vaccine has been manufactured in accordance with cGMP and is currently undergoing quality control (QC) testing.

Clinical Trials of the DNA.HIVA and MVA.HIVA Vaccine Constructs

Clinical testing to date has focused on the HIVA vaccine constructs as a prototype vaccine. The Kenyan site (based at the Kenya AIDS Vaccine Initiative within the faculty of Medicine, University of Nairobi) has undertaken several Phase I/II trials. (Please refer to the table on page 7 for an overview of the clinical trials discussed below.)

▪ In 2003, year one follow-up of the Phase I safety and immunogenicity trials of the MVA.HIVA (trial #004) was completed in Nairobi. A third vaccination was proposed and has obtained regulatory approval to start in early 2004.

▪ The first expanded DNA+MVA prime-boost Phase I/II trial (#006) enrolled 119 volunteers at Oxford St. Mary’s Hospital, Imperial College of Science, Technology, and Medicine in London. The study is assessing the need for a DNA prime, the optimal dose of DNA vaccine and the best interval between the prime and boost inoculations. Data will be available in the second quarter of 2004.

▪ A Phase I trial (#008) completed enrollment in 2003 at the Nairobi site. This is a rollover trial to boost volunteers with MVA.HIVA who received DNA.HIVA in trial #002.

▪ A DNA+MVA Phase I/II trial (#009) at the Uganda Virus Research Institute (UVRI) in Entebbe enrolled 50 people under the supervision of Principal Investigator Dr. Pontiano Kaleebu. This trial will compare one vs. two priming injections of DNA.HIVA followed by MVA.HIVA.

▪ A Phase I/II trial (# 010) underway in the UK and Kenya is evaluating three doses and three routes of injection for MVA.HIVA in persons primed with DNA.HIVA; 70 volunteers were enrolled by the end of the year.

Launch of Trials in South Africa. In August, South Africa’s Medicines Control Council approved IAVI’s MVA trial (#011), a Phase I/II study initiated in South Africa and Switzerland to evaluate different routes and doses of MVA.HIVA without DNA priming. Initiation visits with both the Soweto and Durban sites were held in September and the trial began in mid-November. There has been cross-training and exchange with the UVRI trial site in Entebbe, and the IAVI clinical trials coordinator from Uganda spent several weeks a month in South Africa to assist with the launch of the trials. IAVI’s trial started almost simultaneously with AlphaVax Inc.’s AVX101 VEE candidate (HVTN #040)—for which IAVI provided significant early research and development support—which is being conducted in the same two sites as the IAVI trial. The sites, trial sponsors and the South African AIDS Vaccine Initiative (SAAVI) all worked to ensure close collaboration and minimize confusion.

A trial of the MVA.HIVA vaccine candidate started in 2003 in South Africa, a country with one of the world’s highest HIV infection rates. Above, Dr. Glenda Gray, Principal Investigator of the IAVI trial in Soweto, and Dr. Mampedi Bogoshi, administer the vaccine candidate to a volunteer. (Photo Greg Reynolds)

Additional trials are planned to evaluate higher doses of DNA+MVA, based on results from other programs and our own preliminary results. Studies are being done in parallel in a range of countries to speed up the process of determining the promise of the candidate. Data are expected at the end of 2004 or early 2005, which will allow us to decide whether to
advance the vaccine into efficacy trials or to discontinue support for its development.

**Vaccine Trial Recruitment**

**Volunteer Recruitment in Kenya.** The Kenya AIDS Vaccine Initiative (KAVI) has used a variety of recruitment strategies, including posters placed in shopping malls, hospitals, etc., advertisements on radio and television, community information seminars, and information stands set up at various exhibitions such as the Nairobi International Trade Fare.

Basic information seminars were previously given at institutions of higher learning, followed by weekly detailed seminars at the KAVI site for potential volunteers interested in participating in vaccine trials. However, KAVI recently adopted a new strategy to accelerate current trial enrollment and prepare for future studies. Thirteen peer leaders were selected from their respective communities and trained through monthly one-day workshops. In 2003, information seminars given by KAVI staff were largely organized by the peer leaders, who also provided valuable information on matters of interest or concern within their communities.

KAVI has worked in partnership with other community service NGOs, such as weekend medical camps, to show solidarity with the communities where volunteer recruitment is underway. KAVI also organized an advocacy walk in Nairobi attended by 2,000 walkers to generate interest in the HIV vaccine trials and promote volunteer recruitment.

The introductory community seminars and other activities resulted in nearly 3,000 people expressing interest in the HIV vaccine trials. Of those, 1,257 (including 36% women) attended Wednesday lunch time or Friday evening seminars at KAVI, which give potential volunteers more detailed information about trial participation.

This new strategy resulted in an acceleration of volunteer recruitment for the MVA.HIVA trial (#010) compared to previous studies. A total of 159 people signed screening consent forms and 70 were recruited to participate in the study. Nearly 60 additional low-risk volunteers were deemed eligible for enrolment.

A Community Advisory Board (CAB) has also been established for all KAVI trials.

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**Volunteer Recruitment in Uganda.** The IAVI-sponsored vaccine trial site in Uganda (based at the Uganda Virus Research Institute, Entebbe) has fully enrolled its first HIV vaccine trial (#009 - DNA+MVA Phase I/II study). Fifty volunteers are being vaccinated according to schedule.

In order to continue building community awareness, understanding and support for HIV vaccine trials, the IAVI-sponsored vaccine trials team has developed and been given approval for a volunteer screening/education protocol. This protocol will allow the team to travel to communities in and around Entebbe and Kampala to conduct information seminars. At these seminars, community members are provided with information on HIV, HIV prevention, voluntary counseling and testing (VCT) and basic information on HIV vaccines and vaccine trials. Anyone interested in obtaining more information or in participating in a trial is given an individual appointment for education and counseling with an appropriate member of the team.

The team is also working with other stakeholders in the community and with the CAB to develop additional strategies for increasing public awareness and understanding of HIV vaccine trials. These strategies include identifying and educating peer counselors within the communities, developing and
distributing a quarterly newsletter and partnering with established VCT centers in Uganda to incorporate education and post-test referrals for VCT clients who may be interested in participating in an HIV vaccine trial. The team is also working with the communities to develop strategies for increasing the participation of women in HIV vaccine research.

IAVI sponsors information seminars to educate and engage communities in the vaccine research process and to recruit volunteers for clinical trials. Above, clinical trials physician Dr. Annet Nanvubya from the Uganda Virus Research Institute, leads an information session for Entebbe area residents interested in volunteering for the IAVI-UVRI trial of DNA-MVA.HIVA. (Photo Vanessa Vick)

In the interest of speeding the overall HIV vaccine effort, the UVRI team has shared their experiences and insights on all aspects of conducting a vaccine trial (development of a CAB, volunteer recruitment and education, GCP) with other IAVI and non-IAVI HIV vaccine trial sites in Africa including sites in South Africa and other sites in Uganda.

TGAAC09 (rAAV-HIV) VACCINE (RECOMBINANT ADENO-ASSOCIATED VIRAL VECTORS DELIVERING HIV GENES)

Project Background Summary

Initiated in February 2000, this VDP is led by Principal Investigator Dr. Phil Johnson of the Children’s Research Institute (Ohio, US). The candidate vaccine is being developed by Targeted Genetics Corporation (Washington, US) and is based on HIV-1 subtype C, which is currently circulating in South Africa and neighboring countries, east Africa, and Asia.

This program uses recombinant adeno-associated virus (rAAV) as a vector. In the recombinant AAV vector (rAAV), the rAAV genes have been replaced by HIV genes. The vaccine construct contains the HIV gag-pro genes and a portion of the reverse transcriptase gene from subtype C, the most prevalent HIV strain circulating today. Proof of concept in Phase I trials will be to confirm in humans the immunogenicity of rAAV Gag-Pro-ΔRT observed in monkeys. Additional constructs containing other HIV genes could then be evaluated.

Use of rAAV as a vector for HIV genes is desirable as a vaccine approach for several reasons. First, AAV is not associated with disease in humans. Secondly, a single injection of rAAV-based vectors results in sustained and high-level expression of the foreign genes in mice and macaques, eliciting robust and sustained immune responses. The data from immunogenicity studies of rAAV Gag-Pro-ΔRT in macaques have validated this concept for an HIV vaccine. After a single vaccine dose, the levels of antigen-specific T cell responses approached or exceeded responses observed in SIV-infected macaques, and protection against simian AIDS has been demonstrated. Third, rAAV vectors are heat stable and therefore hold particular promise for use in developing countries.

Progress in 2003

Preclinical Studies. All preclinical studies for the AAV-2 Gag-Pro-ΔRT supporting the Phase I clinical study were completed and reported. A new challenge study is being designed to provide data in support of taking the AAV-2 Gag-Pro-ΔRT vaccine beyond Phase I trials if the clinical data also support this action.

Manufacturing. Filled lots of the vaccine were made available for clinical trials in the fourth quarter of 2003. These lots underwent quality control release.

Regulatory Submission and Selection of Initial Phase I Clinical Sites. Applications were submitted in Germany and Belgium for
initiation of a multicenter Phase I trial to assess the safety and immunogenicity of AAV-2 Gag-Pro-ΔRT. Approvals were obtained from the national Belgian Biosafety Committee (SBB) and the Belgian Ministry of Health.

The first trial volunteer was enrolled on December 8th, 2003 at Centre Hospitalier Universitaire Saint-Pierre in Brussels. In addition, approval was obtained in Germany from the Committee for Somatic Gene Therapy (KSG) and the first German site Ethics Committee. The additional sites in Belgium and Germany await various site, Biosafety or local approvals to begin the study.

(Please refer to the Overview of IAVI-Sponsored Clinical Trials on page 7 for a summary of all IAVI-funded trials currently underway.)

Second-Generation Vaccine. A preliminary design has been developed for a multivalent vaccine containing more genetic components of HIV to potentially elicit broader protection. Work has begun on the development of improved production processes that will allow for reproducible manufacturing of each viral component.

In addition, a new non-human primate immunogenicity study is being conducted to evaluate a different strain of AAV as a possible new vaccine platform after initial studies indicated the possibility of achieving a significant dose-reduction using this alternative serotype. Included in this study is a rollover of the AAV-dose animals to receive a boost of other vaccine platforms to determine if boosts improve overall immunogenicity or duration of response.

MULTIGENIC DNA+MVA PRIME-BOOST VACCINE USING INACTIVATED FULL-LENGTH HIV GENES

Project Background Summary

This project is a partnership with the Aaron Diamond AIDS Research Center (US). The vaccine candidate is a DNA+MVA prime-boost containing HIV genes env, gag, pol, nef, and tat based on clade C circulating in China. Genes have been mutated to prevent potentially harmful biological activities.

This multigenic DNA+MVA vaccine offers potential advantages, including the use of multiple HIV genes for eliciting more robust immunity against HIV, and novel promoter systems to increase expression of HIV genes. Preclinical studies of this candidate with a new adjuvant have shown promising responses.

Inactivated full-length HIV genes are used in this vaccine. Phase I clinical trials and comparative non-human primate studies will be used to assess whether the full-length HIV gene strategy offers advantages.

A dual promoter system with two different plasmids was used for the design of the DNA prime: ADVAX EG-1 expresses HIV env and gag, and ADVAX NTP-2 expresses Pol-Nef-Tat. Both DNAs were constructed and evaluated for safety in preclinical studies in small animals. Construction of the MVA boost component, ADMVA, containing all five HIV genes, was completed in 2002, and immunogenicity for all genes was demonstrated in small animals.

Progress in 2003

Preclinical Studies. Safety studies of the plasmid DNA in small animals requested by regulatory agencies were completed at TherImmune (Maryland, US) and at Althea Technologies (California, US).

Manufacturing. Clinical lots of the DNA vaccines were released by Vical, Inc. (US) in June. The Recombinant MVA was manufactured and is under characterization at Impfstoffwerk Dessau-Tornau GmbH (IDT) (Germany) and at the Aaron Diamond AIDS Research Center (ADARC). Production in serum-free media was successfully completed, representing an important advance in the manufacturing process.

Regulatory Submission. An IND regulatory application to start clinical trials with the DNA vaccine was granted by the US Food and Drug Administration (FDA) in October 2003. A pre-IND meeting on the MVA vaccine was held with the FDA in May 2003 to review preclinical safety studies and the clinical trial plan; no major regulatory roadblocks to Phase I trials are anticipated.

Clinical Testing. A Phase I clinical trial for the ADVAX DNA vaccine was initiated in December 2003; the trial is occurring at two sites in the US, the Rockefeller University and the Rochester University.
**OVERVIEW OF IAVI-SPONSORED CLINICAL TRIALS**

*(Please note that the status of trials given in the Comments section below is as of 31 December 2003.)*

<table>
<thead>
<tr>
<th>IAVI Trial Protocol #</th>
<th>Country Sites</th>
<th>First Participant Enrolled</th>
<th>Total # of Vols. / # Enrolled</th>
<th>Vaccines</th>
<th>Comments / Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>001</td>
<td>UK Oxford</td>
<td>Aug-00</td>
<td>18 / 18</td>
<td>DNA.HIVA</td>
<td>Initial safety, DNA.HIVA dose escalation; study completed.</td>
</tr>
<tr>
<td>002</td>
<td>Kenya Nairobi</td>
<td>Feb-01</td>
<td>18 / 18</td>
<td>DNA.HIVA</td>
<td>DNA.HIVA versus placebo; study completed.</td>
</tr>
<tr>
<td>003</td>
<td>UK Oxford</td>
<td>Mar-01</td>
<td>8 / 8</td>
<td>MVA.HIVA</td>
<td>Initial safety, MVA.HIVA; study completed.</td>
</tr>
<tr>
<td>004</td>
<td>Kenya Nairobi</td>
<td>Feb-02</td>
<td>18 / 18</td>
<td>MVA.HIVA</td>
<td>MVA.HIVA versus placebo; study amended to administer a third dose of MVA.</td>
</tr>
<tr>
<td>005</td>
<td>UK Oxford</td>
<td>Oct-01</td>
<td>9 / 9</td>
<td>MVA.HIVA boost</td>
<td>MVA.HIVA boost for volunteers in trial 001 who received DNA.HIVA; study completed.</td>
</tr>
<tr>
<td>006</td>
<td>UK Oxford, London</td>
<td>Apr-02</td>
<td>120 / 119</td>
<td>DNA.HIVA prime, MVA.HIVA boost</td>
<td>DNA.HIVA dose (placebo, low, medium dose), early boost interval versus late boost interval; enrollment completed and study ongoing.</td>
</tr>
<tr>
<td>008</td>
<td>Kenya Nairobi</td>
<td>Mar-03</td>
<td>10 / 10</td>
<td>MVA.HIVA boost</td>
<td>MVA.HIVA boost for volunteers in trial 002 who received DNA.HIVA; enrollment completed and study ongoing.</td>
</tr>
<tr>
<td>009</td>
<td>Uganda Entebbe</td>
<td>Feb 03</td>
<td>50 / 50</td>
<td>DNA.HIVA prime, MVA boost</td>
<td>1 or 2 doses of DNA.HIVA followed by 2 doses MVA.HIVA; enrollment completed and study ongoing.</td>
</tr>
<tr>
<td>010</td>
<td>Kenya, UK Nairobi, London</td>
<td>Apr 03</td>
<td>111 / 111</td>
<td>DNA.HIVA prime, MVA.HIVA boost</td>
<td>Prime-boost to evaluate 3 doses of and varying routes of administration for MVA.HIVA; enrollment completed and study ongoing.</td>
</tr>
<tr>
<td>011</td>
<td>So. Africa Durban, Johannesburg Switzerland Lausanne Netherlands Amsterdam UK Wales</td>
<td>Nov 03</td>
<td>111 / 30</td>
<td>MVA.HIVA</td>
<td>Dose escalation study to evaluate 3 doses of and 3 different routes of administration for MVA.HIVA; enrollment in first dose-level complete and study ongoing.</td>
</tr>
</tbody>
</table>

**AAV Vaccine Construct**

| A001 | Belgium Antwerp, Brussels Germany Born, Hamburg | Dec 03 | 50 / 1 | AAV | AAV HIV vaccine dose escalation study (low, medium, high) versus placebo; study ongoing. |

**ADVAX DNA Vaccine Construct**

| C001 | US New York, Rochester | Dec 03 | 45 / 5 | DNA | DNA HIV vaccine dose escalation study (low, medium, high) versus placebo; study ongoing. |
Other AIDS Vaccine Product Research

IAVI also continued its preclinical study and assessment of additional vaccine candidates. These three candidates, together with the vaccines now in clinical trials, constitute IAVI’s current AIDS vaccine product portfolio.

Orally-Administered Bacterial Vector

Project Background Summary

This VDP, launched in May 2000, has been a collaboration between IAVI and several research partners: the University of Maryland’s Institute of Human Virology (Drs. Robert Gallo and George Lewis) for development and evaluation of the Salmonella and Shigella vaccines; the Walter Reed Army Institute of Research (WRAIR) for evaluation, development and production of the Shigella vaccine; and Berna Biotech AG, a Swiss vaccine manufacturer, for process development and production of the Salmonella vaccine.

This VDP is seeking to determine whether oral administration of an attenuated (weakened) bacterial vector to deliver a DNA vaccine expressing HIV genes is more effective than injection of naked DNA vaccines. Bacterial vectors offer the potential for induction of both systemic and mucosal immunity, and have the advantage of oral administration. During the past year, new scientific publications have demonstrated with non-HIV antigens that bacterial delivery of DNA is effective in eliciting protection against mucosally delivered pathogens. Additionally, a bacterial vector vaccine would be easily affordable and thus particularly attractive for use in developing countries.

The VDP uses the Oxford–Kenya prototype DNA.HIVA subtype A Gag vaccine administered orally via the bacterial delivery system. Two different bacterial strains—Salmonella and Shigella—are being evaluated as candidate vectors in preclinical studies.

Progress in 2003

Preclinical Studies and Manufacturing. There was a delay in progress of the Salmonella program due to process development issues with the two leading candidates. These problems were addressed with the selection of a third S. typhi strain candidate. This S. typhi pDNA vaccine candidate is under evaluation at Berna Biotech AG (Switzerland) with immunogenicity evaluation in small animals ongoing.

The Shigella candidate was prepared by the Walter Reed Army Institute of Research and is undergoing preclinical safety and immunogenicity testing.

The clinical development plan was discussed with the FDA in July 2003. However, the FDA recently requested that the Shigella and Salmonella vaccine candidates be modified for safety reasons. New constructions are now being considered.

Multigenic MVA Vaccine

Project Background Summary

The goal of this VDP is to evaluate a multigenic MVA vaccine (based on HIV subtype C) and to evaluate it independently and as a booster of other candidates in development. The potential advantage of this construct over a single gene approach is that inclusion of multiple HIV genes would induce broader cell-mediated immunity to various epitopes (protein fragments) of HIV.

This project is a collaboration between the Indian Council of Medical Research (ICMR), IAVI and Therion Biologics Corporation (Cambridge, Massachusetts, US), and was officially launched in March 2001 when IAVI signed a Memorandum of Understanding with the ICMR and the Government of India.

The program aims to produce a multigenic MVA vaccine containing six HIV genes: env, gag, pol, rev, nef and tat. Genes were identified and selected from two sources: (1) HIV isolated from people infected in India, in collaboration with scientists at the National AIDS Research Institute (NARI) in Pune, India; and (2) consensus sequences of the Indian clade C. Genes have been modified to prevent potentially harmful biological activities.

Progress in 2003

Preclinical. Cell mediated immunity has been demonstrated in mice and a study to evaluate antibody response to the vaccine is in progress. A toxicology study was also conducted in mice,
but the results were inconclusive and the study will be repeated in 2004. These studies are required for the regulatory application to initiate the clinical trial, which is planned for submission late in 2004. The clinical trial is expected to begin in 2005.

Manufacturing. Manufacturing of the vaccine and placebo was conducted in 2003 and analysis is ongoing.

**SEMLIKI FOREST VIRUS (SFV) REPLICON DNA AND SFV REPLICON PARTICLE VACCINES**

**Project Background Summary**

IAVI inaugurated this VDP in May 2002 in collaboration with the Swedish biotechnology firm Bioption AB, led by Dr. Peter Liljestrom. This VDP is developing AIDS vaccine candidates using Semliki Forest Virus (SFV) replicons. The vaccine-making technology was pioneered at the Karolinska Institute, Sweden’s premier biomedical research institute.

**Vaccine Design.** Two different vaccines are planned for design using both SFV replicon DNA and SFV particles. The former is aimed at producing more of the vaccine antigen and inducing a more potent immune response than conventional (naked) DNA plasmids; the latter has advantages as it preferentially targets cells of the immune system and has shown to be immunogenic in preclinical studies in combination with MVA.

The project has four objectives:

1. Compare SFV replicon DNA vectors with a conventional DNA plasmid vaccine expressing the HIVA antigen (the Oxford-Kenya DNA.HIVA will be used as reference);
2. Design, construct and test recombinant SFV particles expressing multiple antigens from an Indian HIV clade C isolate;
3. Design, construct and test recombinant SFV replicon DNA expressing multiple antigens from an Indian HIV clade C isolate; and

**Progress in 2003**

**Research Developments.** Several different SFV replicon DNA.HIVA plasmids were constructed and their immunogenicity was assessed in mice. The objective was to compare the different SFV vectors with the conventional naked DNA plasmid expressing the HIVA antigen. The mouse data indicate that SFV-replicon DNA may have an advantage compared to conventional DNA in eliciting cellular immune responses against the model HIVA antigen. A final confirmatory mouse study will provide additional data in early 2004.

Based on completed preclinical data, a single construct has been demonstrated as stable and the GMP campaign has been completed at Cobra Biomanufacturing plc (UK). In parallel, a toxicity study has been launched at Huntingdon Life Sciences (UK). Non-human primate studies are proposed to start in January 2004 to confirm the results observed in small animals.

Dialogue has been opened with east African authorities to explore the feasibility of proceeding directly with a Phase I clinical trial in 2004 with SFV replicon DNA.HIVA compared to conventional DNA in a prime-boost schedule with MVA.

The Indian clade C antigens to be used in the SFV platform have been finalized and codon optimized sequences have been synthesized by Geneart GmbH (Germany). The GagPolNef, RevTat and Env constructs have been completed at Bioption. The double sub-genomic construct (RevTatEnv) should be completed by year-end. Following characterization, the final two constructs (GagPolNef and RevTatEnv) will pass to Cobra Biomanufacturing plc for stability testing in 2004. Alternative cell lines for packaging constructs into SFV particles are being evaluated and lab-scale cell line selection will be completed alongside preclinical evaluation in 2004.

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**Core Immunology Laboratory for Comparison of AIDS Vaccine Candidates**

**Project Background Summary**

The IAVI Human Core Immunology Laboratory (the Core Lab) is based at Imperial College Faculty of Medicine, at the Chelsea and Westminster Hospital in London. The Core Lab’s purpose is to facilitate evaluation of IAVI-sponsored AIDS vaccine candidates. To that end, the Core Lab functions as a central base
for field site laboratories, providing Standard Operating Procedures, standard reagents and training/support of field staff, and as a primary field laboratory for IAVI-sponsored trials underway in London. A percentage of samples from all IAVI-sponsored trials are tested at the Core Lab for standardization purposes.

To ensure that data on immune responses and other parameters from vaccine trials is of high quality—and therefore acceptable to regulatory authorities, the work must be carried out in accordance with Good Clinical Laboratory Practices (GCLP, see below). The Core Lab has continued to ensure that these practices are followed at all laboratories involved in IAVI-sponsored clinical trials.

Progress in 2003

**Good Clinical Laboratory Practices.** The Core Lab, in collaboration with the British Association of Quality Assurance (BARQA) and Qualogy Ltd, has further developed Good Clinical Practices (GCP)—a standard for clinical trials—to make it more relevant to laboratory work. This new set of guidelines, known as Good Clinical Laboratory Practices, has filled a previously existing gap, and has been reviewed by European, Japanese and American agencies.

**Standard Operating Procedures.** The Core Lab continues to produce and implement a number of standard operating procedures (SOPs) to ensure that work on blood specimens from vaccinated individuals is carried out in precisely the same way each time. SOPs cover all procedures performed in the laboratory and include cell separation and freezing of cells, and the ELISPOT and CFC immune assays. These SOPs have been distributed to field sites now hosting ongoing trials (Kenya, Uganda, Belgium, Oxford, Switzerland, South Africa, US), as well as sites selected for upcoming trials (Germany, Wales, the Netherlands and India).

The Core Lab has also continued to provide standardized reagents and equipment to all laboratories participating in IAVI-sponsored AIDS vaccine trials.

**Training.** Core Lab staff provide training and troubleshooting to all laboratory staff involved in IAVI vaccine trials, ensuring that GCLP is followed and the assays to detect immune responses are performed correctly. Also, prior to the start of trials at new sites, a qualifying test run must be successfully completed, in which blood samples are processed at the trial site and sent to the Core Lab, where the viability of the sample and its use in immunogenicity assays is confirmed. This is to ensure that trial samples are processed properly and that immunogenicity results can be obtained from the cells.

Members of the Core Lab staff oversaw the start of trials #009 (see table above) in Uganda and CO01 in the US. On-site training for these trials—and also trials A001 in Belgium, #011 in South Africa/Switzerland, and CO01 in the US—was provided by Core Lab staff. Personnel from two of the three sites for the South Africa trial (#011) and from one of the US sites visited the Core Lab to receive training in various SOPs, and qualifying runs were completed in Belgium, South Africa and the US.

IAVI’s Human Core Immunology Laboratory located at the Imperial College of Science, Technology, and Medicine in London oversees the immunogenicity analyses performed for all IAVI trials, assuring that they are conducted consistently and to international standards. Above, Senior Scientist Dr. Peter Hayes performs quality checks on an ELISPOT analysis, which measures the presence of immune cells elicited by vaccination. (Photo Jens Honoré)

**Monitoring of Samples.** During vaccine trials, many hundreds of cell samples from participants are banked and stored for testing.
and quality control. To enable accurate tracking of these samples, a web-based laboratory inventory management system (LIMS) was implemented at the Core Lab, KAVI, SA, Belgium and UVRI, and access and training was provided to all trial sites. This system, which is compliant with GCLP and FDA regulations, tracks samples and shipments and will also be developed to track the inventory of laboratory supplies.

**Safekeeping of Samples and Reagents.** It is vital to keep stored cell samples and reagents within specific temperature ranges to retain viability. A senior scientist from the Core Lab team implemented a radio-linked monitoring system at UVRI in March during a weeklong staff training visit.

**Quality Assurance Audit.** An external company, Qualogy Ltd (Kettering, UK), has been hired to act as Quality Assurance auditors. This is vital to further ensure that the Core Lab is working to GCLP. Qualogy conducted their first pre-audit of the Core Lab in February 2003. This was followed in July 2003 by a full QA audit that resulted in a positive report requiring only a few minor modifications to ensure full GCLP compliance. These modifications are being implemented, and full GCLP accreditation will be sought in early 2004.

**Storing and Testing Samples from Field Trial Sites.** The Core Lab itself operates a QA program to ensure that valid comparison can be made across vaccine trial sites. Cell samples from all vaccine trial participants are received for storing, and a percentage of these are tested for immune responses. This work continued for the ongoing trials in Oxford (#003, #005 and #006) and Kenya (#004 and #008), and began for the trials initiated in 2003 in Uganda (#009), Kenya/London (#010), South Africa (#011), Belgium (A001) and the US (C001).

**Dual Function as Trial Laboratory.** As noted earlier, the Core Lab also functions as a primary laboratory for two sites with ongoing trials in London. Samples from these trials are sent to the Core Lab daily, requiring cell separation and freezing and the running of immune assays. A percentage of these samples are also stored for future QA testing.

**Trial Site Assessments.** To prepare for new vaccine trials, clinical trial sites must be assessed for suitability based on their potential for new or current laboratory facilities. The Core Lab team created a template to conduct site assessments and site start-ups. In September, members from the Core Lab conducted a site visit/assessment in Rwanda, in anticipation of a Phase I trial beginning in 2004. Other site visits/assessments have been completed in India, also in anticipation of a Phase I trial beginning in 2004, and in multiple Phase I sites in Europe, including Bonn and Hamburg in Germany, Cardiff in Wales (UK), Antwerp and Wavre in Belgium, and one site in China.

**Measuring Immune Responses.** It is important that the measurement of immune responses elicited in vaccine trial participants be standardized so that comparisons can be made of different vaccine approaches. Moreover, the immune assays used should ideally detect all the cells responding to the vaccine. The Core Lab has been instrumental in moving the field forward in both these regards.

The Core Lab uses two main assays to detect immune cells responding to the vaccine—the ELISPOT assay and the cytokine flow cytometry (CFC) assay. These assays identify responding cells through their ability to produce certain proteins known as cytokines, which form part of the immune response.

**CFC Validation.** The first validation report of the CFC assay was completed in June at the Core Lab. This provided valuable data for compliance with GCLP. New technology is being explored in partnership with BD (Becton, Dickinson and Co., US), a company specializing in CFC, to ensure that this test can be processed in high volumes to facilitate vast numbers of samples being tested as large-scale efficacy trials are initiated.

**CFC Standardization.** A number of different methods to perform the CFC assay exist within the field. In an attempt to standardize these, IAVI partnered with the Canadian Network for Vaccines and Immunotherapeutics (CANVAC) to complete the first international collaborative study on CFC. This standardization study included vaccine trial labs from EuroVac, HVTN, Merck, and the VRC, among others. The results of this study were presented and
discussed at an HVTN workshop in May. The Core Lab itself performed quite well in the study, with all data points close to the median values prescribed by the CFC specialty company, BD.

This result, in addition to the strong performance in the ELISPOT collaborative study conducted in 2002, underscores the role of the IAVI Core Lab as a leader in the vaccine trial field.

ELISPOT Equipment Evaluation. An evaluation of the equipment that enables automated reading of ELISPOT assay results was performed in 2003. ELISPOT readers from three companies were compared at the Core Lab over a period of time. A German company, AUTOIMMUN Diagnostika GmbH in Strassberg, was chosen to provide readers custom-made to the Core Lab’s specifications. Machines were purchased and standardized prior to shipping to trial sites in the UK (Core lab and Oxford), Uganda, Kenya and South Africa. In addition, QA ELISPOT plates were developed to ensure analysis of ELISPOT machine performance over time and to allow comparison between sites.

New Assay Development. A key question currently facing the HIV field is whether the commonly used ELISPOT and CFC assays detect the most important cells that respond to a vaccine. This may be important in determining correlates of protection induced by a vaccine. The Core Lab is developing and validating new assays to monitor immune responses. A scientist has been hired to help develop these next generation assays, and assays have been developed to detect memory cell responses as well as the measurement of additional cytokines. The Core Lab is also establishing standardized methods to monitor mucosal responses—which has traditionally been a difficult challenge.

Expansion plans. As IAVI’s clinical program accelerates and expands, there is a need for greater laboratory and specimen storage space. Plans have been commissioned to expand the Core Laboratory and a work plan is in place for construction to begin in 2004.

Good Clinical Practice (GCP) Training. In collaboration with the Johns Hopkins University Bloomberg School of Public Health, the IAVI Medical Affairs team hosted two GCP training workshops (27-28 February in Entebbe, Uganda, and 10-11 April in London, UK) for staff of current and future clinical trial sites in Africa and Europe. The program brought together researchers from several institutions, including the Uganda Virus Research Institute, the Kenya AIDS Vaccine Initiative, Project San Francisco (Kigali, Rwanda), St. Mary's Hospital/Imperial College (London), the Medical Research Council (UK), the John Radcliffe Hospital (Oxford, UK), and Guys and St. Thomas' Hospital (London).

The course was tailored to address issues specific to vaccine trials and the sites of the current IAVI-sponsored AIDS vaccine studies. Program sessions included: concepts of GCP, ensuring safety in vaccine trials, responsibilities for human subject protection, safety assessments, investigator responsibilities, reporting adverse events, protocol components by GCP guidelines, informed consent process, and data quality and control.

Preparations for Large-Scale Efficacy Trials in Africa

As noted earlier, the cornerstone of IAVI’s research and development agenda is to accelerate the development of promising preventive AIDS vaccine candidates. These candidates are being evaluated in small Phase I and Phase II clinical trials for safety and immunogenicity, with the ultimate goal of advancing the most promising of these to large-scale efficacy testing in the developing world.

Conducting an efficacy trial that enrolls thousands of volunteers and lasts several years is a significant challenge. Rigorous adherence to the research protocol is essential and the data must be collected in a meticulous way that will be honored by regulatory authorities in future applications for licensure, should the vaccine prove effective. These challenges are compounded in developing countries, where clinical infrastructure is still limited and capacity for regulatory review of novel products is not always well established.

Site Assessments. IAVI has identified and selected five sites in east Africa—two in Kenya, two in Uganda and one in Rwanda—that may be suitable for large-scale efficacy trials of HIV.
vaccines. Detailed site assessments of potential trial sites in southern Africa have also been performed in Zambia and South Africa following site screening visits performed in 2002 and 2003.

**Building on the Work of Others.** It is important to note that whenever possible, IAVI is attempting to build on the work of other trials sites in order to avoid duplication and ensure optimal utilization of resources.

**Capacity Building.** A specific program to prepare each selected site for efficacy trials has been developed to augment their capability and capacity. These programs include financing the construction of state-of-the-art laboratory facilities and training local researchers in international clinical standards (Good Clinical Laboratory Practices, or GCLP, and Good Clinical Practices, or GCP). Where needed, Voluntary Counseling and Testing (VCT) activities will be strengthened and HIV prevalence and incidence will be defined.

**Feasibility Studies.** Feasibility studies are being initiated in four of the sites to strengthen the capacity for voluntary counseling and testing using rapid HIV tests and to obtain additional information on prevalence, incidence, risk factors and socio-demographic data.

During this capacity building exercise, sites will be required to demonstrate that persons uninfected with HIV and at risk can be counseled, enrolled and followed in a prospective epidemiological study. Community members and leaders will be educated and engaged to support these trials and community advisory boards (CABs) are being formed. In addition, the virus load, CD4 and clinical symptoms of people who become infected during the observational study will be recorded to serve as a basis for planning for the efficacy trial.

Laboratory reference ranges (the range of values considered normal in routine blood work) have not been established for many sites in developing countries. These reference ranges will be determined for the populations expected to participate in these studies to ensure that volunteers are not excluded based on what would otherwise be considered a “normal variation” in each population.

Immunology studies on uninfected volunteers will serve to prepare laboratories as well as obtain baseline information on people that may have been exposed to HIV but have not become infected.

In all areas, referral networks for support, counseling and care will be explored and strengthened in order to support general prenatal care, interruption of mother to child transmission of HIV, and care and treatment of HIV-infected or medically ill people in the community.

IAVI is developing large clinical sites in east Africa to accommodate thousands of volunteers for future efficacy trials. Above, Dr. J.J. Bwayo and his team at the University of Nairobi are partnering with IAVI to develop a site in Kangemi. The site is conducting clinical feasibility studies to identify the optimal design for an efficacy trial in the region. The renovated clinic building will be able to be used by other research teams once IAVI’s studies are completed. (Photo Frans van den Boom)

**Kenya Sites.** There are two sites beginning feasibility studies in Kenya:

- The KAVI-Kangemi Clinic: With IAVI support, the Kenya AIDS Vaccine Initiative upgraded a small building (part of the Nairobi City
Council Health Centre) at Kangemi (a division within Nairobi) to form the KAVI-Kangemi Clinic. The Community Advisory Board has been established. The KAVI-Kangemi Clinic will be used for voluntary counseling and testing and for examination of potential participants. The mapping of the area and risk factors within the community and assessment of attitudes and knowledge has been completed and will be analyzed. From the approximately 1,200 sex workers and clients identified, 180 “peer leaders” were trained in community awareness, HIV/AIDS and AIDS vaccine research in order to disseminate information to the community. Protocols for assessment of prevalence, incidence, natural history (viral load set point, CD4 and clinical end points) of HIV infection in this cohort will begin in 2004.

▪ **CGMRC/KEMRI in Kilifi:** The Centre for Geographic Medicine Research - Coast (CGMRC), affiliated with the Kenya Medical Research Institute (KEMRI), well known for extensive malaria and bacterial diseases research, has begun an active HIV prevention program in Kilifi. Preparations for a feasibility study at this site include renovations of a clinic building, community outreach, medical training, starting a family medicine clinic and upgrading and expanding VCT services to individuals and couples. An HIV prevalence survey with VCT is in progress.

**Uganda Sites.** In Uganda, two sites have begun activities for feasibility studies:

▪ **UVRI/MRC in Masaka:** The Uganda Virus Research Institute (UVRI) and the Entebbe unit of the UK Medical Research Council (MRC) will develop six general population village areas and clinics in the Masaka district to conduct feasibility protocols. They have previously conducted extensive epidemiological surveys of HIV and have excellent incidence and prevalence with relevant demographic data. They have also conducted large clinical trials with other vaccines and interventions and are currently testing microbicides. They are instituting VCT using rapid tests in the field and sensitizing the community to AIDS vaccine research.

▪ **Kakira Sugar Works:** The Joint Clinical Research Centre (JCRC) executed the first HIV ALVAC rgp120 trial in Africa. They have begun the preliminary census and sensitization activities in a general population cohort at Kakira Sugar Works, a private sugar plantation with good health care support of its workers.

**Rwanda Site.** In Kigali, Rwanda, much progress has been made at the Project San Francisco. Site staff completed courses in clinical trials conduct with a focus on HIV vaccines and Good Clinical Practices (GCP) and Good Clinical Laboratory Practices (GCLP); the latter took place at IAVI's Core Lab in London. Clinical safety and immunology laboratories are being developed, equipment is being installed and staff are receiving additional training.

An IAVI-sponsored Phase I vaccine trial (#007) will begin in 2004 to enroll members of couples where both partners are uninfected and at low risk. The protocol has been approved by the University of Alabama and the Ethics Committee in Rwanda. In the trial, a higher dose of the DNA and MVA vaccines will be used in a different regimen to compare with other regimens of the higher dose being evaluated in trials in the UK and planned for Kenya and Uganda. This study will give the staff an opportunity to develop practical skills in conducting a vaccine trial.

The manager Jean Bizimana and technicians Emmanuel Tekirya and Viateur Musengamana of the recently completed IAVI/PSF Immunology Laboratory in Rwanda are seen processing a blood sample as part of preparations for the start of an IAVI Phase I clinical trial in 2004. (Photo Mark Boaz)

The DataFax data management system will be installed and managed by a clinical research
organization (CRO, ICON). A South African branch of the CRO, Quintiles, will provide study-monitoring support. This trial will enable pilot testing of systems that will be used in large-scale efficacy trials in the future.

Addressing Critical AIDS Vaccine R&D Challenges

Non-Human Primate Vaccine Studies

Project Background Summary

IAVI’s non-human primate studies program was launched in 2002 to generate timely data for aiding decisions on general and specific vaccine design or development issues. IAVI believes that data from well-designed non-human primate studies, along with data from human safety and immunogenicity trials, process development studies for manufacturing feasibility, and intellectual property (IP) assessments regarding freedom of use, will collectively provide the most effective data set for prioritizing next-generation candidate vaccines and accelerating the best of these into efficacy trials.

A collaborative network is now in place that includes three participating primate centers, a core laboratory and a data coordinating center. Primates are obtained from USDA-inspected suppliers and all studies are conducted in compliance with regulations pertaining to experimental housing of non-human primates.

In 2002, the non-human primate studies core laboratory was established at BD Biosciences PharMingen. Immunological data generated at the non-human primate core lab will be collected and analyzed by the data coordinating center (EMMES Corporation) using protocols adapted from IAVI’s clinical trials program and customized for the non-human primate studies.

Progress in 2003

Data from the first two studies in support of IAVI-sponsored candidate vaccines, DNA.HIVA and MVA.HIVA (Oxford-Kenya VDP) and rAAV-HIV (Targeted Genetics-Children’s Research Institute VDP), have been encouraging. Further study of the rAAV-HIV immunized animals will look at booster effects of rAAV-HIV, as well as several of the IAVI-sponsored MVA candidates. Comparative immunogenicity testing of a second rAAV-HIV candidate in 2003 confirmed that it is a more potent AAV serotype. Animals are also in place for testing comparative immunogenicity of MVA candidates, and an initial test of SFV replicon DNA, both slated to start in early 2004.

The University of Pittsburgh Primate Research Center is now fully operational as IAVI’s lead primate facility, currently holding 153 animals. Preliminary studies are already underway at the Pittsburgh facility to lay the groundwork for a comprehensive comparative study of antigens required for protection (challenge study). Immunizations for that study will be started in the beginning in 2004 and phased-in challenges will begin later in the year.

Neutralizing Antibody Consortium

Project Background Summary

In collaboration with the National Institutes of Health Vaccine Research Center (VRC), IAVI has formed a consortium of scientists from leading laboratories currently working on neutralizing antibodies. The goal of the consortium is to accelerate the development of candidate vaccines that induce effective neutralizing antibodies against circulating and variable subtypes of HIV. The principal scientists include:

- Dr. Dennis Burton (Program Director) and Dr. Ian Wilson of The Scripps Research Institute;
- Dr. Robert Doms, University of Pennsylvania;
- Dr. John Moore, Weill Medical College, Cornell University;
- Dr. Joseph Sodroski, Dana-Farber Cancer Institute; and
- Dr. Gary Nabel, Dr. Peter Kwong, and Dr. Richard Wyatt of the NIH Vaccine Research Center

The research agenda of the consortium focuses upon finding ways to elicit potent neutralizing antibody responses that can be translated into development of a broadly effective vaccine. Given that five naturally occurring human antibodies have been identified that provide protection against a range of HIV isolates, it is widely believed that this challenge is solvable. Crystal structure information on the envelope
protein, in tandem with the structure of neutralizing monoclonal antibodies, is key to directing these efforts. These data will enable Consortium scientists to develop models, similar to a lock and key, where the structure of the lock is known (the antibody), and the structure of the key (the vaccine) is yet to be discovered. All of the applied research studies are managed by an industrial project manager to assure focus of the effort on usable products. Any promising products developed will immediately move into accelerated clinical development—a comparative advantage of working in such an integrated approach.

By re-engineering the HIV envelope, structures that demonstrate the greatest binding to the effective neutralizing antibodies are accelerated towards production and preclinical testing. A common reagent panel of envelope proteins and monoclonal antibodies will be an essential resource for crystallography and as reference reagents for analyzing the antigenic properties of re-engineered proteins. Developing ways to optimize envelope protein production and purification will also be invaluable. Standardized protocols for small animal immunizations will provide important groundwork for future immunization efforts and the use of high-throughput neutralization assays with the flexibility to test a broad array of HIV strains will assist in determining the unequivocal potency of immune sera.

Progress in 2003

This iterative process, from crystal, to re-engineered protein, to production and purification of candidate vaccines, to preclinical testing, has now yielded several new candidates ready to enter testing in non-human primates. In its second year, the HIV Neutralizing Antibody Consortium has:

- Completed a pilot small animal immunogenicity studies of gp120 envelope proteins and expanded the scope to include novel gp140 proteins to build a reference database for comparative assessment of design improvements.
- Completed a comprehensive analysis of MAb against a panel of 100 viruses, representing the full spectrum of HIV-1 clades, using the high-throughput neutralization assay.
- Initiated a comparison of sera from small animals immunized with first-generation re-designed envelope protein constructs (produced by the Burton, Moore and Wyatt (VRC) laboratories), using the high-throughput neutralization assay.
- Continued to build up the reagent repository to include over 50 monoclonal antibodies and a growing array of envelope proteins representing different strains of HIV, as well as SIV for use in crystallography studies and immunizations.
- Determined and published the structures of several key human MAb against a panel of 100 viruses, representing the full spectrum of HIV-1 clades, using the high-throughput neutralization assay.

- Submitted 30 new samples from the Kwong laboratory (VRC) for crystallization trials on the automated high-throughput platform ("robot").

IAVI Agreement With Maxygen

IAVI entered into an agreement in 2001 with Maxygen, Inc. (Redwood City, California, US) and DBLV, LLC (New York, NY) to explore the use of Maxygen’s MolecularBreeding™ directed molecular evolution technologies to develop novel AIDS vaccines. Maxygen has demonstrated that its proprietary technologies can be used to generate infectious disease antigens that elicit broader and stronger immune responses than do naturally occurring antigens. DBLV, LLC, a venture capital arm of the Rockefeller Foundation (New York, NY), is funding the project. IAVI is lending technical expertise to the project and has been granted a royalty-free license to market any successful vaccines to developing countries.

To date, a large number of novel antigens have been produced and characterized using
Maxygen's proprietary directed molecular evolution technologies. Maxygen’s approaches have allowed over 100 vaccine candidates to be identified, and they are currently being tested in animals. Antibodies against the antigens are currently being evaluated for their ability to inactivate the HIV virus. This study will be completed in early 2004 and will determine whether any of the candidates are promising. At that time a decision will be made whether to continue the partnership.

**GLOBAL AIDS VACCINE SURVEILLANCE EFFORTS**

IAVI has continued to maintain a surveillance system to monitor the progress of global efforts in AIDS vaccine R&D and identify new and promising AIDS vaccine development opportunities. These surveillance activities provide IAVI’s R&D staff—and others in the field—with a detailed and current global overview of the state-of-the-art of AIDS vaccine development. These data are particularly useful in identifying promising new technologies, evaluating them, and in some instances further developing them.

IAVI also provides information on the vaccine pipeline and maintains a database of clinical trials for the scientific community and the public on its website (www.iavi.org/trials).

**Annual Meeting of IAVI’s Scientific Advisory Committee (SAC)**

IAVI’s Scientific Advisory Committee held its annual meeting on 9-10 July 2003. The SAC reviewed and endorsed the four key objectives outlined in the strategic plan:

**Initiating Efficacy Trials.** The SAC endorsed IAVI’s strategy to develop the Proof of Concept efficacy trial concept (“Phase IIb” trials to speed up the determination of promising approaches). At the recommendation of the SAC, the clinical team in R&D is conducting in-depth review on the design, statistics and regulatory issues associated with such trials.

**Prioritization of the Pipeline.** The SAC endorsed the strategy to prioritize IAVI’s vaccine portfolio and focus on a few leading candidates. The SAC emphasized the need for strategic use of non-human primates studies to answer priority questions related to product development decisions. In addition, the SAC encouraged IAVI to conduct studies in order to determine the best prime, best boost, and best combinations regarding cell mediated immunity.

**Addressing Major Scientific Challenges.** The SAC endorsed IAVI’s plan to focus on the expansion of the Neutralizing Antibody Consortium. On the advice of the SAC, the science team in R&D is developing plans to address other key scientific challenges in the AIDS vaccine field.

**Manufacturing.** The SAC endorsed the concept of conducting feasibility studies aimed at enhancing process development capabilities and pilot scale manufacturing facilities for producing clinical trial material.

**INTERNATIONAL SCIENTIFIC MEETINGS**

In 2003, IAVI hosted or participated in a variety of international scientific meetings on AIDS and AIDS vaccines:

- **National AIDS Conference** (18-19 January, Mumbai, India), co-sponsored by IAVI.
- **Standardization and Quality Control of Cell and Gene Therapy Products** (24-25 February, Strasbourg, France), organized by the European Directorate for the Quality of Medicines (EDQM) and the European Pharmacopoeia Commission.
- **15th Annual Drug Information Association European Meeting: e-ternal medical progress in Roma** (5-7 March, Italy), hosted by the Drug Information Association (DIA).
- **Neutralizing Antibody Consortium Meeting - the Path from Crystal to Immunogen** (7 March, Palm Springs, CA, US), a scientific think-tank hosted by IAVI on how to make best use of structural information about HIV and neutralizing antibodies to design a broadly effective vaccine. Presentations from invited experts included electron microscopic “CAT scans” of the HIV envelope glycoprotein as well as detailed crystallographic images of neutralizing antibodies as they are bound to specific sites on the envelope. Data were presented showing the induction of neutralizing antibodies in small animals immunized with a
A prototype vaccine designed to mimic the native trimeric configuration of the envelope glycoprotein.

- **Prospects for Live-attenuated HIV Vaccines** (8 March, Palm Springs, CA, US), a meeting convened by IAVI to consider whether understanding the *mechanism* of protection could guide the development of other, safer approaches to live-attenuated HIV vaccines.

- **Keystone Meeting on HIV Vaccine Development: Immunological and Biological Challenges** (29 March - 4 April, Banff, Canada).

- **HIV Vaccine Clinical Trial Centers** (26-28 May, Bangkok, Thailand), an IAVI-funded scientific study tour for seven Indian scientists to visit various collaborating institutions in Thailand to see how actual trials are run and speak with scientists actively engaged in this work.

- **Clinical Trial Subcommittee Meeting** (24 June, New York), the first of two meetings in 2003 of this Subcommittee of IAVI's Scientific Advisory Committee.

- **Vaccine Science Subcommittee Meeting** (7 July, New York) discussed how IAVI can best tackle the key scientific challenges for HIV vaccine design.

- **IAVI Manufacturing Blueprint Advisory Meeting** (8 September, New York). Attended by the heads of manufacturing from the major vaccine companies, there was consensus that efforts in aid of manufacturing preparedness must begin seven or more years before expected first license and that process development is necessary in order to produce clinical materials representative of the final vaccine and to properly assess manufacturing economics.

- **AIDS Vaccines 2003** (18-21 September, New York). The mission of this conference is to advance research in the field by providing a forum for the sharing of new information regarding the development, delivery, evaluation, production, and implementation of AIDS vaccines and immunotherapies.

- **Neutralizing Antibody Consortium Meeting** (19 September, New York). The components are now in place to implement a generalized protocol for proceeding from protein design to immunogen evaluation and the first-generation NAC vaccine constructs are in the pipeline.

- **Clinical Trial Subcommittee Meeting** (2-3 October, New York). The meeting featured talks by two prominent bio-ethicists, and a distinguished clinical trials statistician, along with discussion on plans for feasibility studies and efficacy trial design.

- **Mucosal Immunity Workshop** (17-18 November, New York), this IAVI-sponsored meeting, chaired by Dr. Ken Rosenthal of the Canadian Network for Vaccines and Immunotherapeutics (CANVAC), brought together scientists with expertise in mucosal biology and immunology with special emphasis on the assessment of mucosal immune responses.

- **WHO Informal Consultation on Characterization and Quality Aspect of Vaccines Based on Live Viral Vectors** (4-5 December, Geneva), the aim of this meeting was to review experience with the development and evaluation of candidate vaccines based on live viral vectors, such as adenoviruses, poxviruses (e.g., avian poxviruses, MVA), Semliki Forest Virus, VEE, Sindbis, yellow fever virus and to discuss related regulatory issues.

**Educating and Engaging Communities in AIDS Vaccine Research**

As the number and scale of IAVI-sponsored AIDS vaccine trials and related activities increases, there is a need to expand local capacity and build expertise in the countries hosting those trials. IAVI has had an office in India for two years and in 2003 opened an East Africa Regional Office in Nairobi, Kenya. This office allows IAVI to better coordinate its activities in the region, including clinical trials, community education, communications and policy/advocacy efforts. Both the India and Kenya offices provide invaluable information regarding the experiences and perspectives of countries participating in AIDS vaccine research.

IAVI has established a Country and Regional Programs department to support fieldwork generally and to strengthen coordination and
communication among field offices and staff. The three overarching goals of this effort are:

1. Support the clinical trial sites by ensuring that there are adequate services, including VCT and referral services, and a supportive community environment.
2. Outreach to stakeholders to strengthen support for vaccine research through increasing awareness, understanding, and participation in the vaccine development process.
3. Accelerate R&D and prepare for future vaccine access by obtaining national level input in the development and implementation of IAVI’s global policy and other cross-cutting initiatives.

Key activities undertaken by the department during 2003 are discussed in greater detail below.

Understanding Women’s Participation in Trials. IAVI is committed to having women participate in AIDS vaccine trials in sufficient numbers to detect differences in efficacy related to gender. However, in many of the countries hosting trials, there are significant barriers to women’s ability to make a free and informed choice regarding trial participation. During 2003, extensive consultations were undertaken in India to better understand and address these barriers. A similar effort is ongoing at the international level and is scheduled to begin in Africa in 2004. A report on the findings to date will be forthcoming in early 2004.

Ensuring Treatment and Care for Trial Participants. During 2003, IAVI consulted with numerous partners and stakeholders—including ethicists and other experts—in developing a baseline guidance document covering the treatment and care of trial participants, including those who become HIV-infected during the course of a trial. This policy is based on a model of shared responsibility that seeks to ensure that both trial participants and communities hosting trials are able to access care and treatment. IAVI’s President Seth Berkley published an article on ethics and treatment in trials in the British medical journal The Lancet, which was IAVI’s first public statement on the issue. A further consultation was conducted in Uganda with vaccine researchers, treatment providers, government officials and community representatives to continue the process of consensus building around appropriate country-specific treatment policies. A similar meeting is planned for India early in 2004.

Materials for Vaccine Literacy. To increase country-level support for and community participation in AIDS vaccines and clinical trials, a set of educational resources and basic curriculum are being developed to translate complex technical information into accurate, consistent materials that can be adapted to the varying needs of individual regions, countries, and communities.

Collaboration with the WHO/UNAIDS African AIDS Vaccine Programme (AAVP). AAVP is a WHO-sponsored organization bringing together African AIDS researchers, including most of IAVI’s research partners on the continent. By working with AAVP, IAVI is able to collaborate on pan-African advocacy for AIDS vaccines and to exchange information, expertise and lessons learned with partners in countries where IAVI is not working directly. In 2003, IAVI collaborated with AAVP on several activities:

- Regional Media Workshop. A media workshop on AIDS vaccines for 25 African journalists from 12 countries was held in Kenya and included a tour and briefing with the researchers at the Kenya AIDS Vaccine Initiative. Within two weeks of this workshop, multiple articles and broadcasts appeared in print and electronic media in Botswana, Cameroon, Kenya and Zambia that highlighted both the need for and progress towards an AIDS vaccine.

- Community Preparedness Working Group. IAVI continues to provide technical assistance to the Working Group’s strategic plan and operations to ensure community participation is integrated into AAVP’s scientific agenda.

- Annual Conference. IAVI participated in developing the agenda, participant list and presentations for AAVP’s annual conference held in Addis Ababa, Ethiopia, in June. The meeting—entitled “Strategies for the Development of HIV Vaccine Trial Sites in Africa: Challenges And Opportunities”—brought together over 130 researchers, policy makers and community representatives engaged in AIDS vaccine research and development in Africa to share
experiences and build collaborations. IAVI sponsored a number of participants from its trial sites in Africa and hosted a satellite meeting to review progress to date and establish mechanisms for increased community involvement and multi-site collaboration.

- **National Vaccine Plans.** IAVI’s East Africa Regional Office and Uganda-based staff participated in an AAVP workshop to develop a template for National AIDS Vaccine Plans. IAVI representatives contributed content for the final draft documents and will continue working closely with the AAVP initiative.

- **NGO Network.** Based on discussions with a number of national and international NGO partners, IAVI is developing a network of community-based partners and NGOs to guide several initiatives, including:
  - the development of training and outreach materials;
  - the establishment of a resource center to facilitate dissemination of materials; and
  - the documentation and dissemination of lessons learned/best practices with community outreach in vaccine trials.

- **International Conference on AIDS and STDs in Africa (ICASA).** For the September conference in Kenya, IAVI worked with the ICASA Secretariat and various partners to develop a range of vaccine activities that included a scientific round table, a community satellite meeting, a Ugandan Parliamentarians meeting, and a skills building workshop.

### Country Programs

#### Kenya

IAVI has developed strong relationships with KAVI and other potential trial sites in the region to continue a number of Phase I studies and to develop capacity for future efficacy trials. While local capacity is increasingly strong, national recognition of the local effort and the importance of vaccines in general has in the past been disappointing. However, with the opening of the regional office and the change of government in Kenya, IAVI is now seeing some success in making vaccines a much higher priority for Kenya and the region.

#### East Africa Regional Office.

In August, IAVI opened an office to support its activities in Africa. Dr. Samuel Kalibala, a distinguished Ugandan physician with a long history of managing research in Africa, was hired as Regional Representative. An excellent multidisciplinary team is now in place and working throughout the region.

- **Political Support.** IAVI has been working to secure the support of the new Kenyan government. The Minister of Health, Hon. Charity Ngilu, and her staff have shown great interest and commitment, and recently convened a full-day meeting that brought together all of the groups working on AIDS vaccine research in Kenya. As one result of that meeting, a working group has already begun to outline a National HIV Vaccine Plan.

- **NGO Network.** The Regional office has agreed to a workplan with the Kenyan AIDS NGO Consortium (KANCO) to work with member NGOs in areas of Kenya where IAVI is working to build community support for HIV vaccine research.

- **Information Needs Assessment Among Kenyan NGOs.** In an effort to tailor educational materials on HIV vaccines and trials to local constituents, an information needs assessment was conducted among 61 NGOs in the four regions where IAVI is working. Preliminary findings were promising:
  1. knowledge of AIDS vaccines among the NGOs interviewed is higher than expected;
  2. there is need for clarification of technical scientific concepts (e.g. clinical trial processes);
  3. there is less skepticism and fear surrounding AIDS vaccines than expected;
  4. media messaging surrounding the KAVI trials is reaching NGOs as a targeted audience;
  5. NGOs interviewed would be willing partners in AIDS vaccine advocacy; and
  6. there is a need for targeted trainings and development of a strategic work plan for incorporating vaccines into these NGOs’ existing program activities.

#### Uganda

There is strong political commitment for AIDS vaccines in Uganda and excellent relationships
have been forged with the Uganda Ministry of Health, other potential trial partners and the Uganda AIDS Commission. Within two years, IAVI has built, equipped and trained a clinical trials site, received rapid political, regulatory and community approval, and fully enrolled its first Phase I AIDS vaccine trial. The team is working to ensure that the IAVI/UVRI site builds further on its Phase I expertise and that additional sites are developed for possible efficacy trials. The IAVI/UVRI CAB has been particularly active and provides a strong model for work in other locales.

**Inauguration of the Vaccine Trial Unit.** On 25 July, IAVI and UVRI inaugurated a new Phase I trial facility in Entebbe. The construction of the unit was funded by IAVI and contains immunology laboratories and counseling and clinical examination rooms. The IAVI/Uganda Phase I vaccine trial data is generated at this site and the entire IAVI/UVRI team is stationed there. Minister of State for Health, the Hon. Mike Mukula, officiated at the ceremony, which was attended by the US Ambassador, the British High Commissioner, the President of IAVI, and representatives from government organizations and NGOs. Members of the CAB and several vaccine trial volunteers were also present and received special recognition. “The volunteers are truly the unsung heroes of this effort and the world owes them an enormous debt of gratitude for their altruism,” said IAVI’s President Seth Berkley.

**Standard of Care Consultation.** The Ugandan Ministry of Health and IAVI convened a high-level, expert consultation to better define the appropriate care and treatment for clinical trial participants and host communities. This discussion takes on added importance as IAVI and its local partners explore the feasibility of conducting large-scale vaccine trials in Uganda. This consultative meeting resulted in the formation of a working group consisting of leading Ugandan HIV researchers and representatives from the Uganda AIDS Commission, the Ministry of Health and the AIDS Control Program. With IAVI acting as secretariat, this group will draft a document to provide guidance to the government and to research sponsors on the issue of providing care to individuals who become HIV infected while participating in AIDS clinical trials.

**Research on Product Introduction.** IAVI and the Institute for Public Health (IPH) in Uganda initiated a joint research project on how new health technologies have been approved and adopted within the country. This study, which will be completed in early 2004, will lay the groundwork for an access agenda in Uganda and will also be the basis for similar research in other countries.

**Community Advisory Board.** The IAVI/UVRI CAB is playing an increasing role in designing and implementing a recruitment strategy to accelerate enrollment in future trials. Members of the CAB assist in identifying appropriate communities where the IAVI/UVRI team may conduct information seminars on HIV vaccines and vaccine trials. CAB members are active in attending these seminars and in explaining their role in advocating for both the community and potential trial participants. A community newsletter on HIV vaccines and vaccine trials in Uganda was launched in 2003 and is distributed quarterly to a wide network of CBOs, NGOs, parliamentarians, policy makers and other stakeholders. CAB members contribute to this newsletter and also provide input into IAVI’s new global community newsletter, VAX.

**Medical Professionals Briefing.** Recognizing the importance of keeping local members of the medical profession informed of its efforts, the Uganda team conducted a one-day training program for more than 200 health professionals.
from Entebbe and Kampala. The purpose of the briefing was to provide basic information on IAVI-sponsored HIV vaccine trials and to present AIDS vaccine research within the context of a comprehensive AIDS prevention strategy.

**Media Briefing.** The Uganda team also held an IAVI-sponsored vaccine update for 45 media professionals to assist them in reporting on vaccine research. The workshop resulted in strong press coverage to support volunteer recruitment.

**National Vaccine Plan.** The IAVI/UVRI team continued close collaboration with the Ugandan AIDS Commission to contribute to the development of the final draft of the Ugandan National AIDS Vaccine Plan, which now includes an expanded section on community preparedness. This Plan is a critical foundation for all vaccine-related activities in Uganda, serves as a model for other countries, and will now be circulated to a broader range of stakeholders for final consultation.

**South Africa**

IAVI was instrumental in the start-up of the South African AIDS Vaccine Initiative (SAAVI) and continues to maintain strong relationships in South Africa, not only because of the severity of the epidemic there, but also because of the country’s scientific, manufacturing and political leadership in the region and globally. As reported earlier, in August, the Medicines Control Council approved IAVI’s MVA trial (IAVI #011), just after it approved AlphaVax’s VEE trial (HVTN #040), a candidate whose early development was also supported by IAVI. Initiation visits with the Soweto and Durban sites were held in September and the trial began in mid-November.

**Media Preparation for Trial Launches.** IAVI and SAAVI co-hosted a communications and media workshop for the principal investigators of the two Phase I studies. Both the quantity and quality of press coverage for both trial launches was excellent. This has been largely attributed to intensive collaboration between the trial sites, SAAVI, HVTN and IAVI. Throughout the launches, the stories focused on both trials getting underway and the importance of conducting multiple trials of different vaccine products.

**SAAVI / IAVI Collaboration.** IAVI and SAAVI held a series of strategic planning meetings to outline areas of collaboration on community education activities in South Africa and to link these activities into a broader regional network. SAAVI received a grant from the EU for ongoing and expanded community preparedness, and IAVI is specifically included in this project as a partner to link SAAVI’s effort regionally and internationally. Similarly, SAAVI is part of IAVI’s expanded vaccine preparedness efforts in east Africa that are also being partially funded by the EU.

**Efficacy Trials Site Assessments.** IAVI staff made additional site assessment visits in South Africa and neighboring countries to review possible efficacy trial sites for the region. A report was prepared and a southern Africa strategy is being developed for implementation in 2004.

**Gender and Ethics.** These cross-cutting thematic issues are a key part of IAVI’s activities in South Africa. There is a growing collaboration with the SA HIV Vaccine Ethics Group of the University of Natal (HAVEG) to link the efforts of both organizations. As part of its gender program, IAVI sponsored a special vaccine panel at the 10th annual South Africa Reproductive Health Priorities Conference and delivered a presentation on gender and AIDS vaccine research and development.

**Rwanda**

IAVI has worked closely with the University of Alabama-Birmingham (UAB) and Project San Francisco (PSF) to develop a new trial site in Kigali, Rwanda. An initial Phase I trial (IAVI #007) has been approved and the site has been initiated. In this process, the regional office and the trial sites in Kenya and Uganda have been actively engaged to ensure that experience and solutions are transferred among sites and that there is programmatic coherence across the region. It is anticipated that this initial Phase I trial will help prepare the site for future efficacy trials.

**Stakeholder Outreach.** IAVI’s Medical Affairs and Vaccine Preparedness programs participated in a high-level meeting convened by key stakeholders in Rwanda to review IAVI’s Phase I vaccine trial protocol and broader goals for local efficacy trials. The meeting included the Minister of Health, the Minister of State for
HIV/AIDS, other key Ministry officials, religious leaders and members of the media.

**Good Clinical Practices.** In anticipation of the start of trial #007, PSF staff were trained in Good Clinical and Laboratory Practices. IAVI’s Core Lab and Medical Affairs teams have worked extensively with local staff to ensure the successful launch and conduct of the Phase I trial in 2004.

**Couples’ Voluntary Counseling and Testing.** IAVI is working closely with PSF and UAB to capitalize on the success of the Couples’ Voluntary Counseling and Testing (CVCT) program. A CVCT workshop was held in November to review local experiences to date. IAVI sponsored trial staff from other sites in the region to attend the workshop so that CVCT techniques could be evaluated for possible integration into other trial sites. These other trial staff prepared a “vaccine day” workshop following the CVCT event to familiarize the Rwandan site staff and government officials with the practicalities of conducting vaccine clinical trials. The President of Rwanda, Hon. Paul Kagame, opened the workshops with a moving speech highlighting the importance of both CVCT and vaccine research.

> **Needless to say, we are committed to supporting any effort that may contribute to finally stemming the AIDS pandemic. We do so in the understanding that an HIV vaccine is possible. And that when a safe and effective vaccine is discovered, Rwandans will have made their contribution.**
> 
> **Hon. Paul Kagame**
> **President of Rwanda**

**India**

Opened in early 2002, IAVI’s India office now has full representative office status. IAVI’s strategy in India has been guided by an integrated approach of building strong political and community support concurrent with building technical capacity for clinical trials. Based on strong partnerships with the Indian Council of Medical Research (ICMR), its subsidiary, the National AIDS Research Institute (NARI), and the National AIDS Control Organization (NACO), IAVI has developed broad support from the President—who mentioned the organization, its focused pursuit and the need for AIDS vaccines during several speeches—as well as from ministers and parliamentarians. The government has repeatedly committed to a shortened timeline for regulatory review and other means of accelerating trials.

**Expanded Testing of AIDS Vaccines.** As a direct result of the support expressed by India’s President and Prime Minister at IAVI’s December 2002 Board Meeting in Delhi, IAVI and the Government of India have agreed that up to three or four vaccine candidates can enter Phase I trials in India as soon as the products are ready for human testing. The Government also agreed that IAVI could immediately establish two “cohort plus” studies in preparation for expanded efficacy trials. The planning and assessment for the cohort studies is nearly complete and work is expected to begin in the first half of 2004. These cohorts would ideally be available for efficacy trials of any vaccine candidate agreed upon between ICMR, NACO and IAVI.

**Preparations for Phase I Vaccine Trial.** India’s first Phase I AIDS vaccine trial is planned for 2004 in Pune. Numerous preparatory activities occurred in 2003, including preparation and pre-testing of outreach and education materials for volunteer recruitment.

**Clinical Trials Site Development.** The clinical trial site now being developed is the National AIDS Research Institute (NARI) in Pune, Maharashtra, headed by Dr. R.S. Paranjape. Dr. Sanjay Mehendale will serve as the lead clinician for the clinical trials and Dr. Madhuri Takhar, (immunologist) will lead the GCLP compliant laboratory in Pune. Renovation of the clinic and laboratory spaces is complete and equipment for the immunology lab has been ordered. Clinic and laboratory staff have been recruited and the lab staff will receive training in Good Clinical Laboratory Procedures (GCLP) at the IAVI Core Lab in London in January 2004. The volunteer recruitment plan, led by behavioral scientists Seema Sahay and Nita Mawar, has also been established.

**State Level Meetings.** India’s diverse cultures require that health intervention programs take a state-level approach to adapt to each area’s unique considerations. As part of a process to build consensus among civil society regarding the need for an AIDS vaccine, IAVI held public
interactive meetings in collaboration with NACO and ICMR in six high prevalence states. Preparing for these meetings involved outreach to literally thousands of people in these areas.

**NGO Network.** A working group comprised of five nationally networked NGOs was set up to help build additional networks and collaborations at both national and international levels. The working group organized an initial workshop for over 40 NGO representatives in Bangalore in August entitled "Developing Coalitions and Partnerships for HIV Vaccine Development and Access". This new national NGO network feeds into IAVI’s global NGO network, thus facilitating information sharing. The mandate of the NGO coalition includes advocacy and information dissemination for AIDS vaccines and vaccine trials among the communities. The working group further agreed to convene meetings of NGOs working at the community level in their respective states. The initial focus will be in Maharashtra and Tamil Nadu, where Phase I trials are being planned.

**Engaging the Corporate Sector.** IAVI had numerous interactions with the private sector in 2003, culminating in a business leaders’ roundtable with President Seth Berkley in December. Work on HIV vaccines was strongly endorsed, including several offers of support.

**China**

As vaccine R&D efforts move forward in China, IAVI has been working to devise an appropriate institutional structure for selected vaccine preparedness activities to begin in 2004. This will include an initial workshop to introduce the concept of vaccine preparedness to researchers, officials, and other stakeholders, and several other preparatory activities.

**Brazil**

Although IAVI’s work in Brazil is not based on clinical trials, this country has much of the technical, political and community capability and capacity that IAVI seeks to build in areas where trials are planned. With limited investment, IAVI has forged strategic partnerships with Brazil’s very active NGO community and the National AIDS Program (NAP) to keep vaccines on Brazil’s agenda and link its efforts with others around the world. Brazil’s leadership in the HIV/AIDS field, particularly in the area of treatment, also makes it a vital partner for vaccine advocacy.

**Foro 2003 (Latin American AIDS Conference).** IAVI, in collaboration with the Brazilian National AIDS Programme (NAP), released a policy briefing document in English, Spanish and Portuguese focusing on developing country governments and communities. IAVI also helped coordinate a round-table discussion on vaccine activity in the region.

**NGO Relations.** IAVI sponsored and attended a satellite meeting held at the National AIDS NGO Conference, fostering collaboration between all Brazilian NGOs that do work related to AIDS Vaccines. The meeting was organized by Grupo de Incentivo à Vida (GIV). As part of its community education activities, IAVI supports the publication of GIV’s National AIDS vaccine newsletter, which reaches over 9,000 people per issue. IAVI has also provided a grant to Grupo Pela Vidda, an NGO based in Rio de Janeiro, to support the development and distribution of an innovative vaccine education toolkit targeted at health care professionals.

**Media Outreach.** A workshop for journalists sponsored by IAVI and the NAP was held in June. The workshop also involved local community partners, national HVTN trial sites and other key players in the AIDS vaccine field in Brazil. As a follow up to the workshop, an in-depth analysis of the media coverage of AIDS
vaccines in the country over the past three years was conducted by a local contractor and will be used as a resource for guiding and evaluating media outreach activities at the national level.

Parliamentarians Briefing. In September, IAVI presented at the launching of a new parliamentarians working group on AIDS at the National Congress. The working group, which brings together over 50 Members of Parliament and works closely with the NAP, focuses on advancing legislation that supports the development of AIDS policies. Leading parliamentarians have expressed significant interest in incorporating vaccine issues into the working group’s agenda.

Mobilizing International Support and Assuring Future Vaccine Access

PUBLIC POLICY

Overview. IAVI’s public policy program supports the development and implementation of public policies at both national and international levels to accelerate the development of HIV vaccines for the world and to ensure swift global access once a safe and effective preventative vaccine is developed. Priority areas for the public policy program are: building political support for AIDS vaccine development; mobilizing funding to accelerate vaccine development and use; understanding demand and need; and developing strategies to ensure swift access to AIDS vaccines, particularly in developing countries.

New Vice President of Public Policy

In May 2004, IAVI’s Public Policy department looks forward to welcoming Dr. Robert Hecht, who will lead efforts to develop and advocate for public policies to accelerate the development of a preventive AIDS vaccine and ensure future global access. Dr. Hecht comes to IAVI from a 20-year tenure at the World Bank, where he most recently served as Manager of the Bank’s central unit for Health, Nutrition, and Population, which is responsible for global strategies, knowledge, technical services and partnerships. (Please see page 41 for more information on Dr. Hecht’s background.)

Additional New Staff. Another welcome addition to the public policy staff is Dr. Chutima Suraratdecha, who joined IAVI in August 2003 to manage policy activities directed at understanding demand for an AIDS vaccine. Prior to joining IAVI, Dr. Suraratdecha held a joint appointment as an Associate Professor of Economics at Sukhothai Thammathirat Open University and as a researcher at the International Health Policy Program, Thai Ministry of Public Health.

Policy Advisory Committee. IAVI’s Policy Advisory Committee (PAC)—comprised of experts from a range of fields including public health, vaccine development, and international governance—met for the first time in New York City on 4 September. At the meeting, members of the PAC were briefed about IAVI’s public policy program and feedback was sought on options for moving this work forward and for gaining a better understanding of the political and scientific environment in which HIV vaccines are now being developed and how they will be used in the future. The PAC will convene again in mid-2004. (Please see page 46 for a complete list of the PAC members.)

POLICY ADVOCACY

In 2003, IAVI undertook a number of activities aimed at increasing global awareness of the need for an AIDS vaccine and for the adoption of policies to support rapid vaccine development and future use.

Evian 2003 G8 Summit. In advance of the G8 summit held in June in Evian, France, IAVI worked with French partner organization AIDES, the Access to Medicines Team at the UK’s Department for International Development (DFID), and partner organizations in the US and Canada to advocate for language in the 2003 G8 Communiqué emphasizing the urgency of increasing research and development on diseases primarily affecting developing countries. The final communiqué includes an action plan which encourages G8 members to meet the commitments in the UNGASS Declaration of Commitment on HIV/AIDS and urges them to: increase R&D efforts for therapeutic and preventive health technologies for diseases chiefly impacting the poor, to support research and public-private partnerships, and to explore options for creating incentives to facilitate private sector involvement.
US Prevention Technologies Collaboration. IAVI continues to play a leading role in an ad-hoc coalition of groups to promote a bi-partisan legislative proposal in the United States Congress to accelerate the search for new prevention technologies against AIDS, TB and malaria and to prepare for global access to these products. The coalition includes microbicides groups, public-private partnerships for TB and malaria vaccines, organizations such as BIO (the biotechnology industry trade association), the AIDS Vaccine Advocacy Coalition and other advocacy groups. The group has secured a commitment from a Congressional Democrat to sponsor the legislation and is seeking additional bipartisan cosponsors. It is hoped that the legislative proposal will serve as a model for similar action to accelerate research and development in other countries.

European Commission. The European Commission’s Directorate General for Development (DG Development) is exploring options for European incentives directed at encouraging private sector investment and engagement in R&D for diseases affecting developing countries. IAVI staff have been involved in the ongoing discussion and IAVI has been invited to participate in early discussions regarding possible options and criteria for prioritization.

World Economic Forum 2003 (23-27 January, Davos, Switzerland), IAVI President and CEO Dr. Seth Berkley attended this annual meeting of global leaders, at which he led discussions on three panels that covered the economic impact of HIV/AIDS, the vital importance of vaccines and organizational leadership.

VaxGen Trial Announcements. In February, VaxGen, a California-based biotechnology company, announced the results from the Phase III trial of their clade B AIDS vaccine. In advance of the announcement IAVI made strategic outreach efforts to policymakers, NGOs and others to ensure that they had sufficient background information to understand the scientific and policy implications of the results. In addition, IAVI worked closely with its international partner organizations to develop and widely distribute key messages reinforcing the need for the global community to intensify the search for a vaccine.

Global Alliance for Vaccines and Immunization (GAVI). IAVI continues to serve as the NGO representative to the GAVI Financing Task Force. In addition, Public Policy staff met with the GAVI Secretariat in Geneva in February to explore possible areas for coordinated advocacy efforts.

International Conference on R&D for Neglected Diseases (29 April, Geneva). In April, IAVI presented on the global responsibilities and partnerships required to develop AIDS vaccines at a meeting organized by Médecins sans Frontières (MSF), Consumer Project on Technology (CPTECH), OXFAM, Health Action International (HAI) and Third World Network (TWN). The meeting, held as a precursor to the World Health Assembly’s May discussions on intellectual property rights and innovations in public health, focused on developing new models to intensify and accelerate R&D efforts for neglected diseases.

Outreach to Parliamentarians. IAVI co-sponsored a roundtable meeting of members of the Indian Parliament and US Congressional Representatives in Washington, DC in June. The briefing discussed the critical leadership roles of India and the US in research and development of HIV vaccines. Over 45 policymakers, non-governmental organization representatives, policymakers, business leaders, and vaccine advocates attended the meeting, which was co-convened by the Global Health Council, the Center for Strategic and International Studies, the Indo-US Parliamentary Forum (IUPF), the US-India Business Council, the Federation of Indian Chambers of Commerce and Industry, and the AIDS Vaccine Advocacy Coalition.

IAVI also supported a meeting in October of the Asian Forum of Parliamentarians on Population and Development devoted to HIV/AIDS and vaccines in Bangkok. Parliamentarians from 11 Asian countries participated and issued a declaration in support of parliamentary action on HIV vaccines. IAVI also sponsored the participation of officials from Uganda and South Africa to increase cross-regional exchange.

BIO 2003 Annual Conference (22-25 June, Washington, DC). IAVI participated in a panel discussion on public policy options to accelerate research into microbicides and vaccines for AIDS, TB and malaria at the annual
conference of BIO, the biotechnology trade association. Discussions focused on potential policy actions to create incentives for industry to invest in the research and development of new preventative health products.

**Brainstorm 2003 (28-30 July, Aspen, Colorado),** a forum convened by Fortune magazine, brought together business, technology, and world affairs leaders to tackle some of the world’s most difficult issues, including political, religious, and military tensions; global warming; the global economic divide; and the social responsibilities of corporations. Dr. Seth Berkley served on a panel entitled “Epidemics: AIDS, SARS—What’s next for the world’s health? How should we respond?”

**UNGASS Review.** In September, the UN General Assembly assessed progress on the 2003 and 2005 targets set forth in the 2001 UNGASS Declaration of Commitment of HIV/AIDS. IAVI lobbying helped ensure that AIDS vaccines were incorporated in the initial UNGASS declaration. In advance of the 2003 meeting, IAVI wrote to the Permanent Missions of countries supportive of AIDS vaccines, expressing its commitment to the UNGASS Declaration and highlighting the concerted global effort still required to move the AIDS vaccine field forwards.

**The Search for New Medicines (15-16 Sept., London).** IAVI attended a meeting on the role of alliances in bridging the gap between access and innovation at the Royal Institute of International Affairs (Chatham House). IAVI also participated in a related seminar series held by the Royal Institute.

**Canadian HIV/AIDS Legal Network (17-19 Nov., Montreal).** IAVI co-sponsored an international consultation on opportunities for collaboration between treatment, microbicides and vaccine advocates and researchers to speed development efforts and ensure global access to new health technologies. The meeting, hosted by the Canadian HIV/AIDS Legal Network, brought together experts from 12 countries to address the need for coordinated efforts by those working in treatment, vaccines, and microbicides to develop an effective comprehensive response to HIV. Participants strategized on areas for collaborative work and a Joint Statement of Commitment is being drafted.

**Global Health Forum (2-5 Dec., Geneva).** IAVI attended the Seventh Global Forum for Health Research. The annual meeting brings together a range of stakeholders from the public and private sector, including aid agencies, researchers, government representatives, foundations and NGOs to examine issues related to health research in developing countries. The 2003 meeting included discussions on the consolidation of the public-private partnership field, underpinnings of the World Health Organization’s ‘3 by 5’ initiative, and the role of intellectual property management in ensuring social benefits when taking potential products from the research to product development stage.

**Financing Access to Medicines (4 Dec., New York).** IAVI participated in a workshop at Columbia University discussing possible strategies to promote access to medicines and financing drug and medicine development for neglected diseases. Discussion centered on ways to address the market’s failure to drive investment into medicines for diseases primarily affecting the poor, and evaluated several innovative financing options for advancing promising research and ensuring access to medicines.

**POLICY RESEARCH & DEVELOPMENT**

**Understanding Vaccine Demand and Use.** Public Policy is currently reviewing work done to date on topics central to understanding potential demand and use of a preventive AIDS vaccine; these include demand and need estimates, AIDS vaccine modelling, willingness to be vaccinated, and willingness to pay for vaccination.

IAVI awarded a consultancy to Prof. Dale Whittington of the University of North Carolina at Chapel Hill to analyze the household data collected by the International Health Policy Program of the Thai Ministry of Public Health with support from the World Bank and European Commission. The analysis will look at the key determinants of household demand.

**Global Spending on AIDS Vaccine Research and Development.** IAVI is nearing completion on an analysis of global spending on AIDS vaccine R&D. The review seeks to quantify the levels and variety of global investment in AIDS vaccine R&D by sector (public, private and not-for-profit), funders, and major product
developers. The analysis should serve as a useful baseline for evaluating future spending by different sectors, as well as providing valuable information on the effectiveness of incentives intended to encourage private sector involvement. Preliminary findings were presented at the 2003 AIDS Vaccines Conference held in New York City in September.

Ensuring Vaccines are Available and Accessible. The pace at which national governments approve vaccines for local use and the speed with which they are adopted are key determinants of the demand profile over time for an AIDS vaccine. A grant has been awarded to the Institute of Public Health at Makerere University in Kampala to explore Uganda’s experience of approval and uptake of a number of existing health commodities. The project was approved by the Ugandan National Committee for Science and Technology and work started in December. This project will help identify stakeholders, issues and challenges that will need to be addressed to ensure rapid approval and successful introduction of a future AIDS vaccine. If appropriate, the project may be expanded and/or replicated in other countries.

OTHER INTERNATIONAL COLLABORATIONS

In 2003, IAVI continued to build political and financial commitment to AIDS vaccine development and delivery through numerous, other international collaborations.

Canada

IAVI enjoys many multi-faceted relationships in Canada.

The Canada Fund for Africa Secretariat of the Canadian International Development Agency (CIDA). As one of IAVI’s leading government donors with a contribution of CAD $45 million over 3 years, Canada provides vital support to IAVI’s vaccine development efforts and community work in Africa. This grant is funded by the Canada Fund for Africa Secretariat within the Canadian International Development Agency (CIDA), with whom IAVI shares the vision of a sustained, long-range approach to HIV/AIDS.

In June 2003, IAVI President Seth Berkley met with then Minister for International Cooperation Susan Whelan and many of her staff to discuss the impact of this grant and to exchange ideas about future challenges and possibilities. IAVI also welcomed several senior CIDA staff members to its donor meeting held in September 2003 at the International Conference on AIDS and STDs in Africa (ICASA) in Nairobi. Following this meeting, the CIDA representatives had the opportunity to tour IAVI’s Kangemi site and meet local staff.

IAVI’s communications department has strengthened its relationship with CIDA’s communication team in terms of sharing news about Canada’s important global contributions on HIV vaccines. There were several key changes at CIDA in the past year: in June, IAVI welcomed the arrival of new CIDA President Paul Thibault, and in December, the new Minister for International Cooperation Eileen Carroll.

Partnerships with Canadian NGOs. In Canada, IAVI enjoys strong relationships with three NGOs that play critical roles in the AIDS vaccine movement: the Canadian AIDS Society, the Canadian HIV/AIDS Legal Network, and the International Council of AIDS Service Organizations. These relationships were enhanced through numerous interactions throughout the year. In March, IAVI met with these NGOs in Ottawa, Montreal and Toronto, respectively, to review progress and challenges in their various IAVI-funded grants. In May, representatives from these NGOs participated in IAVI’s Global Team Meeting in New York, where they had the opportunity to interface with other NGOs from developing countries and the rest of the IAVI team.

In September, IAVI attended the Annual General Meeting of the Canadian HIV/AIDS Legal Network in Montreal, which offered the opportunity to strengthen links with other NGOs, government representatives from CIDA and Health Canada, and participants from UNAIDS.

In October, Seth Berkley met with the HIV/AIDS Legal Network’s leadership in Montreal to discuss future directions for AIDS vaccines and potential roles for Canada. Dr. Berkley then traveled to Ottawa to speak at an NGO breakfast hosted by the Canadian AIDS Society and entitled, “Towards an HIV Vaccine: The Role of Canadian Communities”. This intimate
gathering was attended by NGOs representing various spheres, including HIV/AIDS, development, and Aboriginal issues.

Finally, IAVI participated in the one-day Microbicide Symposium, hosted by the Interagency Coalition on AIDS and Development (ICAD) on 30 October 2003. This event, co-sponsored by CAS, CIDA and Health Canada among others, brought together people from various sectors with a shared interest in microbicide research and development, both inside and outside of Canada. IAVI presented on some of the overlaps between HIV vaccines and microbicides.

Health Canada. IAVI also continues a collaborative relationship with Health Canada around policy development issues. In June, Seth Berkley met with Health Canada’s International Affairs Directorate in Ottawa to discuss Canada’s domestic and international roles in the AIDS vaccine movement, both present and future, as well as the importance of forming a global AIDS vaccine movement and engaging a broad range of partners around the world.

IAVI applauds Canada’s leadership in working to create a domestic plan for HIV vaccine development and delivery. To this end, IAVI participated in the inaugural National HIV Vaccine Planning Meetings led by Health Canada in June and December 2003. At the December 2003 meeting, IAVI was invited to join the four-member HIV Vaccine Plan Steering Committee that is overseeing Canada’s ambitious plan.

Department of Foreign Affairs and International Trade (DFAIT). IAVI continued to develop its relationship with DFAIT in 2003, including liaising with new DFAIT staff members in order to learn more about Canada’s participation in the G8.

Relationships with Canadian Researchers. IAVI’s relationships with Canadian HIV vaccine researchers continue to grow. In April, IAVI participated in the 12th Annual Canadian Conference on HIV/AIDS Research in Halifax, Nova Scotia. In June, IAVI attended the Annual Scientific Meeting of the Canadian Network for Vaccines and Immunotherapeutics (CANVAC). Seth Berkley is a member of the CANVAC Board of Directors and attended the October meeting in Montreal.

IAVI has also engaged in specific collaborations, including a project exploring African perspectives on HIV vaccines to guide future vaccine preparedness and community development work. To this end, IAVI funded CANVAC anthropologist Dennis Willms to conduct a research project at the International Conference on AIDS and STDs in Africa that was held in Nairobi in September.

In November, CANVAC scientist Ken Rosenthal chaired the New York-based Mucosal Immunity Think Tank that brought together leading scientists, including several others from CANVAC, to review the state of the field and identify gaps in knowledge. Dr. Rosenthal described the meeting as a major success, saying that he hoped the momentum would spark renewed interest in the importance of mucosal immunity in HIV vaccinology.

In addition, IAVI collaborated with Canadian scientists and NGOs—including CANVAC, CAS and the HIV/AIDS Legal Network—to present a half-day workshop on HIV vaccines at the Canadian HIV/AIDS Skills-Building Meeting in Calgary in November.

Europe

IAVI’s European presence and outreach continues to grow. These efforts are aimed at building political commitment; improving the policy environment for AIDS vaccine R&D, clinical trials and future vaccine access; fostering community advocacy; and increasing financial support for the global AIDS vaccine effort and IAVI’s R&D program. In 2003, there was a significant increase in the involvement of European groups in IAVI’s clinical trials programs: in addition to the ongoing trials underway in the UK, trials started in Switzerland and Belgium, and are slated to begin in Germany and the Netherlands in early 2004.

Collaborating with NGO partner organizations remains a central means for building support for AIDS vaccine R&D and delivery at the country as well as the European level. The number of NGOs that IAVI currently works with is eight, with the newest organizations being gTt (Spain), AIDES (France) and Noah’s Arc-Red Cross Foundation (Sweden). In addition, a
partnership with the Belgium AIDS organization SENSOA is currently being discussed and several joint activities have already taken place in connection with IAVI’s AIDS vaccine trials in Belgium.

In order to work effectively in Europe, it is essential to develop materials in different languages. To this end, IAVI’s new VAX bulletin was launched in 2003 and made available in four languages: English, French, Spanish, and Portuguese. IAVI’s partner organizations are actively involved in the production and wide circulation of these materials, which in turn greatly benefits their advocacy efforts and those of the IAVI European office.

**European Commission (EC)**

*DG Development*

In 2003, IAVI staff continued to work with the EC’s Directorate General for Development (DG Development) and AIDCO staff on securing funding from the European Union (EU) to build local capacity and ownership in the South in preparing for AIDS vaccine trials. In December, IAVI was notified by AIDCO that it had been awarded its first project funding from the EU.

IAVI staff have been contributing to ongoing DG Development discussions regarding incentives to increase investment in R&D for neglected diseases. IAVI staff also attended a high-level roundtable meeting hosted by DG Trade on Access to Medicines in Brussels in April.

*DG Research and EDCTP*

IAVI representatives met with Dr. Octavi Quintana-Trias and Dr. Manuel Romaris from the EC’s Directorate General for Research (DG Research) in February to explore possible areas of collaboration. Both parties agreed that The European Developing Countries Clinical Trial Partnership (EDCTP)—established as an independent entity in 2003 to allow for increased European involvement in clinical trials—could provide an excellent platform for such collaboration, which would benefit global efforts to maximize the use of resources to accelerate the development of HIV/AIDS vaccines.

IAVI representatives met in September with Dr. Piero Olliaro soon after his appointment as Executive Director of the EDCTP and had very constructive discussions on a possible collaboration in preparing for and conducting large-scale clinical trials in Sub-Saharan Africa. IAVI has provided a concept sheet mapping out the activities and efforts required to achieve this goal. Dr. Olliaro visited the IAVI European office in December to discuss the collaboration in more depth, with a focus on site development and clinical trials. IAVI will submit a follow up concept sheet for review by EDCTP’s Partnership Board in January.

**European Parliament**

IAVI organized a successful symposium in the European Parliament on 17 June. The British Member of the European Parliament (MEP) and IAVI Board member Glenys Kinnock chaired the meeting and presenters included: IAVI President and CEO Dr. Seth Berkley; EC officials from DGs Development and Research, including Lieve Fransen from DG Development and Kurt Vandenberghe from the Cabinet of Commissioner Busquin, DG Research; Wanjiku Kamau from the Stop AIDS Alliance; IAVI Board Chair Geoffrey Lamb; and IAVI Board members Ciro de Quadros and Kapil Sibal. The meeting was well attended by MEPs, Commission staff and NGOs and provided an excellent forum to discuss how the EU can strengthen European contributions to global HIV vaccine efforts.

IAVI worked closely with the Danish MEP, Ulla Sandbaek of the Development Committee, on Parliament’s consideration of the proposal to establish the EDCTP, which included a meeting with Commissioner Busquin.
IAVI also worked with members of the Development Committee on drafting a report on the progress of the Programme for Action on HIV/AIDS, TB and Malaria.

**The Netherlands.** The Government of the Netherlands continues to be a leading supporter of AIDS vaccines as part of its comprehensive HIV/AIDS agenda.

Following the announcement of the contribution of €13.6 million to IAVI for the period 2004-2007, the Dutch Minister for Development Cooperation, Agnes van Ardenne, once again expressed her commitment to AIDS during the 2004 budget discussions with Parliament. The Minister also expressed support for the development of new preventive technologies such as vaccines and microbicides, affirming the government’s continued commitment to AIDS vaccine development and IAVI despite the challenging political and budgetary climate.

IAVI’s joint work with AIDS Fonds, its Dutch partner organization, focuses on strengthening collaboration and expanding Dutch support towards AIDS vaccines and IAVI’s work. IAVI actively participated in the meeting on the need for political leadership in the fight against HIV/AIDS and organized a vaccine workshop during the 7th National AIDS Congress on HIV/AIDS and STIs during World AIDS Day on 1 December. Professor Elizabeth Ngugi from the Kenya AIDS Vaccine Initiative gave a presentation at the core international session on community involvement in vaccine and microbicides trials.

**United Kingdom.** The UK remains a leading supporter of vaccines as part of its comprehensive AIDS agenda.

DFID’s Policy Division has been divided into a number of multi-disciplinary teams, including HIV/AIDS, Access to Medicines and a Central Research Unit. Early in 2003, IAVI met with Robin Gorna, HIV/AIDS Team leader, and with Emma Back, the new Access to Medicines Team Leader. In December, IAVI met with Paul Spray, the leader of the Central Research Unit. IAVI has continued policy dialogue with the DFID policy teams throughout the year. This included consultation regarding the Evian G8 meeting in June and participation in a meeting on DFID’s HIV-related research portfolio.

In December, Dr. Seth Berkley and IAVI staff members met with the Parliamentary Undersecretary of State for International Development, Gareth Thomas MP, and his advisors. Dr. Berkley also led a two-hour seminar on HIV vaccines with DFID Policy Division staff and met with members of the All-Party Parliamentary Group on AIDS.

A meeting was also held in December with Crusaid, a UK non-profit organization and long-time supporter of IAVI, resulting in an invitation for Dr. Berkley to give a keynote speech at a special VIP donor reception. While in London, Dr. Berkley also gave interviews for the BBC World Service and *The Economist*.

The European team is looking forward to working with Deborah Jack, the new Chief Executive of the National AIDS Trust (NAT), IAVI’s partner organization in the UK. IAVI and NAT have agreed on a joint work plan through mid-2004, focusing on policy and political advocacy.

**Norway.** Norway continues to be a strong supporter of IAVI’s AIDS vaccine effort. IAVI met in June with Norwegian NGOs, the Ministry of Foreign Affairs, the Committee on Foreign Affairs, and the Committee on Social Affairs and Health; the latter two will visit Uganda and IAVI’s regional office in Kenya in January 2004.

**Denmark.** IAVI’s Danish NGO partner AIDS-Fondet has successfully engaged the international development organization Danish Church Aid in AIDS vaccine advocacy work. In March, Danish Church Aid, together with the leading Danish newspaper *Politiken*, organized a panel discussion on AIDS vaccine R&D and access. IAVI was represented by European Director Frans van den Boom, who was interviewed afterwards by several leading Danish newspapers and TV stations.

An advocacy initiative with AIDS-Fondet, Danish Church Aid, the development NGO Ibis and *Politiken* are calling for an increased government contribution to the development of AIDS vaccines.

AIDS-Fondet also held meetings with a number of Danish parliamentarians from both the left and the right to secure increased political support for preventive AIDS vaccines.
In December 2003, HIV-Denmark—the NGO for people living with HIV/AIDS—organized a seminar for its members and constituencies. IAVI was invited to make a presentation on the search for a preventive AIDS vaccine. The seminar was well attended and there was a very good response and a shared sense of urgency that more needs to be done in AIDS vaccine research.

Ireland. Ireland remains very committed to the global AIDS vaccine effort and to IAVI’s work. In February, Dr Seth Berkley and Frans van den Boom met with Tom Kitt TD, Minister of State at the Department of Foreign Affairs, and representatives of Development Cooperation Ireland (DCI) to update them on IAVI’s work. DCI representatives participated in IAVI’s donors’ briefing in Nairobi and the meeting with the Development Assistance Committee (DAC) of the Organisation for Economic Co-operation and Development.

In December, IAVI received notice of continued support from DCI in the form of a three-year contribution of €7.5 million.

IAVI is discussing plans with Development Cooperation Ireland, the Dutch Ministry of Foreign Affairs, the European Commission and the International Partnership for Microbicides for a high-level political meeting in summer 2004 on the critical importance of investment in vaccines and microbicides.

Sweden. In 2003 Sweden scaled up its work against HIV/AIDS globally by appointing Lennarth Hjelmåker as Special Ambassador for HIV/AIDS. Ambassador Hjelmåker assumed his position in late 2003 and there are signs that other EU member states and the EU will follow this example.

In late May, Dr. Seth Berkley and members of IAVI’s European team visited Sweden for a series of meetings with development cooperation organizations, representatives of SIDA/Sarec, Members of Parliament, and the State Secretary for Development, Ms Annika Söder. A follow-up meeting is planned for February 2004 with Dr. Berkley and the Minister for Development, Carin Jämtin.

IAVI continues to collaborate closely with Noah’s Arc in Sweden, which is contributing to advocacy work with government officials and parliamentarians on the implementation of the new strategic element of Sweden’s fight against HIV/AIDS.

IAVI gave a presentation on its global activities during World AIDS Day in Stockholm. IAVI also addressed a conference organized by the Swedish International Development Cooperation Agency (Sida), Noah’s Ark and the SADC Ambassadors to Sweden, to launch their joint HIV/AIDS initiative called Together. Government officials, ambassadors and community groups attended the conference.

Germany. In 2003, IAVI and its German partner organization, Deutsche AIDS-Stiftung (DAS), intensified their efforts to build support in Germany for IAVI’s mission, including raising public awareness, strengthening overall political commitment, encouraging more involvement by other NGOs, increasing financial support for AIDS vaccines from the public and private sectors, and ensuring involvement of the relevant stakeholders in the clinical trials that will start in 2004.

In April, IAVI and DAS organized a meeting with some of Germany’s leading AIDS researchers and chaired by former German Minister of Health, Ms. Andrea Fischer. The Robert Koch Institute (RKI) organized a follow-up symposium in October attended by Germany’s leading vaccine and HIV/AIDS scientists. The event, which was well covered in the media, resulted in AIDS vaccine development becoming more prominent on the German scientific agenda. At the press briefing held in conjunction with the event, a call was made for increased German government funding for AIDS vaccine research and development.

IAVI and DAS also met with the Deutsche Gesellschaft für Technische Zusammenarbeit (GTZ) GmbH, which has extensive worldwide operations, to discuss possible areas of collaboration. Ulrich Heide, CEO of Deutsche AIDS-Stiftung, subsequently met with the German Minister for Development in May, and again during a World AIDS Day TV-special, when he briefed her on IAVI’s work and the upcoming clinical trials in Germany.

Fulbright Commission Conference: “Health as Foreign Policy”. In November, Dr. Seth Berkley presented an update on AIDS vaccine development and IAVI’s views on the role of public-private partnerships (PPPs) in the global
battle against devastating diseases such as HIV/AIDS at the Fulbright Commission conference on “Health as Foreign Policy” in Berlin. The conference was attended by German government officials, ambassadors from developing countries and health professionals from around the world. Dr. Berkley was interviewed by the leading newspaper Berliner Tagesspiegel and the national TV station 3SAT as part of their World AIDS Day coverage.

France. In November, high-level meetings were organized with Michel Kazatchkine (Director of ANRS, the National Agency for AIDS Research), Jerôme Bonnafont (President Chirac’s Technical Adviser on Health), Laurent Vigier (chargé de mission), and IAVI’s French partner organization AIDES (Director Hélène Rossert and Emmanuel Trenado, Director of International Programmes).

The meeting with Kazatchkine was helpful in gaining better insight into the ANRS program on vaccines. The meeting with Bonnafont and Vigier helped provide a better understanding of the French government’s priority areas in the fight against HIV/AIDS. IAVI also submitted a letter to President Chirac on the eve of World AIDS day presenting the case for a preventive AIDS vaccine in order to inform his meeting with French scientists. In media quotes that followed, Chirac proposed combining European efforts regarding R&D on preventive AIDS vaccines.

Spain. IAVI’s partnership with the Spanish NGO, Grupo de Trabajo sobre Tratamientos del VIH (gTt) continued building momentum throughout 2003. Joint activities are focused on disseminating the IAVI/AIDS vaccine message throughout Spain and the Spanish-speaking world, and on building support from the autonomous Governments of Catalunya and the Basque Country, as well as from the national Parliament and Government in Madrid.

IAVI, gTt and its Basque partner NGO Itxarobide had a positive first meeting with Javier Madrazo, the Minister for Housing and Social Affairs, and responsible for Development Cooperation of the Basque Autonomous Government. After a follow up meeting with Mr. Igor Irigoyen Fuentes, the head of the Development Cooperation Office, potential options for funding are being explored and a concept note will be submitted in early 2004.

Joan Tallada of gTt met with all the principal Catalan political parties to request explicit support for AIDS vaccines R&D in their election programs. The socialist party, which subsequently became a member of the new coalition government and holds the Presidency of the Government, inserted the wording proposed by gTt in its election program.

Together with gTt, IAVI hosted a Parliamentary briefing in Madrid on 27 November. Parliamentarians representing the entire Spanish political spectrum expressed their commitment to include AIDS vaccines in a Parliamentary resolution in 2004, and to explore the possibility of providing financial support from the Spanish Central Government.

The press conference that followed the briefing was very well attended and preventive AIDS vaccines and IAVI’s work received excellent coverage in all major Spanish generalist and specialized newspapers (El Mundo, El País, El Periodico de Catalunya, Diario Medico and La Vanguardia), as well as on TV5, one of the main private TV stations of the country. In addition, the Health Minister of Spain, Dr. Ana Pastor, appeared during prime time on a main TV channel during World AIDS Day and mentioned the importance of supporting the development of new technologies such as vaccines for the prevention of HIV and AIDS, a first in Spain.

IAVI also met with the recently appointed Director of the Spanish AIDS Plan (SAP), Dr. Lourdes Chamorro, who showed a keen interest in IAVI’s work and in including AIDS vaccines in the new strategy of the Plan, to be released in 2005.

Finally, both IAVI’s and gTt’s digital and printed information and education tools in Spanish increased dramatically in 2003, including IAVI’s VAX Bulletin, fact sheets and press releases, as well as gTt’s news services and a redesigned AIDS vaccines section within gTt’s website.

Belgium. As reported earlier, an application was submitted in Belgium for initiation of a multicenter Phase I trial to assess the safety and immunogenicity of the tgAAC09 (rAAV-HIV) vaccine candidate. Approvals were obtained from the national Belgian Biosafety Committee.
(SBB) and the Belgian Ministry of Health. On 8 December 2003, the first trial volunteer was enrolled at Centre Hospitalier Universitaire Saint-Pierre in Brussels.

IAVI and the Belgian NGO SENSOA used the trial to inform Ministries, NGOs and health professionals about IAVI and AIDS vaccine research. IAVI was subsequently invited by the Government of Belgium to provide information on the current status of HIV/AIDS vaccine R&D, IAVI’s role, and potential areas for support.

Switzerland. On 12 November, a Phase I study (IAVI #011) began in Lausanne, Switzerland to evaluate different routes and doses of the MVA.HIVA vaccine. The Principal Investigator for the Swiss trial is Dr. Giuseppe Pantaleo. IAVI is exploring the potential for collaboration with The Swiss Centre for International Health at the Tropical Institute in Basel.

Secretary General Juan Somavia of the International Labor Organization (ILO) visited IAVI in May to discuss the role of vaccines in addressing the AIDS epidemic. A model of cooperation was discussed in the area of clinical trial preparations and policy formulation. Subsequent meetings in Geneva are planned.

The IAVI Report

Overview. The IAVI Report newsletter and the new VAX bulletin represent the only media focused exclusively on global efforts to develop an AIDS vaccine. The IAVI Report continues to fill a critical information niche by providing comprehensive coverage of the field from the research, policy, advocacy and community perspectives, while the monthly bulletin VAX addresses the need for a publication geared to a wider, non-technical audience. Both provide news and analysis, adding context and highlighting trends and gaps in the search for a vaccine. Published six times a year (in print and online), the IAVI Report together with the monthly VAX bulletin reach over 8,500 subscribers in 140 countries, with thousands of additional readers accessing the online editions. To further open up content to an expanding and global readership, the VAX bulletin is now regularly translated into French, Spanish and Portuguese.

The Report bolstered its commitment to creating a robust, searchable and user-friendly web presence with the hiring of a full-time Web Editor, Dr. Roberto Fernandez-Larsson, former editor of the AIDScience website of Science magazine. The first phase of the Report’s web development has been completed, with a new open design, indexed article database and subscription options for delivery of publications in the medium most convenient for the reader.

VAX

In the last half of 2003, the IAVI Report began a major new initiative with the launch of a new monthly publication, VAX, intended to make news covered in the IAVI Report more accessible to non-scientific audiences, particularly in community settings that include potential trial volunteers. VAX is designed to serve as a tool to engage communities and to support other IAVI initiatives.

In addition to articles on vaccines, VAX features glossary definitions for any technical words used, along with “Primers” answering key questions pertinent to understanding the scientific challenges to AIDS vaccine development. Topics covered to date include the trials approval process, routes of transmission and viral diversity.

Using a master layout template, partner organizations can produce print-ready copy for the English or translated versions, with the option of including local-specific news to foster community ownership. Several of these organizations have become distribution partners—for example, IAVI’s partner in Spain, the Barcelona-based NGO Grupo de Trabajo sobre Tratamientos del VIH (gTt), translates, typesets and hosts the Spanish VAX on the homepage of its website (http://www.gtt-vih.org/), offering both HTML and PDF formats. Similarly, IAVI is collaborating with the national French NGO, AIDES, and with Brazil’s Grupo de Incentivo a VIDA [GIV], for the French and Portuguese versions of VAX respectively.

The Report has begun establishing in-country print and distribution centers, with French and English versions of VAX currently being printed and distributed for east Africa (Kenya, Rwanda and Uganda), a project managed by IAVI’s East Africa Regional Office in Nairobi. Plans are also
underway to create distribution centers in South Africa and Brazil. Additional centers will be set up as need dictates.

**Database of AIDS Vaccines in Human Trials.** Created and updated by the *IAVI Report* staff, the database is today the most comprehensive and inclusive source of trials information available. A robust, searchable research tool on ongoing human AIDS vaccine trials, the human trials database also functions as a unique and important living archive of the AIDS vaccine candidates in humans.

Since its first publishing in September 2003, the Clinical Trials Watch poster—a time-stamped snapshot of all ongoing trials derived from the database—has significantly raised awareness of the database in the scientific community; it is now often cited in conference presentations on AIDS vaccines as the best source of this information. This poster, which is regularly updated and available on the website as a PDF, is the most frequently downloaded item on the entire IAVI website, and was viewed by over 12,000 people in 2003.

**IAVI Report Online.** The *IAVI Report*’s section of the IAVI website has been redesigned to display the latest stories and to help users easily find articles on related themes. In addition to these enhancements, the new web page will offer a choice of online subscriptions in formats best suited to subscribers’ needs (i.e., HTML or plain text electronic delivery of VAX and the IAVI eAlert, to accommodate varying bandwidth access).

The site has been designed with an eye to making the content easy to receive across a wide range of internet access, with mailback features built in, so readers whose internet connectivity is limited can use email by subscribing to the *IAVI Report* eAlert service.

**Communications Activities**

**Media Coverage Highlights.** IAVI continued media outreach activities to promote awareness and understanding of the search for an AIDS vaccine and IAVI's programs. In areas where trials are conducted, accurate media coverage assists in recruiting volunteers and generating local support for vaccine research and development.

**Coverage of IAVI.** Throughout the year, IAVI’s programs around the globe garnered positive media coverage:

In February, the start of an IAVI-sponsored trial of the HIVA.DNA-MVA candidate at the Uganda Virus Research Institute (UVRI) attracted positive press attention, including in news outlets throughout east Africa and in the *Guardian* (UK) and on the Agence France-Presse, Associated Press and Reuters wire services. A February feature story in *The New Yorker* magazine about AIDS vaccine research and development closely followed IAVI’s work in Uganda and extensively quoted IAVI President and CEO Dr. Seth Berkley and UVRI Principal Investigator Dr. Pontiano Kaleebu.

In July, several newspapers including the *East Africa Standard* (Kenya), *The New Vision* (Uganda) and *The Star* (South Africa) published stories about the inauguration of the new IAVI-UVRI Phase I trial facility in Entebbe, attended by Dr. Berkley. These outlets also covered Dr. Berkley’s visits to Tanzania and Kenya. Throughout his tour of the three countries, Dr. Berkley stressed the importance of AIDS vaccine research and development, Africa’s leadership in the effort and the need for volunteers to participate in trials.

In November, the start of an IAVI-sponsored trial of the HIVA.MVA vaccine candidate in South Africa resulted in considerable media attention on the country’s television stations and in newspapers such as *The Star*, *The Sowetan* and *Business Day*. The start of this trial followed the launch of a trial of a vaccine candidate developed by AlphaVax, Inc. (for which IAVI provided early support); together the two vaccine candidates were the subject of much media attention in the country.

In December, announcements of the start of IAVI-sponsored trials in Belgium and the US attracted significant attention. The trial of the tgAAC09 (rAAV-HIV) vaccine candidate was particularly well covered in Seattle, the hometown of co-developer Targeted Genetics Corp., and in Brussels, the trial site. Publications covering the start of this trial included *The Seattle Times* and *La Libre Belgique* (Belgium). Separate from the announcement of the rAAV trial, IAVI's media presence in Europe expanded this year with feature magazine stories in several countries,
including German Tagesspiegel, Swedish Svenska Dagbladet, Danish Politiken and Finnish Kuukausiliite.

In the last half of the year, media coverage of IAVI in India intensified as site assessments for upcoming IAVI-sponsored AIDS vaccine trials began. Many articles—in publications such as The Hindu, The Times of India, Financial Express and The Telegraph—focused on the upcoming trials and public remarks by Indian government officials supporting AIDS vaccine research.

Coverage of the field. In addition to publicizing its own programs, IAVI worked to increase awareness about general issues surrounding AIDS vaccine research and development.

In February, VaxGen, Inc. announced that its vaccine candidate AIDSVAX B/B did not prove effective in preventing HIV infection or AIDS in a Phase III trial that took place in North America and Europe. In November, VaxGen made a similar announcement concerning a Phase III trial of AIDSVAX B/E in Thailand. Following both announcements, IAVI released statements to help put the results in context. IAVI stressed that, although AIDSVAX was not efficacious, the trials themselves were successful because they demonstrated that a large-scale AIDS vaccine trial can recruit and retain a large number of volunteers and be conducted safely and ethically.

The VaxGen announcements - and IAVI’s statements - were the subject of several news stories in outlets such as The Economist, the Guardian (UK), The Wall Street Journal, The San Francisco Chronicle and ABC News.

In June, the journal Science published the paper “The need for a global HIV vaccine enterprise,” calling for a massive expansion of the resources dedicated to AIDS vaccine research and development, and for greater coordination among researchers. The paper was authored by Dr. Richard Klausner of the Bill & Melinda Gates Foundation and co-signed by leading AIDS vaccine development agencies, including IAVI.

Also in June, Science published the findings of a team at Scripps Research Institute detailing the structure of HIV neutralizing antibody 2G12, thought to be a key clue to the design of a highly effective vaccine. The Scripps team, led by Drs. Dennis Burton and Ian Wilson, is part of the IAVI-sponsored Neutralizing Antibody Consortium.

In October, more than 50 Washington, DC-based journalists and policymakers attended an IAVI-sponsored briefing at the National Press Club, “Progress toward a vaccine to prevent AIDS.” Among the news organizations in attendance were Nature, Science, Voice of America and the Bloomberg, Reuters and Scripps-Howard newswires. In addition, the briefing aired multiple times on C-SPAN. The briefing included presentations from IAVI on the major scientific challenges facing AIDS vaccine development: advancing the candidates now in small-scale trials to large-scale trials in the developing world; improving on the candidates now in trials; and planning for large-scale manufacturing.

At the close of the year, IAVI offered information about AIDS vaccines in honor of World AIDS Day. IAVI released a press statement on the latest epidemiological statistics from UNAIDS, accompanied by a fact sheet chronicling the past year’s progress in vaccine research and development. A special section of the IAVI website also linked to other organizations with World AIDS Day content.

Resource Development

The year 2003 brought renewed and increased funding from government and multilateral donors, the news that the European Union would fund IAVI for the first time, and new partnerships and support from the private sector, including a renewed and increased commitment by one of IAVI’s founding donors. Specific awards and grants included:

Renewed and Increased Funding from Governments and Multilateral Donors

- Denmark. In June, Denmark, which had become a donor for the first time in 2002, reconfirmed its commitment to IAVI by pledging DKK 10 million (US $1.5 million) in support for fiscal year 2003.

- Ireland. In December, Development Cooperation Ireland awarded an increased multi-year grant of €7.5 million over the

- **Norway.** Also in December, the Norwegian Government made an increased commitment of NOK 12.5 million (US $1.9 million) for the period December 1, 2003 through December 31, 2004.

- **The Netherlands.** In October, the Government of the Netherlands committed €13.6 million to IAVI for the period 2004-2007, bringing their total cumulative contribution to €33 million since 1999.

- **The World Bank.** In June, the World Bank announced US $700,000 in renewed support through the Global Forum for Health Research.

- **United States.** In the wake of President Bush's January 2003 announcement that the US government has committed to spending $15 billion over the next five years on global AIDS programs, Congress earmarked a significant increase in funding over the $10.4 million provided to IAVI for 2003. The language of the relevant bill states, “not less than $26,000,000 should be made available for the International AIDS Vaccine Initiative.” This includes $10 million designated specifically to fund increased collaboration with and support for European AIDS vaccine research projects coordinated with the European Union's new 5-year program, the AIDS Vaccine Integrated Project, and in cooperation with the Partnership for AIDS Vaccine Evaluation (PAVE) operating under the aegis of the US Department of Health and Human Services.

**First Funding from the European Union**

- In December, IAVI received notice that the European Commission's Directorate General for Development will provide €3 million in matching funds for vaccine preparedness activities in east Africa over the three-year period, 2004-2006. The funded program, *Partnerships for Preparedness: Building local capacity and ownership in the development of AIDS vaccines*, will assist IAVI and east African partner organizations in building local clinical and social research capacity and in preparing communities for preventive AIDS vaccine trials and subsequent access to a licensed vaccine.

**Private Sector Funding**

- Through the efforts of IAVI's German partner organization, Deutsche AIDS-Stiftung, German athlete and extreme sportsman Joachim Franz contributed €51,000 raised from a biking tour he undertook from Paris to Dakar that was supported by various sponsors, including Volkswagen AG.

- In August, one of IAVI's founding donors, the Until There’s A Cure Foundation, committed US $40,000 in funding for 2004. In a difficult economic environment, this renewed support represented a significant investment by a funder committed to supporting not only the global vaccine effort but also many community-based AIDS service organizations.

- In October, IAVI received a bequest of US $500,000 from the Estate of Mercedes Hotle.

- In November, The Starr Foundation, another of IAVI's founding donors, renewed and increased its support by awarding a two-year grant of US $5 million through November 2005.

- In December, DHL, the world's leading express delivery and logistics company, initiated a partnership with IAVI by donating essential courier service to and from IAVI's Core Lab in London. This first phase of what both parties hope will be a growing collaboration represents a significant in-kind contribution by DHL as the Core Lab serves as a central resource for all of IAVI's vaccine trial sites.

- Also in December, the Perls Foundation made a grant of US $75,000 to be used in support of the HIV testing component of feasibility studies at the Kakira sugar cane plantation in Uganda in preparation for HIV vaccine trials. This was the Foundation's first grant to IAVI.

In addition, BD (Becton, Dickinson and Company), who made a generous five-year pledge of $1 million to IAVI in 2001, produced a series of two- and four-page promotional advertisements highlighting their support for IAVI's work under the theme, “Helping All People Live Healthy Lives.” The advertisements appeared in a number of
industry publications and business magazines including *The Economist*.

**Overview**

With these grants and contributions, IAVI has received cumulative funding and commitments totaling nearly US$340 million. This support comes from a broad array of sources and ranges in size from relatively modest gifts from concerned individuals to a multi-year commitment of US$100 million from the Bill and Melinda Gates Foundation. In addition to the donors mentioned above, IAVI currently receives significant support from the governments of Canada, the United Kingdom, and Sweden, all of whom have recognized the urgent need to fund AIDS vaccine R&D and preparatory activities. Other key financial support has come from the Alfred P. Sloan and the Rockefeller Foundations; from corporate donors such as Glaxo Wellcome and Levi Strauss; from leading AIDS organizations including the Elton John AIDS Foundation, Crusaid, and Aids Fonds; from UNAIDS; and from a growing number of individuals.

Even with this broad support, however, funding IAVI’s programs through 2008—*which by no means represents an end to the marathon effort of discovering and delivering a safe and effective vaccine*—is currently projected to cost more than US$590 million. This means that IAVI must raise more than $250 million in new commitments over that period.

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Given this challenge, IAVI continues to work to build political and financial support for AIDS vaccines. Activities in 2003 to keep current donors informed and engage potential new funders included:

**Organisation for Economic Co-operation and Development (OECD).** In June, IAVI met with Deputy Secretary General Richard Hecklinger and senior staff of the OECD to discuss building broader OECD support for preventive AIDS vaccine development. This was followed by a return visit in November when Seth Berkley briefed the Development Assistance Committee (DAC) on the need for broad OECD member country support for AIDS vaccine research. The DAC establishes overseas development assistance priorities for OECD countries and monitors their implementation. Over 20 officials from the US, Japan, EC, Korea, Mexico, Belgium, Ireland and elsewhere participated in the meeting. In a subsequent meeting with senior OECD officials and US Ambassador Constance Morella, IAVI discussed a proposal for an OECD work program taking advantage of the unique role the OECD plays as a think tank for the industrialized world in economics, science and technology, statistics, trade, development, and policy.

**European Parliament.** Also in June, IAVI organized a symposium in Brussels for members of the European Parliament. IAVI Board member Glenys Kinnock, MEP, chaired the meeting and presenters included Seth Berkley, EC officials from the Directorate Generals of Development and Research, and members of IAVI’s board of directors.

**Outreach to the Pharmaceutical Industry.** As part of an initiative to develop closer ties to the pharmaceutical industry on policy, R&D and resource development issues, IAVI staff met with the European Vaccine Manufacturers (EVM) and the European Federation of Pharmaceutical Industries and Associations (EFPIA) policy staff. In addition, meetings were held with representatives of PhRMA, the US industry associations, and the International Federation of Pharmaceutical Industry Associations (IFPMA). Follow-up meetings are planned.

**Nairobi Donor Briefing.** In September, in advance of the ICASA Conference in Nairobi, IAVI organized a briefing to update attending government and corporate donors, as well as others in the international community. The briefing covered IAVI’s current research program, community outreach, clinical trials programs, and policy and access agendas. The meeting was hosted by IAVI partner organization, the Kenya AIDS Vaccine Initiative (KAVI), at their facility at the University of Nairobi, and featured a series of presentations by IAVI staff as well as by representatives of KAVI and the Uganda Virus Research Institute.

**Funders Concerned About AIDS Briefing.** In December, IAVI organized a briefing on the state of AIDS vaccine efforts for a foundation audience in collaboration with Funders Concerned About AIDS (FCAA). FCAA is a group of leading foundations and corporations that support AIDS causes. Planned as FCAA’s World AIDS Day event, the briefing was sponsored by the New York Community Trust and hosted by
the Ford Foundation and included updates on the current state of the vaccine effort from local, national and international perspectives. Panelists included IAVI President and CEO Dr. Seth Berkley; His Excellency Zac Nsenga, Rwandan Ambassador to the US; and Edd Lee, Director of Community Education and Outreach for the AIDS Vaccine Advocacy Coalition (AVAC). The panel was moderated by Dr. Elaine Gallin, Program Director for Medical Research at the Doris Duke Charitable Foundation.

To supplement these briefings and symposia, IAVI’s Resource Development department provided government and foundation donors with updates and reports, including the independent evaluation supported in part by the World Bank, the 2002 Annual Progress Report, detailed FY 2002 Annual Financial Reports, IAVI’s FY2002 Audited Financial Statements, and the 2003 Mid-Year Progress Report.

Governance, Operations and Finance

INDEPENDENT EVALUATION

An independent evaluation of the organization was undertaken in 2002 in accordance with IAVI’s grants from the World Bank, Development Cooperation Ireland (formerly Ireland Aid) and the Rockefeller Foundation.

The evaluation team consisted of Mr. Richard Skolnik, the Director of the Center for Global Health of the George Washington University, who was the team leader; Dr. Ayo Ajayi, the Regional Director for Africa of the Population Council; Dr. Subhash Hira, the Director of the AIDS Research and Control Center in Mumbai, India (ARCON) and a Professor of Infectious Diseases at the University of Texas in Houston; and Dr. John LaMontagne, the Deputy Director of the National Institute of Allergy and Infectious Diseases at the United States National Institutes of Health (NIH).

The evaluation panel’s final report was completed and published in April 2003 and copies were mailed to representatives at IAVI’s donor institutions and to numerous other key supporters.

The evaluation examines the extent to which IAVI has met the objectives of its strategic plans. The evaluation also highlights the manner in which its efforts on advocacy, policy, access, and research and development have contributed to reaching IAVI’s overarching goal of helping the world gain access to a safe and affordable AIDS vaccine that will meet the needs of the developing world. The evaluation offers useful suggestions about steps IAVI might take to meet key challenges and enhance its efforts through more strategic staffing, continued deepening of its country partnerships, strengthening its management team, and continuing to refine its partnerships in flexible and innovative ways. In addition, the evaluation offers comments about how the landscape for AIDS vaccines might be different in the absence of IAVI. Overall, the evaluation concludes that IAVI has made a unique and significant contribution to the world’s search for an AIDS vaccine and that its efforts have speeded up that search in very important ways.

The following is an excerpt from the Concluding Comments of the evaluation’s Executive Summary:

“The panel believes that IAVI has met or exceeded most of its key goals and has been a very positive and effective force in the development of an AIDS vaccine and the likelihood that such a vaccine will be used in a timely manner where it is most needed. IAVI has helped to spur research and development on AIDS vaccines. It has helped to raise the political profile of HIV/AIDS and increase the attention of policy makers to the need for an AIDS vaccine that would meet the needs of the developing world. IAVI has also begun to involve developing country policy makers, scientists, and civil society in AIDS vaccine efforts in essential ways in which they were never involved before. IAVI has taken pioneering approaches to the idea that an AIDS vaccine must be available simultaneously throughout the world, including innovative approaches to intellectual property. IAVI has also done some pioneering work on policy and access issues related to the eventual uptake of an AIDS vaccine and the notion that the world must prepare early for future vaccines. While doing all of this, IAVI has also been the world leader in information on AIDS vaccines.”

“The panel also believes that IAVI deserves enormous credit for having achieved so much in such a short period of time. This is even more
the case when one considers that IAVI was started as a new form of organization and that it has carried out its work in a period of extraordinary changes in the world of HIV/AIDS. The panel appreciates the quality of IAVI’s leadership and the urgency that it has imbued in the organization."

The complete report of the independent evaluation is available at IAVI’s web site (www.iavi.org/about/).

ENHANCING SENIOR LEADERSHIP

As the scope and complexity of IAVI’s global programs and operations have grown, so too has the need to recruit additional senior-level management to help lead the organization through the new challenges that lie ahead. These strategic new additions include:

Dr. Emilio A. Emini, Senior Vice President and Chief of Vaccine Development. In March 2004, Dr. Emilio A. Emini joins the leadership in IAVI’s R&D program. As noted earlier, Dr. Emini comes to IAVI after 20 years at Merck & Co., Inc., where he gained recognition as one of the world’s preeminent AIDS vaccine scientists. As Merck’s Senior Vice President of Vaccine Research, Dr. Emini was responsible for Merck’s overall basic vaccine research program including diseases other than AIDS. During his tenure, he led the company’s AIDS vaccine efforts, advancing five different vaccine candidates to human trials. In addition to searching for an AIDS vaccine, Dr. Emini led the Merck team that developed one of the first highly effective antiretroviral agents for the treatment of people living with HIV.

Dr. Emini obtained his Ph.D. in 1980 at the Cornell University Graduate School of Medical Sciences where he studied the molecular basis of Venezuelan encephalitis virus pathogenesis. His postdoctoral studies focused on understanding the mechanism of antibody-mediated neutralization of polioviruses. In 1983, Dr. Emini joined the Merck Research Laboratories where he participated in studies that led to the licensure of the recombinant hepatitis B vaccine. He subsequently pursued his interest in vaccine research by initiating programs to assess the feasibility of designing vaccines for the Epstein-Barr virus as well as for Hepatitis A.

Dr. Robert Hecht, Senior Vice President of Public Policy. In May, IAVI will welcome Dr. Robert Hecht to lead the organization’s public policy efforts. As noted earlier, Dr. Hecht joins IAVI from a 20-year tenure at the World Bank, where he most recently served as Manager of the Bank’s central unit for Health, Nutrition, and Population, which is responsible for global strategies, knowledge, technical services and partnerships. His other positions at the Bank included Chief of Operations for the World Bank’s Human Development Network, Principal Economist in the Latin America region and one of the authors of the 1993 World Development Report, “Investing in Health.” From 1987 to 1996, Dr. Hecht was responsible for a number of the Bank’s studies and projects in health in several countries in Africa and Latin America, most notably in Zimbabwe and Argentina. In the late 1990s, Dr. Hecht served as an Associate Director of the Joint United Nations Programme on HIV/AIDS (UNAIDS).

Mike Goldrich, Chief Operating Officer. In November, Mike Goldrich came to IAVI from a distinguished 33-year career of managing scientific programs and research institutions. Most recently, he was the senior Vice President for Research Operations at the Beth Israel Deaconess Medical Center at Harvard Medical School, in Boston. Prior to that he spent five years as the COO of the Institute for Human Virology at the University of Maryland. Before that he had a distinguished 25 year career at the National Institutes of Health which included COO of the Warren Magnuson Clinical Center, Director of Management and Operations of the National Institutes of Allergy and Infectious Diseases and Administrative Director for Cancer Treatment at the National Cancer Institute. Mr. Goldrich received his BA from the University of Maryland (Magna Cum Laude) and his MBA from Loyola College (Summa Cum Laude). He is a member of numerous honorary academic societies (Phi Beta Kappa and Beta Gamma Sigma) and has received many performance related awards during his career including the Presidential Meritorius Award while at the National Institutes of Health.

Mollie Shields-Uehling, Vice-President of Development. Mollie Shields-Uehling joined IAVI in February 2003, bringing extensive experience in international business, commerce and government affairs. She has spent many
years living, working and studying abroad. She worked in the pharmaceutical industry, leading the international policy departments for Bristol-Myers Squibb and Lederle and women’s healthcare issues for Wyeth. She also served in the Foreign Commercial Service, representing US government and commercial interests. She worked in the Executive Office of the President where she headed the Office of Private Sector and Intergovernmental Liaison in the Office of the US Trade Representative. Her undergraduate degree is from American University and her graduate work was at the University of Oklahoma and Oxford University. She sits on the board of the Business Council for International Understanding.

BOARD OF DIRECTORS

IAVI’s Board of Directors welcomed two distinguished new members for three-year terms:

▪ John D. Evans (Board Treasurer), Chairman & CEO, Evans Telecommunications Co. and The John D. Evans Foundation

▪ Michel Greco, Former Deputy CEO, Aventis

The following additional changes also became effective in 2003 (a complete Board list is provided on p. 44.):

▪ Richard Feachem, Gordon Douglas, Jacques-François Martin, and Jaap Goudsmit completed their terms.

▪ Peter Piot completed eight years of service and was changed to an ex-officio advisory member.

▪ Ian Gust, in his capacity as new chair of IAVI’s Scientific Advisory Committee, became the SAC liaison (ex-officio).

Committees of the Board. As the organization has grown, there has been a concomitant need for increased Board participation. Board committees that were previously established to focus upon specific areas, such as the Finance Committee, have expanded and new committees have been established:

▪ Audit and Finance Committee. Increasingly, IAVI is conducting business involving, for example, clinical trials in multiple countries and thus greater emphasis has been placed on issues such as risk management and liability mitigation. The Finance Committee was broadened and reconstituted as the Audit and Finance Committee with an expanded charter to accommodate these changes plus the need to be responsive to requirements set by the Sarbanes-Oxley Law governing the relationship between Boards and company officials.

▪ Resource Mobilization Committee. A Resource Mobilization Committee was formed to respond to the Board’s increasing interest in IAVI’s ability to raise funds to support its expanded programs.

▪ Compensation Committee. This committee was formed to deal with personnel compensation strategies and programs corresponding with nearly 100% growth in the organization’s staff.

The Nominating Committee, which considers the addition of new directors as current terms expire, was unchanged.

OPERATIONS AND FINANCE

Annual Financial Audit. Ernst & Young, LLP (E&Y) completed the FY2002 financial audit of IAVI in March 2003. Their approach focused on internal control procedures and testing IAVI’s financial systems. The audit yielded no material adjustments and IAVI received a clean audit opinion stating that our financial statements present fairly the organization’s financial position. E&Y also completed their first A-133 audit of IAVI (required for all United States government fund recipients to ensure that proper financial control is exercised over such funds). The A-133 audit yielded no material findings and a clean audit opinion was received.

Risk Management. As IAVI continues to transition products from the research to the product development stage, the organization has initiated an ongoing program of risk management and assessment. After a comprehensive selection process, IAVI retained the services of the insurance and risk management firm of McManamey & McManamey to work with a cross-departmental Risk Management Team to conduct a review of current insurance levels and liability risk. Based on the team’s findings, IAVI expanded its international clinical insurance to prepare for
the increasing numbers of trials and products in clinical testing. The team is also looking into ways of partnering with organizations similar to IAVI to reduce insurance costs and better address risk across the field.

The Risk Management Team also conducted a preliminary risk assessment and evaluation of departments and activities across IAVI. The team presented its risk mitigation recommendations in the areas of communications, contracts and business development, manufacturing and medical affairs to the Senior Management Team and IAVI currently is instituting several of the initiatives. In addition to recent risk management programs, IAVI is continually reviewing operational risk and increasing the monitoring and oversight of key partners in the product development process.

**Strategic Planning.** Given the organization’s rapid growth, as well as the dramatic changes underway in the AIDS external environment, IAVI decided to begin its strategic planning a year ahead of the normal planning cycle. In the second half of 2003, IAVI worked closely with an experienced health-care and management consultant, Dr. Vikram Narasimhan, to create and implement new evaluative and planning tools for the organization. This valuable exercise provided an important focus for IAVI’s long-range strategic planning process, which is expected to be complete by the middle of 2004.

**Non-Profit Corporate Governance.** The New York State Attorney General’s office has proposed stringent regulations for non-profit organizations. A number of internal initiatives are underway in order to prepare for this new regulatory environment and to manage effectively the increased volume, size and complexity of IAVI transactions. Among other changes, an Internal Audit function has been created to ensure that all global internal control and finance management policies are followed, that IAVI field sites are employing adequate internal controls, and that field financial staff have appropriate accounting systems and are suitably trained.

**Grant Monitoring Program.** On an annual basis, internal control reviews of selected IAVI funding recipients are performed by E&Y to ensure that appropriate controls are in place and identify any issues related to financial and accounting procedures.

**New York Headquarters.** In response to the steady and rapid growth of the organization’s R&D and other programs, IAVI expanded its New York office space in 2003 by an additional 14,500 square feet to accommodate increased staffing needs. Construction on the new space was completed in September. IAVI’s landlord contributed substantially to this effort, covering nearly a third of the costs associated with the expansion. In addition, IAVI applied for grants for companies expanding in the downtown area after the World Trade Center disaster and recouped approximately $400,000 in expansion costs.

**IAVI’s Global Field Operations.** With the organization’s work becoming more focused on activities in the field, IAVI is implementing a process to decentralize key programmatic and infrastructure activities, while at the same time retaining fiscal control, consistency of strategic purpose and high quality communications. The following is a summary of these activities in 2003:

- **Department of Global Operations.** In 2003, IAVI established a Department of Global Operations (formerly the Department of International Finance) to manage the organization’s expanding portfolio of grants and contracts. The department is also responsible for financial oversight of all field programs and the development of fiscal infrastructure and business management systems.

  In the last quarter of 2003, the Department began the process of fully automating the grants and contracts authorization and payment process. It also developed new tools of business analysis and financial planning, and initiated a review of the IAVI procurement process. Finally, working collaboratively with colleagues in Research and Development, the Department coordinated a request for proposal (RFP) that lead to the hiring of a new IAVI out-sourced risk manager.

- **Field Operations Manual.** IAVI began the process of establishing a Field Operations Team, composed of department representatives based in New York, representatives from our field offices and
professionals from other international field organizations. This group is working through the process of decentralization to clearly define the roles and responsibilities of IAVI personnel worldwide. The team is also developing a field operations manual that will govern our activities in the field.

- **Grants of Authority and Indirect Costs**

  **Policy.** IAVI undertook an organization-wide analysis of the policies and procedures by which it authorizes grants, contracts and payments at all levels and locations within the organization. This process resulted in the creation of a *Grants of Authority* document that clearly defines the powers and responsibilities of the various parties managing IAVI’s strategic relationships. The organization also researched and drafted a comprehensive policy on the payment of indirect costs for IAVI’s grantees and business partners.

- **European Office.** A larger and less costly office space was leased for IAVI’s European office commencing in January 2003 in order to meet IAVI’s expanded European staffing needs through 2007.

- **India Office.** Working with the Indian offices of Ernst & Young and Indian consultants, IAVI completed an application for recognition as a liaison (representative office) and filed it with the Reserve Bank of India. The application is being processed by various ministries and departments within the Indian government.

- **East Africa Regional Office.** Working with local consultants, IAVI applied for and received a Certificate of Compliance from the Kenyan government providing the organization’s regional field office with legal recognition within the country. During this period, IAVI also opened a local bank account, located and leased appropriate office space in Nairobi, and began hiring local field staff.

- **Information Technology (IT).** IAVI’s IT team assisted in establishing the IT infrastructure in the New Delhi office, including system integration and the new Indian website project, and set up the basic network infrastructure and purchased all of the equipment necessary for the newly established field office in Kenya.

  The database system (LIMS System) for tracking blood samples and inventorying storage freezers for IAVI’s Core Lab was deployed in the UK; the system is currently being tested for the field labs in Uganda and Kenya. The test results are expected to demonstrate good performance due to the fact that LIMS is a Citrix-based system, which is particularly well suited for bandwidth-constrained environments.

  In order to support preparations for a future large-scale efficacy trial in east Africa, a Data Management Task Group (DMTG) was created to evaluate key considerations for data management and bio-statistical support. The group has selected three Contract Research Organizations (CROs) as final candidates to assist IAVI in this regard. The lead candidate will work with IAVI in a Phase I trial in Rwanda (#007) in order to assess whether the company is able to support large-scale trials. Additionally, the DMTG has concluded that Data Fax is the most suitable data management system for African countries, considering bandwidth constraints and availability. This system will also be used in the above-mentioned Phase I trial in Rwanda.

- **A Document Control Center** has been established at the New York headquarters office to provide a controlled filing center and database for R&D documents (protocols and contracts for clinical trials), which are compliant with FDA regulations and subject to inspections by that regulatory agency.

**Human Resources**

In 2003, IAVI filled nearly 50 positions at diverse levels and functions across the globe. The staffing strategy of direct sourcing with support from research firms continues to minimize dependency on agencies and other costlier recruiting methods, and the IAVI website is now fully leveraged to attract external candidates and promote internal career development. An increased focus on international human resources activities led to the creation of a senior position within the department to deal with international labor practices, policy development and related matters.

In mid-2003, it was noted that more than 50% of IAVI staff were from outside the US—the organization’s personnel represents 37 different countries.
IAVI’s Board of Directors provides strategic guidance and oversight for the organization. This year, four members completed their two terms and extensions: Gordon Douglas, Richard Feachem Jacques-François Martin, and Jaap Goudsmit. After serving for eight years, Peter Piot became an ex-officio advisory member and Ian Gust, in his new capacity as chair of IAVI’s Scientific Advisory Committee, became the SAC liaison (ex-officio). The Board also welcomed two new members: John D. Evans and Michel Greco.

- **Seth Berkley, MD**, President and Chief Executive Officer, IAVI
- **Awa Marie Coll-Seck**, Executive Secretary, Roll Back Malaria Partnership, WHO, Geneva; Former Director, Policy, Strategy and Research, UNAIDS
- **Ciro de Quadros, MD, MPH**, Director, International Programs, Sabin Vaccine Institute; Former Director, Vaccines and Immunization, Pan American Health Organization
- **John D. Evans, Treasurer**, Chairman & CEO, Evans Telecommunications Co. and The John D. Evans Foundation
- **Michel Greco**, Former Deputy CEO, Aventis
- **Geeta Rao Gupta, PhD**, President, International Center for Research on Women
- **Ian Gust, MD, Ex-officio, Chair, IAVI Scientific Advisory Committee**, Department of Microbiology & Immunology, The University of Melbourne; Former Director of R&D, CSL Ltd.
- **Glenys Kinnock**, Member of European Parliament, Wales
- **Chripus Kiyonga, MD**, Minister without Portfolio, Uganda; Former Chair of the Global Fund to Fight AIDS, Tuberculosis, and Malaria; Former Minister of Health, Uganda
- **Paul Klingenstein**, President of Aberdare Ventures
- **Geoffrey Lamb**, Board Chair, Vice President for Concessional Finance and Global Partnerships, The World Bank
- **Malegapuru William Makgoba, MBShB, DPhil, FRCP, FRSSAf, MASSAf**, Vice Chancellor, University of Natal; Former President, Medical Research Council, South Africa
- **Peter Piot, MD, PhD, Ex-officio**, Executive Director, Joint United Nations Programme on HIV/AIDS
- **Philip Russell, MD, Secretary**, Special Advisor, Vaccine Development and Production, US Department of Health and Human Services; Professor, International Health, Johns Hopkins University
- **Kapil Sibal, JD**, Member of Parliament, India
- **Lee Smith, Founding Chairperson**, Former President, Levi Strauss International; Former Chairperson, US National Leadership Coalition on AIDS
- **Sir Richard Sykes, DSc, FRS**, Rector, Imperial College of Science, Technology, and Medicine; Former Chairperson and Chief Executive Officer, GlaxoSmithKline plc

**Members Emeritus**

- **Michèle Barzach, MD**, Former Minister of Health, France
- **Gordon Douglas, MD**, Consultant, Vaccines, Infectious Disease and Global Health, Former President, Merck Vaccines, Merck and Co., Inc.
- **Richard Feachem, PhD, DSc (Med)**, Executive Director, Global Fund to Fight AIDS, Tuberculosis, and Malaria; Founding Director, Institute for Global Health, University of California
- **Jaap Goudsmit, MD, PhD**, Executive Vice President, Research & Development, Chief Scientific Officer, Crucell NV; Co-Founder, European Vaccine Effort Against HIV/AIDS
- **Jacques-François Martin**, President, Vaccine Fund; Former Chief Executive Officer, Pasteur-Mérieux
- **Shudo Yamazaki, MD, PhD**, Director-General Emeritus, National Institute of Infectious Diseases, Japan
**Scientific Advisory Committee**

An internationally recognized Scientific Advisory Committee (SAC) meets annually to review the state-of-the-art in AIDS vaccine development and to advise IAVI on new initiatives under consideration. Subcommittees of the SAC meet quarterly, or as needed, to provide additional advice regarding the state-of-the-art in AIDS vaccine research, project management, and the conduct of clinical trials of AIDS vaccines in the developing world.

- **Dennis Burton, PhD**, Professor, Immunology, Scripps Research Institute
- **John G. Curd, MD**, President & Chief Medical Officer, Novacea, Inc.
- **Michel De Wilde, PhD**, Executive Vice President, Research and Development, Aventis Pasteur SA
- **Ronald C. Desrosiers, PhD**, Professor, Microbiology & Molecular Genetics, Harvard Medical School; Director, New England Primate Research Center
- **Ian Gust, MD, Chair**, Professor, Microbiology and Immunology, University of Melbourne; Former Director of R&D, CSL Ltd.
- **Philip Johnson, MD**, President, Columbus Children’s Research Institute, Columbus Children’s Hospital
- **Liming Lee, MD, MPH**, President, Chinese Academy of Preventive Medicine
- **Norman Letvin, MD**, Chief, Viral Pathogenesis, Beth Israel Deaconess Medical Center; Professor, Medicine, Harvard Medical School
- **Andrew McMichael, MD, PhD**, Director, Weatherall Institute of Molecular Medicine, University of Oxford
- **Rosemary Mubanga Musonda**, Acting Director General, Zambia National AIDS Council
- **Neal Nathanson, MD**, Vice Provost for Research, University of Pennsylvania; Former Director, Office of AIDS Research, US National Institutes of Health
- **Helen Rees, MBCh**, Executive Director, Reproductive Health Research Unit, Chris Hani Baragwanath Hospital
- **Jerald C. Sadoff, MD**, President & CEO, AERAS Global Tuberculosis Foundation; Former Clinical Director for Vaccine Development, Merck and Co. Inc.
- **Mauro Schechter, MD, PhD**, Professor, Infectious Diseases, Federal University of Rio de Janeiro
- **Hans Wigzell, MD, DSc**, President, Karolinska Institute

**Vaccine Research & Design Subcommittee**
- Rafi Ahmed, Emory University
- Dennis Burton, Scripps Research Institute
- Ronald Desrosiers, Harvard Medical School
- Kim J. Hasenkrug, NIAID, NIH
- Shiu Lok Hu, University of Washington
- Philip Johnson, Chair, Columbus Children’s Hospital
- Kelly MacDonald, University of Toronto
- Doug Nixon, Gladstone Institute of Virology and Immunology
- Quentin Sattentau, University of Oxford
- Bruce Walker, Massachusetts General Hospital
- David Watkin, University of Wisconsin Medical School
- Lindsey Watkins, Scripps Research Institute

**Project Management Subcommittee**
- Kenneth R. Brown, Gordon College
- John Curd, Novacea
- Marie-Paule Kiery, Chair, WHO/IVR
- Jack Melling, Consultant
- John Petricciani, CancerVax Corp.
- Stanley Plotkin, Aventis Pasteur
- Jerry Sadoff, AERAS Global Tuberculosis Foundation
- Vijay Samant, Vical Inc.
- Michel De Wilde, Aventis Pasteur SA

**Clinical Trials Subcommittee**
- Donald S. Burke, Johns Hopkins University
- Beryl Koblin, New York Blood Center
- Ira Longini, Emory Univ. School of Public Health
- Helen Rees, Chair, Univ. of the Witswatersrand
- Wasima Rida, Statistics Collaborative, Inc.
- Mauro Schechter, Federal University of Rio de Janeiro
- Haynes W. Sheppard, California Department of Health Services
- Hilton Whittle, MRC Laboratories
- James Whitworth, The London School of Hygiene & Tropical Medicine
POLICY ADVISORY COMMITTEE

IAVI strengthened its policy capacity by establishing a Policy Advisory Committee in 2002 to serve as a sounding board on key issues and assist the policy team in setting priorities, reviewing policy research proposals, and expanding IAVI’s network in the field. IAVI received over 155 nominations for the committee—encompassing a broad range of experts from 23 countries—making the selection process extremely challenging. The 14 founding members of the committee are listed below.

▪ David Kihumuro Apuuli, MD
  Director-General, Uganda AIDS Commission

▪ Amie Batson, MPPM
  Senior Health Specialist, World Bank and Co-chair of Global Alliance for Vaccines & Immunization Financing Task Force

▪ Donald S. Burke, MD
  Director, Center for Immunization Research, Department of International Health, Johns Hopkins University School of Hygiene & Public Health

▪ Chris Collins (Observer)
  Executive Director, AIDS Vaccine Advocacy Coalition

▪ Ciro de Quadros, MD, MPH
  Member, IAVI Board of Directors; Director of International Programs, Albert B. Sabin Vaccine Institute

▪ R. Gordon Douglas Jr., MD
  Member Emeritus, IAVI Board of Directors; Director, Strategic Planning, Dale & Betty Bumpers Vaccine Research Center, US National Institutes of Health; Former President, Merck Vaccines, Merck and Co. Inc.

▪ Christopher J. Elias, MD, MPH
  President, Program for Appropriate Technology in Health

▪ Lieve Fransen, MD, PhD
  Head, Social & Human Development Policy & Programming, Directorate-General Development, European Commission

▪ David L. Heymann, MD (Observer)
  Executive Director, Communicable Diseases, World Health Organization

▪ Purnima Mane, MA, MPhil, PhD
  Chief Fund Portfolio Director & Director for Asia, The Global Fund to Fight AIDS, Tuberculosis & Malaria

▪ Jean-Marie Okwo-Bele, MD, MPH
  Senior Advisor & Team Leader, Immunization Plus, UNICEF

▪ Bernard Peçoul, MD, MPH
  Executive Director, Drugs for Neglected Diseases Initiative (DNDi)

▪ Seung-il Shin, PhD
  Senior Advisor, International Development, VaxGen Inc.

▪ Jean Stéphenne
  President & General Manager, GlaxoSmithKline Biologicals

▪ Joseph Stiglitz, PhD
  Professor of Economics & Finance, Columbia University

▪ Mark Wainberg, PhD
  Director, McGill University AIDS Centre
# Glossary of Vaccine-Related Terms

**AAV** aden-associated virus.

**Adjuvant** A substance sometimes included in a vaccine formulation to enhance or modify its ability to stimulate immune responses.

**Animal model** In research, the use of animals to mimic a human disease or condition in order to evaluate safety and potential efficacy of an experimental vaccine or treatment.

**Antibody** An infection-fighting protein in the blood or secretory fluids that recognizes, neutralizes, and helps destroy disease-causing microorganisms, or toxins as part of an immune response to antigens or foreign bodies. Antibodies are made and secreted by B lymphocytes in response to stimulation by antigens. Generally, each antibody binds only to the specific antigen that stimulated its production. Antibodies are coordinated by helper T cells. See neutralizing antibody.

**Antigen** Any substance that is recognized by a component of the immune system. Antigens are often agents such as invading bacteria or viruses.

**Assay** Determination of the amount of a particular constituent of a mixture, or determination of the biological or pharmacological potency of a drug.

**Attenuated** Weakened.

**Biodistribution** The extent to which a substance is distributed throughout tissues and organs.

**Booster** A second or subsequent vaccine dose given after the prime dose, to increase immune responses. A booster vaccine may or may not be the same as the primary one.

**Canarypox** A virus that infects birds and is being used as a vector to carry HIV genes into human cells in several HIV vaccines now in clinical trials. Canarypox virus cannot grow in human cells, an important safety feature.

**CBO** Community-based organization.

**CD4+** See Helper T cell.

**CD8+** See CTL.

**Cell line** Human cells that have been adapted to grow continuously in culture without dying out.

**Cell-mediated immunity (cellular immunity)** An immune response that targets host cells infected with microorganisms such as viruses, fungi, and certain bacteria. It is coordinated by CTLs and helper T cells.

**CFC (cytokine flow cytometry) Assay** An assay that identifies responding cells through their ability to produce certain proteins known as cytokines, which form part of the immune response.

**Challenge** In vaccine experiments, the deliberate exposure of an immunized animal to the infectious agent. Challenge experiments are never done in human HIV vaccine research.

**Clade** A group of related HIV isolates classified by their degree of genetic similarity. There are two major groups of HIV-1 isolates, called M and O. Group M consists of at least eight clades, A through H.

**Clinical trial** A human trial.

**Combination vaccine** A vaccine consisting of multiple constructs. A prime-boost vaccine is a combination vaccine.

**Construct** Design of a vaccine.

**Controlled trial** In a controlled vaccine trial, a control group receiving a placebo is compared with one or more groups of volunteers given experimental vaccines.

**Correlates of immunity (correlates of protection)** The specific immune responses that correlate with protection from a certain infection. The precise correlates of immunity for HIV are unknown.

**CTL (cytotoxic T lymphocyte, killer CD8+ cell)** A component of cell-mediated immunity that destroys host cells infected with viruses, fungi, or certain bacteria. CTLs carry the CD8+ surface marker and are thought to play an important role in immunity to HIV, but this is still unproven.

**Cytokine** A group of soluble, hormone-like proteins produced by white blood cells and that act as messengers between cells. Cytokines can stimulate or inhibit the activity of immune cells and may prove useful as immunologic adjuvants.

**Delivery system** See vector.

**DNA (deoxyribonucleic acid)** The genetic material of all living things, except for RNA-carrying viruses, such as HIV. DNA is a double-stranded, helical molecular chain found within each cell. It contains the information needed for
cells to produce proteins, molecules that enable cells to reproduce and carry out their functions.

**DNA vaccine (naked DNA vaccine)** An experimental vaccine technology in which one or more genes coding for specific antigen(s) are directly injected into the body, where they hopefully produce antigen(s) in the recipient and trigger immune responses.

**Efficacy** In clinical vaccine research, the ability of a vaccine to protect vaccinated subjects against a specific infection or disease. A vaccine may be tested for efficacy in Phase III trials if Phase I and Phase II trials show it to be safe and promising. Efficacy is distinct from immunogenicity.

**ELISPOT** (Enzyme-Linked Immuno-Sorbent spot) A blood test that detects antibodies and is often used to test whether a person is infected with HIV.

**env** A gene of HIV that codes for gp160, the precursor molecule that gets split into the envelope proteins gp120 and gp41. env is under consideration as a component of an HIV vaccine.

**Envelope** Outer surface of a virus, also called the coat.

**Epitope** A specific site on an immunogen that stimulates specific immune responses.

**Expression system** See vector.

**First-generation AIDS vaccine candidate** AIDS vaccine candidate currently in clinical trials; distinct from second-generation candidate.

**gag** An HIV gene that codes for p55. p55 is the precursor of HIV proteins p17, p24, p7, and p6 that form HIV's core. gag is under consideration as a component of an HIV vaccine.

**GCP** International standards for Good Clinical Practices.

**Genetic engineering** The laboratory technique of splicing together genes to produce specific proteins, for example, to use as vaccines or medicines.

**GLP** International standards for Good Laboratory Practices.

**GMP** International standards for Good Manufacturing Practices.

**gp120** The glycoprotein on the outer surface of the HIV envelope; gp120 binds to the CD4+ molecule on helper T cells during infection. It has been studied as an experimental HIV vaccine because the outer envelope is the first part of the virus “seen” by antibodies. See gp41.

**gp41** A protein embedded in the outer envelope of HIV that anchors gp120. gp41 plays a key role in HIV's entry into helper T cells by facilitating the fusion of the viral and cell membranes.

**Helper T cell (helper CD4+ cell)** T lymphocyte bearing the CD4+ cell surface marker. Helper T cells are the chief regulatory cells of the immune system, controlling activities such as coordinating cell-mediated immunity and turning antibody production on and off. They are the main targets of HIV infection.

**HIV (Human Immunodeficiency Virus)** The etiologic agent that causes AIDS.

**HIVA** An AIDS vaccine under investigation by IAVI that consists of the gag gene of HIV subtype A, p24, p17 and a series of mini-genes representing the CTL epitopes from env-gag-pol-nef. HIVA is intended to be combined with RENTA.

**Immune response** The body's reaction to foreign antigens. This response may neutralize or eliminate the antigens. See cell-mediated immunity, mucosal immunity, neutralizing antibody.

**Immunogen** A substance capable of provoking an immune response.

**Immunogenicity** The extent to which an immunogen stimulates immune responses. Immunogenicity is distinct from efficacy.

**Inactivated** Altered to prevent harmful biologic activity.

**IND** Investigative New Drug regulatory application required by the US FDA.

**Informed consent** An agreement signed by all volunteers participating in a clinical trial, indicating their understanding of: (1) why the research is being done; (2) what researchers hope to learn; (3) what will be done during the trial, and for how long; (4) what risks are involved; (5) what, if any, benefits can be expected from the trial; (6) what other interventions are available; and (7) the participant’s right to leave the trial at any time.

**Isolate** A particular strain of HIV from a person (primary isolate) or cultured cell line (laboratory isolate).

**Lymphocyte** A type of white blood cell.
Monoclonal antibodies  A collection of identical antibodies that recognizes the same single epitope.

Mucosal immunity  Immune response conferring resistance to infection across the body's mucous membranes. Mucosal immunity depends on antibodies and other immune components present in the linings of the reproductive and gastrointestinal tracts and other moist body surfaces exposed to the outside world, the most frequent routes of HIV infection.

Multigenic  Containing more than one gene.

MVA  Modified Vaccinia virus Ankara, under consideration as a vector.

 nef  A gene present in HIV that is not required for but regulates viral reproduction, now being studied as a component of an HIV vaccine.

Neutralizing antibody  An antibody that prevents virus from infecting a cell, usually by blocking viral entry points on the virus.

NGO  Non-governmental organization.

OECD  Organization for Economic Cooperation and Development.

p17, p24, p7, and p6  Proteins that form HIV's core. See Gag.

Phase I vaccine trial  A clinical trial with a small number of healthy volunteers, typically at low risk for HIV infection. Phase I trials test a vaccine's safety in humans, including its metabolic and pharmacologic actions and any side effects seen with increasing doses. Phase I trials may gather data on the vaccine's immunogenicity.

Phase I/II vaccine trial  A preliminary safety and immunogenicity clinical trial that is larger than a Phase I trial.

Phase II vaccine trial  Controlled clinical trial to identify common short-term side effects and risks associated with the test vaccine and to collect information on its immunogenicity. Phase II trials can include up to several hundred participants.

Phase III vaccine trial  Large controlled clinical trial to determine the ability of a vaccine, at an optimally selected dose and schedule, to provide efficacy. These trials also gather additional information about safety needed to evaluate the overall benefit-risk relationship of the vaccine. Phase III trials usually include several hundred to several thousand volunteers. Placebo  An inactive substance given to some participants in a controlled clinical trial, while others receive the test substance. Placebos provide a basis for comparison.

Plasmid  Circular DNA molecules that multiply independent of the host chromosome and transmit desired genetic information through cell divisions. See DNA vaccine.

pol  An HIV gene that codes for reverse transcriptase and other molecules that the virus uses to replicate. pol is under consideration as a component of an HIV vaccine.

Preclinical  In vaccine research and development, the stages before clinical trials.

Prime-boost (priming)  Giving one vaccine dose to induce certain immune responses, to be followed by or together with a second type of vaccine, a booster. A prime-boost combination may induce different types of immune responses and/or enhance overall responses beyond those seen with only one type of vaccine.

Process development  The optimization of the processes for manufacturing a vaccine.

Protocol  The detailed plan for a clinical trial, outlining its rationale, purpose, methodologies, and other aspects of trial design.

QA  Quality assurance.

QC  Quality control.

R&D  Research and development.

rAAV  Recombinant Adeno-Associated Virus, under consideration as a vector.

Reagent  A substance used to produce a chemical reaction so as to detect, measure, or produce other substances.

Recombinant  A cell or an individual with a new combination of genes not found together in either parents; usually applied to linked genes. See genetic engineering.

RENTA  An AIDS vaccine under investigation by IAVI that consists of genes expressing inactivated HIV clade A tat and nef, the reverse transcriptase gene, and the two most immunogenic regions of env. RENTA is intended to be combined with HIVA.

Replicon  A unit of DNA that contains an initiation point and a termination point and is capable of self-replication. See DNA vaccine.
An HIV gene that helps regulate the virus’ life cycle, now being studied as a component of an HIV vaccine.

**Reverse transcriptase** A retroviral enzyme that is capable of copying RNA into DNA, an essential step in the life cycle of HIV. See **pol**.

**RNA (ribonucleic acid)** A single-stranded molecule composed of chemical building blocks similar to those of DNA. RNA is the sole genetic material of retroviruses, including HIV, and an intermediary in making proteins in all living things.

**Salmonella typhi** A genetically engineered, harmless derivative bacteria that can live in the human gut, under consideration as a vector.

**Second-generation AIDS vaccine candidate** AIDS vaccine candidate now in preclinical development; distinct from first-generation candidate.

**SFV** Semliki Forest Virus, under consideration as a vector.

**Shigella** A genus of gram-negative, facultatively anaerobic, rod-shaped bacteria of the family Enterobacteriaceae, under consideration as a vector.

**Simian Immunodeficiency Virus (SIV)** An HIV-like virus that infects monkeys and causes an AIDS-like disease in some species.

**Strain** See clade, isolate.

**Subtype** See clade.

**tat** An HIV gene that helps regulate the virus’ life cycle, now being studied as a component of an HIV vaccine.

**T-cell** One of two main types of white blood cells critical to the immune system. They include CD4+ and CD8+ T-cells. The "T" stands for the thymus, where T-lymphocytes mature. (See lymphocyte.)

**Vaccinia** A cowpox virus, formerly used in human smallpox vaccines and now as a vector in some experimental HIV vaccines. See MVA.

**VDP** IAVI AIDS Vaccine Development Partnership.

**Vector** A bacterium or virus that does not cause disease in humans and is used in genetically engineered vaccines to transport antigen-encoding genes into the body to induce an immune response.

**VEE** Venezuelan Equine Encephalitis, under consideration as a vector.

**Viral load** The level of HIV circulating in the bloodstream. Viral load is inversely correlated with HIV disease progression.
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BD (Becton, Dickinson and Company)
Crusaid
The European Union
Joachim Franz
The Bill & Melinda Gates Foundation
The Estate of Mercedes Hotle
The Perls Foundation
The Starr Foundation
Until There’s A Cure Foundation
The World Bank / Global Forum for Health Research

and eight national governments

Canada Fund for Africa Secretariat of the Canadian International Development Agency
Ministry of Foreign Affairs of Denmark
Development Cooperation Ireland
Netherlands Ministry of Foreign Affairs
Norwegian Royal Ministry of Foreign Affairs
Swedish International Development Cooperation Agency
U.K. Department for International Development
U.S. Agency for International Development