



AAVP NEWS

THE FOURTH EDITION OF THE AFRICAN AIDS VACCINE PROGRAMME (AAVP) NEWSLETTER

Editorial

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Supported by WHO and UNAIDS, the African AIDS Vaccine Programme (AAVP) was conceived, in 2000, as a network of African scientists working together to promote and support HIV vaccine research in Africa, through capacity-building and regional and international collaboration.

Officially launched in June 2002, AAVP has played important roles in building community and political support and strengthening HIV vaccine research capacity in Africa. AAVP has established effective partnerships with major research agencies and others working on HIV vaccine research and development in Africa. Our partners include, for example, the US National Institutes of Health/HIV Vaccine Trials Network (NIH/HVTN), l'agence nationale de recherches sur le SIDA (ANRS), the US Centers for Disease Control and Prevention (CDC), the Walter Reed HIV/AIDS Program, the International AIDS Vaccine Initiative (IAVI), the European Developing Countries Clinical Trial Partnership (EDCTP), and the South African AIDS Vaccine Initiative (SAIVI).

AAVP and its partners have achieved much but there is a continuing pattern of under-investment in HIV vaccine-related research in Africa. This means that AAVP must become an ever more active player in efforts to mobilize African and international stakeholders at the community, political and scientific levels.

HIV vaccines: The best hope and a major challenge



The AIDS epidemic has presented Africa with a major public health and socio-economic development crisis that calls for new approaches to health care. The past few years of experience have taught crucial lessons about how to reduce the risk of new infections and improve the quality of care for people living with HIV/AIDS. There have been major advances in providing education on safe sexual behaviour, effective counselling and testing, and access to antiretroviral therapies. There are still huge challenges that must be met in order to turn the tide of the epidemic, reduce its socio-economic impact and thus contribute to achieving the Millennium Development Goals.

Among the challenges are to develop safe, effective and broadly affordable biomedical tools for prevention. Microbicides, applied as topical ointments, hold great promise for preventing sexual

transmission of the virus. The best single hope is for HIV vaccines that will protect people against infection with HIV. Microbicides and HIV vaccines would not replace existing HIV/AIDS prevention, care and treatment programmes and strategies at any time in the foreseeable future. Instead, they would be immeasurably valuable complements to those programmes.

Vaccine researchers from around the world are joining forces to accelerate progress towards safe, effective and affordable HIV vaccines. Dr Marie-Paule Kieny, Director, Initiative for Vaccine Research, World Health Organization (WHO), has said, "With so many HIV vaccine clinical trials testing novel products ongoing and planned by a wide variety of investigators, it is time to intensify global collaboration. Lessons learned must benefit all working in this challenging, but advancing, field."

Vaccine trials underway in four African countries and planned in five more

When AAVP was launched in June 2002, only one candidate HIV vaccine was undergoing phase I trials in Uganda. AAVP aimed to ensure that additional candidate vaccines were ready by the end of 2004 and that small-scale phase I and II trials - testing for safety and measurement of immune responses - were initiated or completed in four African countries by the end of 2005.

At the AIDS Vaccine 2004 International Conference held from 30 August to 1 September 2004 in Lausanne, Switzerland, it was reported that, by the end of 2004, there would be more than 30 candidate vaccines being tested in phase I and II trials in 19 countries and four of them were being tested in African countries: Botswana, Kenya, South Africa, and Uganda. In addition, trial sites were under development in seven more, of which five were in Africa: Cameroon, Malawi, Rwanda, United Republic of Tanzania, and Zambia. Soon, nine of the world's 26 AIDS vaccine trial sites will be in Africa. Currently, IAVI, the Kenya AIDS Vaccine Initiative (KAVI), the United Kingdom's Medical Research Council (MRC), and the Uganda Virus Research Institute (UVRI) are completing phase I

and II trials of two candidate vaccines developed by Oxford University and KAVI at sites in Kenya, South Africa, and Uganda, as well as in the United Kingdom. Phase 1 (recombinant AAV vaccine, IAVI- Targeted-Genetics) trials have been approved in South Africa and are due to start soon. The Botswana-Harvard AIDS Institute Partnership (BHP) began phase I trials - to assess safety, tolerability and ability to induce immune responses - of the EP HIV-1090 DNA Vaccine in both the United States of America and Botswana in 2003. By March 2004, 14 volunteers were enrolled and vaccinated in Gaborone, Botswana. In April 2004, the BHP team and the HIV Vaccine Trials Network (HVTN) began an HIV vaccine preparedness study to determine their ability to recruit HIV negative persons with defined risk criteria into a standardized protocol that would keep them prepared for future large-scale HIV vaccine trials. In December 2004 a phase I trial testing multi-clade DNA vaccines started in collaboration between the Makerere University, the Walter Reed HIV/AIDS Program and the Vaccine Research Center (VRC). SAAVI and the HVTN, among others, are conducting trials of another candidate vaccine, developed by AlphaVax Inc, in South Africa and the United States of America.

Vaccine trials demonstrate research capacity in Kenya and Uganda

At the AIDS Vaccine 2004 International Conference in Lausanne, scientists from IAVI, the Kenya AIDS Vaccine Initiative (KAVI) and the Uganda Virus Research Institute (UVRI) reported on HIV vaccine trials they were conducting in partnership with the United Kingdom's Medical Research Council (MRC). The team had been testing two candidate vaccines called DNA.HIVA and MVA.HIVA. Five trials, involving 277 volunteers, conducted over 30 months had shown the vaccines to be safe and well tolerated but they had induced cellular immune responses in, at most, 18% of the volunteers and these responses were not long lasting. At the outset,

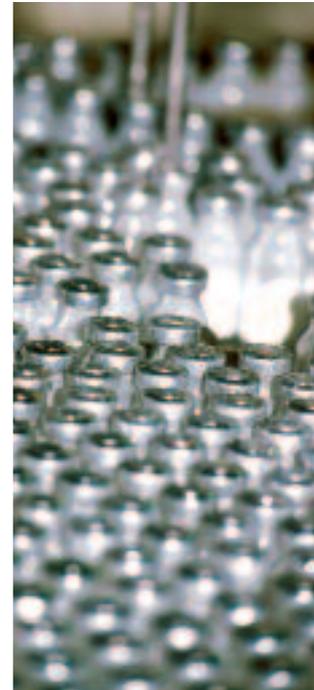
the team had stipulated that a 60% response would be required to qualify a candidate vaccine for further development. Though the trial results had not met expectations, the team deemed them important since they demonstrated the ability to recruit and retain volunteers and to produce data of high quality. In advance of the trials, IAVI had worked with KAVI and UVRI to build their research capacity. Today, KAVI and UVRI have two of Africa's few state of the art labs for measuring cell-mediated immunity. These labs now have highly trained and experienced professional staff and their work has strong political and community support.

Sweden supports research capacity development in Africa

In 2002, Sweden became the first donor country to support AAVP. The country's support for HIV/AIDS research is administered by the Swedish International Development Cooperation Agency (Sida), through the Department for Research Cooperation (SAREC). As Head of Sida/SAREC's Division of Human Sciences for Social Development, Dr Barbro Carlsson oversees the agency's involvement in the AAVP.

In a recent interview, Dr Carlsson explained, "AAVP is a perfect fit with our philosophy. We believe the best long term strategy is to help African countries build capacity to do their own research and not just have our scientists do research for them. We support bilateral partnerships between Swedish and African institutions so that, for example, Africans can get training in their own universities and do not have to go abroad. This approach builds capacity in African universities and also provides more appropriate training, where people acquire the knowledge and skills to work with whatever limited resources their countries may have. We also support development of research libraries, laboratories and capacity to administer research grants."

Over the past 15 years, much of Sida/SAREC's support for HIV/AIDS research has focused on the United Republic of Tanzania. TANSWED, a collaboration of Muhimbili University College of Health Sciences in Dar es Salaam and Sweden's Center for Infectious Disease Control and Karolinska Institute, has developed simple diagnostic tools, tracked the spread of infection in the United Republic of Tanzania and looked for strategies for preventing spread of HIV infection from mother to child through breast milk. TANSWED has been involved in studies showing that vaccination can evoke strong immune response in apes. A vaccine based on that research is now undergoing phase I trials in Sweden. Tanzanian police officers who get tested regularly for HIV have been prepared to serve as volunteers in phase I/II trials. "By supporting AAVP," Dr Carlsson said, "we support the development of more bilateral and multi-lateral partnerships that will increase the capacity of African countries to do their own health research, whether focused on HIV/AIDS or other problems. A priority, right now, is to build this capacity quickly so that African countries will be prepared for phase III trials as soon as a suitable HIV candidate vaccine is found."



IAVI says research labs for African scientists are needed

The International AIDS Vaccine Initiative (IAVI) is a not-for-profit organization working with partners in 23 countries to ensure the development of HIV vaccines suitable for use throughout the world. It was founded in 1996 to fill a gap left by the pharmaceutical industry, which could see little profit in work on HIV vaccines for developing countries. IAVI has been an active partner of AAVP from its start in 2002.

Dr Samuel Kalibala, a Ugandan medical doctor who specializes in sexually transmitted diseases, is IAVI's Representative for East and Southern Africa. In a recent interview, he discussed the importance of research in Africa by Africans and the part AAVP plays in promoting and supporting such research.

"At first, IAVI left the science to biotech firms in Europe and the United States of America while it focused on advocacy for funding to get more candidate vaccines in the pipeline but, in 1998, it began getting involved in the science and clinical trials. The reason was to ensure that more of the science and clinical trials took place in developing countries, involving research institutions and scientists from those countries. We work with AAVP to achieve this aim in Africa.

"AAVP is highly respected in Africa, by African scientists, political leaders and the general public. This puts it in a position to do things that IAVI and other HIV vaccine researchers cannot do at the country and regional level. For example, AAVP can help build the capacity of national regulatory authorities to review and approve vaccine research proposals in timely manner.

"IAVI has prepared five East African sites (two in Kenya, two in Uganda and one in Rwanda) to stand ready for large-scale phase III trials as soon as a candidate vaccine is found. These sites are located where there are people who would make potential cohorts for vaccine trials. For example, one is at a sugar plantation and another is in a poor urban neighbourhood where commercial sex workers reside. IAVI's African partners help coordinate and maintain these efforts. AAVP works with its partners to develop the necessary skills for this kind of community mobilization and cohort development .

"AAVP helps us tackle sensitive gender and age issues, such as how to recruit and retain women for trials when they know they cannot get pregnant during the trial period and how to recruit minors, under age 18, when they need consent of their parents and guardians. AAVP also facilitates South to South dialogue between researchers. AAVP in collaboration with IAVI have facilitated the participation of selected investigators in Africa to the "African Investigators Meeting" organized by the US-Army in Bangkok, Thailand from 3-7 November 2004. To support our partnership with AAVP we contribute to their regular operating budget and, in East Africa, we also participate in and contribute directly to the costs of their activities in the region.

"As for the future, I foresee AAVP helping us with what, in my opinion, is the top priority. That is to establish well-equipped research labs at institutions such as the Kenya Medical Research Institute, in Nairobi, and the Uganda Virus Research Institute, in Entebbe, so African scientists can do all the work necessary in supporting the development of candidate vaccines."

Canada supports development of health infrastructure in Africa

In 2002, at the Group of 8 (G8) Summit in Kanaskis, in the Canadian province of Alberta, the G8 leaders approved the Africa Action Plan and linked it to the New Partnership for Africa's Development (NEPAD). NEPAD aims to move Africa from the margin to the mainstream of economic development in the 21st century and emphasizes African leadership and control of the development process.

At Kanaskis, Canada announced that its contribution to the G8 Africa Plan would include a five-year Canada Fund for Africa of CAN \$ 500 million. In 2003, the Canadian International Development Agency (CIDA) announced that CAN \$ 5 million of the Fund would go to support AAVP.

Ms Peggy Thorpe, Health Specialist in the Africa and Middle East division of CIDA, oversees Canada's participation in AAVP. In a recent interview, she said, "The Canada Fund is also part of our contribution to the achievement of the Millennium Development Goals, including the goal to reverse the HIV/AIDS epidemic by 2015. The link to NEPAD gives us unique flexibility in administering the Fund, allowing us to accept more direction and control from African countries."

"We are cautiously optimistic about the development of an HIV vaccine appropriate for Africa but think it is important to be realistic and not hold out the promise that an effective vaccine will be found any time soon. Meanwhile, when we support development of African countries' capacity to do vaccine research, we also support development of their whole health infrastructure. Accelerating the development of that infrastructure is one of the keys to achieving the Millennium Development Goals."

"Among the things CIDA would like to see happen through AAVP is more involvement of and collaboration among African universities and other research institutions, as well as partnerships with institutions in donor countries. We would like to see the strengthening of continent-wide and regional structures to promote and support such involvement and collaboration."

AAVP to meet four challenges in 2005

Challenge One: To ensure a transparent, coordinated and collaborative environment in which all partners from the public and private sectors, from African countries and the international community, can work together to achieve the AAVP's mission.

This will require 1) advocating for and supporting the formation of new partnerships and networks within and among communities, countries, regions and the international community and 2) supporting development and implementation of policies and strategies that address needs of countries and vulnerable communities.

Challenge Two: To promote African ownership or co-ownership of HIV vaccine programmes in Africa and to maintain them as sustainable, long-term efforts supported by regional AAVP management infrastructures.

This will require 1) developing policies that enable African countries to play active roles in planning and implementing HIV vaccine-related projects and 2) exploring ways to develop appropriate regional AAVP management infrastructures to support regional and country activities.

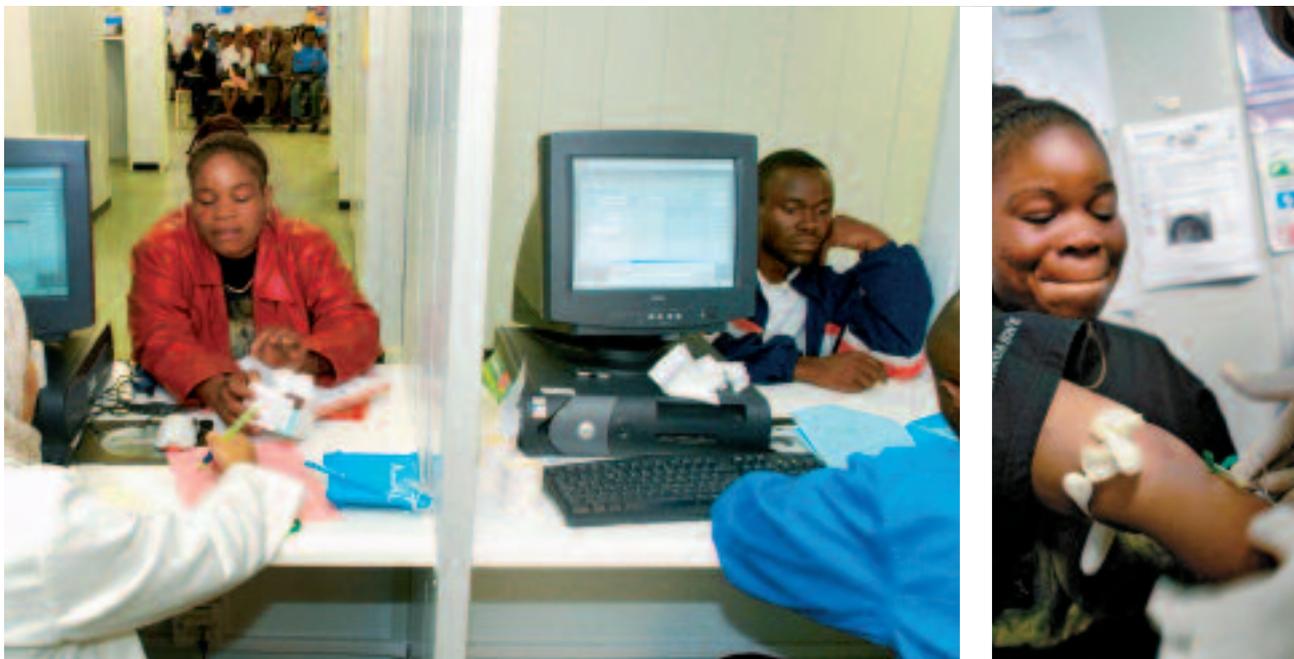
Challenge Three: To lay grounds for research and clinical trials to be conducted in Africa according to the highest scientific and ethical standards and with the utmost respect for human rights.

This will require 1) continuing to develop and implement National AIDS Vaccines Plans in order to strengthen the capacity of human resources and research infrastructure in selected African countries and 2) supporting development of regional and national normative frameworks that define and enforce scientific and ethical standards.

Challenge Four: To facilitate the integration and coordination of HIV vaccine-related activities with HIV/AIDS prevention, treatment and care programmes.

AAVP is committed to 1) working closely with agencies responsible for HIV/AIDS prevention, treatment and care programmes and 2) sharing experiences, ideas and resources to make optimal use of limited resources.

Gender, ethnicity and age present challenges for HIV vaccine researchers



From 26 to 28 August 2004, a consultation hosted by WHO and UNAIDS in Lausanne, Switzerland, considered issues related to gender, ethnicity and age in HIV vaccine research and clinical trial recruitment. Discussion revolved around the experiences and lessons learned from a variety of vaccine research programs, trials and studies in different countries. The lack of sufficient research and the fact that HIV is usually transmitted sexually led to the conclusion that it is important to involve people of both genders and all ages and ethnicities in vaccine trials in approximate proportion to their presence in populations at risk of HIV infection.

The number of women and girls with HIV infection grew from under 2 million in 1985 to nearly 18 million in 2004. Women and girls now account for almost half of all cases of HIV infection. In sub-Saharan Africa, they account for 57% of cases and for 76% of cases among young adults (15 to 24). The reasons for women's greater vulnerability to HIV/AIDS are biological, social, and cultural. The same social and cultural factors that make women and girls especially vulnerable to infection can also work against their volunteering for HIV vaccine trials. The bigger problem,

though, is that they may be reluctant to carry through on their agreement to participate in trials when they learn they will not be able to get pregnant during the trial period. This will be a particular problem with phase III trials, which generally last for three years.

Recruiting legal minors under age 18 for trials also presents problems, when they require consent and when communication about sexually transmitted disease between minors and their parents or guardians is often awkward. Upcoming concerns will be how to recruit mother-baby pairs to test vaccines for the prevention of mother to child transmission and how to recruit children to test vaccines that might protect them against infection before they enter adolescence and their most sexually active years.

The consultation concluded with a full set of recommendations addressing the legal, ethical and logistical problems involved in recruiting appropriate volunteers for HIV trials and protecting them from harm. These recommendations will provide guidance to, among others, AAVP staff as they work with their African partners.

Global policy consultation recommends national and regional frameworks

On 2 and 3 September 2004, a consultation hosted by WHO and UNAIDS in Lausanne, Switzerland, reviewed AAVP's draft guidelines for countries to refer to as they develop their own National HIV Vaccine Plans. The guidelines incorporated lessons learned from AAVP's experience supporting its country-level partners in Botswana, Cameroon, Kenya, South Africa, United Republic of Tanzania and Uganda as they worked on developing

such national plans. The consultation concluded by recommending both national and regional frameworks for HIV vaccine research and development. Regional frameworks would be developed through collaboration of host countries and institutions within a region and with sponsor countries and institutions addressing complex scientific, regulatory, ethics, legal and human rights challenges in HIV vaccine research.

Global partners strengthen collaboration to accelerate progress

The first WHO-UNAIDS Sponsored Meeting of Global Partners Promoting HIV Vaccine Research and Development was held in Montreux, Switzerland, on 2-3 February 2005. Attending were some 50 vaccine experts - including members of the AAVP Steering Committee - from developing and industrialized countries.

The experts gave progress reports on their research projects, including the results of several phase I and II trials of candidate vaccines, and discussed the Global HIV/AIDS Vaccine Enterprise Scientific Strategic Plan, published in January 2005. The Plan sets a number of milestones to be reached through collaboration of all global partners.

A number of challenges were identified. One is to increase capacity to conduct clinical trials worldwide, including trials of particular candidate vaccines at multiple sites where there are different patterns of transmission and where different strains of the HIV virus are prevalent. The second is to ensure that candidate vaccines are tested at the most appropriate sites regardless of who developed the product or strengthened the site. A third is to ensure access to antiretroviral treatment where HIV vaccine trials are taking place and a fourth is to ensure that trial sites are available for other HIV preventive research, where appropriate. "Overcoming these challenges will require intense international collaboration and coordination," said Dr Saladin Osmanov, Coordinator ad-interim, WHO-UNAIDS HIV Vaccine Initiative.

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