



November 27, 2016

## QUESTIONS AND ANSWERS

### The HVTN 702 HIV Vaccine Study

**1. What is the HVTN 702 study?**

The HVTN 702 study is a large, advanced-stage clinical trial that aims to determine if an investigational HIV vaccine regimen is safe, tolerable and effective at preventing HIV infection among South African adults. The Phase 2b/3 study is the largest and most advanced HIV vaccine clinical trial to take place in South Africa and the only current HIV vaccine efficacy trial worldwide. The experimental vaccine regimen is based on the one tested in the only study to-date to show that a vaccine can protect people from HIV infection—the [RV144 clinical trial](#) in Thailand led by the U.S. Military HIV Research Program and the Thai Ministry of Health. The HVTN 702 vaccine regimen has been adapted to the HIV subtype that predominates in southern Africa, where the pandemic is most pervasive.

**2. How effective was the vaccine tested in the RV144 clinical trial?**

The experimental vaccine regimen tested in the RV144 trial was found to be 31 percent effective at preventing HIV infection over the 3.5 years of follow-up after vaccination. In the HVTN 702 study, the design, composition and schedule of the RV144 vaccine regimen have been adjusted in an attempt to increase the magnitude and duration of vaccine-elicited protective immune responses, and to extend the higher level of protection seen at one year in RV144 throughout the entire three-year follow-up period of HVTN 702.

**3. Who will enroll in HVTN 702?**

HVTN 702 will enroll approximately 5,400 healthy, sexually active men and women aged 18 to 35 years old. To ensure a balance of the sexes, at least 40 percent of enrolled participants will be male and at least 40 percent will be female.

**4. Where is HVTN 702 taking place?**

The study is taking place at 15 clinical sites in five provinces in South Africa: Gauteng, KwaZulu-Natal, North West, Eastern Cape and Western Cape.

**5. When did HVTN 702 begin and when will it end?**

The first participant was enrolled on Oct. 26, 2016, and results are expected in late 2020.

**6. Who is sponsoring and funding HVTN 702?**

The National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, is the sponsor of HVTN 702, which is co-funded by NIAID, the Bill & Melinda Gates Foundation (BMGF), and the South African Medical Research Council (SAMRC).

**7. Who is conducting and leading HVTN 702?**

The NIAID-funded HIV Vaccine Trials Network (HVTN) is conducting the trial.

Glenda Gray, M.B.B.C.H., F.C.Paed. (SA), is chair of the HVTN 702 protocol. Dr. Gray also is president and chief executive officer of the SAMRC, a research professor of pediatrics at the University of the Witwatersrand, and a director of the Perinatal HIV Research Unit at Chris Hani Baragwanath Hospital in Soweto, South Africa.

The protocol co-chairs are Linda-Gail Bekker, M.D., Ph.D.; Fatima Laher, M.D.; and Mookho Malahleha, M.B.Ch.B., M.P.H. Dr. Bekker is deputy director of the Desmond Tutu HIV Centre at the University of Cape Town and chief operating officer of the Desmond Tutu HIV Foundation in Cape Town, South Africa. Dr. Laher is a director of the Perinatal HIV Research Unit at Chris Hani Baragwanath Hospital. Dr. Malahleha is deputy director of Setshaba Research Centre in Soshanguve, South Africa.

**8. What is the study design?**

Half of the HVTN 702 study participants will be randomly assigned to receive the investigational HIV vaccine regimen, and the other half will receive a placebo. Neither the volunteers nor the study team know who receives which type of injection until the end of the trial. Participants will receive a total of five injections over one year and then will be followed for another two years.

**9. What HIV preventive care do study participants receive?**

Study participants are being offered the standard of care for preventing HIV infection, including condoms and lubricant, counseling on how to reduce behaviors that increase risk for infection, access to management of other sexually transmitted infections, information on voluntary medical male circumcision and referral to circumcision services, and counseling and referral for antiretrovirals to take immediately following suspected exposure to HIV (post-exposure prophylaxis).

In addition, study participants are being referred to available local programs where they may obtain the oral medication Truvada to take daily for HIV prevention, a highly effective practice called pre-exposure prophylaxis (PrEP). HVTN 702 has been designed so investigators will be able to discern a preventive effect from the vaccine regimen even if some participants are taking PrEP.

**10. What will happen to study participants who acquire HIV infection during the trial?**

More than 1,000 people in South Africa become infected with HIV each day. Study participants who become HIV-infected in the community will be referred to local medical providers for care and treatment and will be counseled on how to reduce their risk of transmitting the virus. The study team will follow these participants for about six months after confirmation of diagnosis.

### **11. How is the study team ensuring the safety of study participants?**

An independent Data and Safety Monitoring Board (DSMB) will carefully monitor participants' safety. A DSMB is composed of clinical research experts, statisticians, ethicists and community representatives who meet periodically during a study to review safety and efficacy data as it is gathered. A statistician who is not part of the study team presents interim data to the DSMB. Because the study team is blinded to interim study data, they are excluded from portions of meetings when data are presented. The DSMB alerts the study team if anything appears to compromise the safety of study participants, if there is compelling evidence that the study intervention is effective, or if it becomes clear that the study cannot answer one of the questions it was designed to address.

In addition, a Protocol Safety Review Team (PSRT) designated for HVTN 702 is conducting ongoing oversight of the safety of study participants. The PSRT includes a medical officer from NIAID's Division of AIDS, the study's protocol chair and co-chairs, and principal investigators and clinicians from study sites. Regular reports of safety data will be sent to the Medicines Control Council, the South African national regulatory authority for medications.

### **12. What are the components of the HVTN 702 investigational vaccine regimen? How are they intended to improve upon the regimen tested in the RV144 clinical trial?**

The HVTN 702 vaccine regimen consists of two experimental vaccines: a canarypox-vector based vaccine called ALVAC-HIV and a two-component gp120 protein subunit administered in an adjuvant to enhance the body's immune response to the protein subunit. The vaccines do not contain HIV and therefore do not pose any danger of HIV infection to study participants. Both ALVAC-HIV (supplied by Sanofi Pasteur) and the protein subunit (supplied by GSK) have been modified from the versions used in RV144 to be specific to HIV subtype C, the predominant HIV subtype in southern Africa. Additionally, the protein subunit in HVTN 702 is combined with MF59 (also supplied by GSK), a different adjuvant than the one used in RV144, in the hope of generating a more robust immune response. Finally, the HVTN 702 vaccine regimen will include booster shots at the one-year mark in an effort to prolong the early protective effect observed in RV144.

### **13. Has the HVTN 702 vaccine regimen been tested previously?**

Yes, the HVTN 702 vaccine regimen was previously tested in the [HVTN 100 study](#). HVTN 100 is an early stage, Phase 1/2 clinical trial that sought to determine whether or not the investigational vaccine regimen was safe and elicited a set of key immune responses that were comparable to the immune responses elicited by the RV144 vaccine regimen. Once it was clear that the regimen in HVTN 100 met these criteria, the study's funders decided to go

forward with plans to test the safety, tolerability and efficacy of the regimen in the much larger HVTN 702 clinical trial.

HVTN 100 is ongoing, and investigators will continue to monitor the data emerging from it to inform HVTN 702.

#### **14. What is the P5 and its relationship to HVTN 702?**

P5 stands for the Pox-Protein Public-Private Partnership, a diverse group of public and private organizations committed to building on the success of the RV144 trial. The P5 aims to produce an HIV vaccine that could have a significant public health benefit and to advance scientists' understanding of the immune responses associated with preventing HIV infection. HVTN 702 is part of the P5 research program.

P5 members are NIAID, BMGF, SAMRC, HVTN, Sanofi Pasteur, GSK and the U.S. Military HIV Research Program. NIAID, BMGF and SAMRC fund the P5.

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