



23 October 2007

Update on the STEP and Phambili HIV vaccine trials

On 21 September 2007, the United States' National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), the pharmaceutical company Merck & Co. Inc., and the NIAID-funded HIV Vaccine Trials Network (HVTN) announced that immunisations in the HIV vaccine clinical trial known as the STEP study — also referred to as the HVTN 502 or Merck V520-023 study — would be discontinued ('Immunizations Are Discontinued in Two HIV Vaccine Trials' http://www3.niaid.nih.gov/news/newsreleases/2007/step_statement.htm). The decision was based on recommendations made by an independent Data and Safety Monitoring Board (DSMB), which concluded that the vaccine did not prevent HIV infection nor reduce the amount of virus in those who became infected with HIV. The STEP study was conducted in the USA, Australia, South America and the Caribbean in countries where the predominant circulating HIV subtype is B. This study enrolled mostly men who had sex with men.

As a result of those findings, immunisations and enrollment in a separate clinical trial in South Africa, known as Phambili, which was evaluating the same Merck test HIV vaccine was paused to allow for further analysis of these findings. Based on that additional review of the STEP data, an independent DSMB has now concluded that there is no basis for anticipating more favourable results in the South African clinical trial known as HVTN 503, or the 'Phambili' study. Therefore, the HVTN 503 oversight committee has permanently suspended immunisations and enrolment in the study in South Africa.

The DSMB also recommended that all volunteers be told whether they received the vaccine or placebo and be strongly encouraged to return to their study sites for further related tests and ongoing counselling. This week participants will be called back to receive this information.

Based on data from the STEP Study, there is a possibility that people in the vaccine arm may have increased susceptibility to acquiring HIV infection. Study volunteers in either the Phambili or the STEP study will be counselled about this possibility. The vaccine itself cannot cause infection. HIV infections would be the result of unprotected sexual relations.

Based on the information from STEP, the investigators believe it is prudent to stop the trial. Volunteers who became infected with HIV during the trial will receive appropriate medical treatment and care. The Phambili trial had enrolled 801 participants.

“We are very disappointed by the outcome of STEP,” said Ms Elise Levendal, Interim Director of SAAVI. “We hope that the data that eventually emerges from this study will help us in future vaccine designs.”

The trial partners will release more information concerning the study findings as it becomes available in the coming weeks.

Prof. Glenda Gray of the Perinatal HIV Unit at Chris Hani-Baragwanath Hospital, the National Principal Investigator for the Phambili trial, stressed that as the vaccine had not worked in the companion trial it does not make sense to continue the Phambili trial in South Africa. She emphasised that the well-being of the participants remains the main priority. “As the well-being of our participants is paramount, we will continue to follow up participants and offer individualised risk reduction counselling, which is integral to the trial.”

“The path to find an HIV vaccine is a hard one,” says Prof. Anthony MBewu, President of the Medical Research Council. “The difficulties are common in science. It took almost 50 years to find a polio vaccine and HIV is proving to be a tricky adversary. However, every trial that is conducted gives us additional and valuable information about how to fight this virus.”

The Phambili trial was approved by the Medicines Control Council, the ethics committees of the University of the Witwatersrand, University of Cape Town, University of KwaZulu-Natal and the University of Limpopo. The institutional biosafety committees and the GMO committee in the Department of Agriculture reviewed and approved the trial in South Africa

For additional information about the HVTN 502 and HVTN 503 studies, see http://www3.niaid.nih.gov/news/QA/step_qa.htm

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About SAAVI (www.saavi.org.za)

SAAVI is an initiative of the South African government, and a lead programme of the Medical Research Council. Founded in 1999 by Eskom, the Department of Health, and the Department of Science and Technology, SAAVI seeks to co-ordinate the research, development and testing of HIV vaccines in South Africa to arrive at an effective, safe, affordable and locally relevant AIDS vaccine as quickly as possible. SAAVI funds and co-ordinates activities of investigators at South African academic institutions. The activities include: laboratory development of vaccines; immunology; testing of vaccines in clinical trials; ethics and behavioural research; community education and mobilisation; and bioinformatics. An emphasis has been on creating novel biotechnology platforms to develop and test HIV vaccines, and developing the clinical and social environment conducive to running HIV vaccine trials. SAAVI works and collaborates with key national and international partners, and has both an internal research and development arm aimed at investigating and developing novel candidate vaccines, as well as extensive and widespread clinical infrastructure for testing both our own and vaccines developed internationally.

About NIAID

NIAID is a component of the National Institutes of Health. NIAID supports basic and applied research to prevent, diagnose and treat infectious diseases such as HIV/AIDS and other sexually transmitted infections, influenza, tuberculosis, malaria and illness from potential agents of bioterrorism. NIAID also supports research on basic immunology, transplantation and immune-related disorders, including autoimmune diseases, asthma and allergies.

The National Institutes of Health (NIH)—*The Nation's Medical Research Agency*—includes 27 Institutes and Centers and is a component of the U. S. Department of Health and Human Services. It is the primary federal agency for conducting and supporting basic, clinical and translational medical research, and it investigates the causes, treatments and cures for both common and rare diseases. For more information about NIH and its programs, visit <http://www.nih.gov>.

About the HIV Vaccine Trials Network (www.hvtn.org)

The HVTN is an international collaboration of scientists and institutions whose goal is to accelerate the search for an HIV vaccine by sharing trial results and facilitating parallel, concurrent testing. The HVTN is a unique hybrid that combines the depth and diversity of the academic community and the flexibility of a commercial drug company. Working with industry and government, the HVTN seeks to expedite and co-ordinate the trial process, advancing vaccine candidates and building a body of knowledge around HIV vaccine trials. The HVTN is funded and supported by the National Institute of Allergy and Infectious Diseases of the National Institutes of Health, an agency of the US Department of Health and Human Services (DHHS). The HVTN comprises more than 25 research institutions worldwide, co-ordinated from its headquarters at the Fred Hutchinson Cancer Research Center in Seattle.

About Merck (www.merck.com)

Merck & Co., Inc. is a global research-driven pharmaceutical company dedicated to putting patients first. Established in 1891, Merck discovers, develops, manufactures and markets vaccines and medicines in over 20 therapeutic categories. Merck scientists have been conducting research to develop an HIV vaccine for nearly 20 years. The company also devotes extensive efforts to increase access to medicines through far-reaching programmes that not only donate Merck medicines but help deliver them to the people who need them. Merck also publishes unbiased health information as a not-for-profit service.