Px Wire: A Quarterly Update on HIV Prevention Research

AVAC
AIDS Vaccine Advocacy Coalition

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AVAC's Take

Greetings! This is the last issue of *Px Wire* in 2008—and what a year it has been. The AIDS vaccine field has started to move ahead with different goals and refined strategies in the wake of disappointing data from 2007. Multiple PrEP trials were launched or expanded, the microbicide field began to focus considerably more on the implications of ARV-containing products, and the scale-up of male circumcision started in some countries.

At the International AIDS Conference in August, and in a provocative *Lancet* article (*Lancet*, doi:10.1016/S0140-6736(08)61697-9) by WHO staff, including Kevin De Cock, director of the HIV/AIDS program, the notion of ARV treatment as prevention seized the spotlight. This newly highlighted strategy will continue, we predict, to help shape the field in 2009.

Also in 2009, AVAC will work with other prevention stakeholders to put the spotlight on HIV testing, which is the cornerstone for almost all of the new and emerging prevention strategies. As we continue the search for new options, it's imperative that testing programs continue to expand in ways that are innovative, responsive to community priorities, and sustainable.

In 2008, the best work that's happened has been through efforts that brought scientists and communities together in conversations that haven't always been easy but have always been important. We've been honored to be part of these conversations—and look forward to having many more of them in the year to come.

Warmest wishes,
AVAC

Data Dispatch: HVTN 505

For the past few months, the US-based conversation around vaccine research has kept circling back to a trial now known as HVTN 505.

In brief, HVTN 505 is a proposed "exploratory" study by the NIH-funded HIV Vaccine Trials Network (HVTN) to test a vaccine strategy developed by the US Vaccine Research Center.

The strategy to be tested consists of two different vaccines. The first three immunizations are with a DNA "prime" that stimulates anti-HIV immunity. The prime also prepares the immune system for the "boost," a single immunization that consists of synthetic fragments of HIV packaged into a disabled cold virus known as adenovirus serotype 5, or Ad5.

Ad5 may ring some bells with *Px Wire* readers. A similar, though not identical, form of this cold virus was used in the Merck vaccine candidate, MRK-Ad5, which was evaluated in the Step and Phambili studies. The initial results of the Step study were published in November 2008 in the *Lancet* journal (*Lancet*, doi:10.1016/S0140-6736(08)61591-3).

In the Step study, MRK-Ad5 had no overall benefit in terms

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At a Glance: Moving right along

- An FDA panel of independent advisors recommended approval of the newly formulated female condom (FC2) in December, green-lighting the less expensive and physically streamlined second-generation product by the Female Health Company. Donors, governments and implementers should take advantage of this lower cost option and take long overdue action to dramatically increase access to and information about the female condom as part of all HIV prevention and family planning programs.

- The Phase III clinical trial "Partners in Prevention" completed all study visits in November 2008 and the data are now being analyzed. The study sought to determine whether suppressing HSV-2 in HIV-positive people reduced the risk of passing HIV to their HIV-negative partners. The study enrolled 3,000 serodiscordant heterosexual couples. The HIV-positive partners were randomized to receive ongoing acyclovir (HSV-2 treatment) or a placebo. Public release of data from the trial is anticipated in mid-2009.

- In November, a Data and Safety Monitoring Board conducted a scheduled safety review of the phase IIb CAPRISA 004 tenofovir gel microbicide study and recommended that the trial continue. The study aims to determine whether the use of the gel can help prevent male-to-female vaginal transmission of HIV. The study is enrolling 930 women in South Africa and is expected to be completed in 2010.

- The iPrEx study of oral tenofovir+emtricitabine (TDF/FTC) has begun enrolling volunteers at trial sites in Brazil. The study is evaluating the safety and effectiveness of TDF/FTC as oral pre-exposure prophylaxis (PrEP) in roughly 3,000 HIV-negative gay men and other men who have sex with men. In addition to sites in Brazil, the study is enrolling volunteers in Ecuador, Peru, South Africa and the United States. It will begin enrolling volunteers in Thailand in early 2009. Results are expected in late 2010. ■

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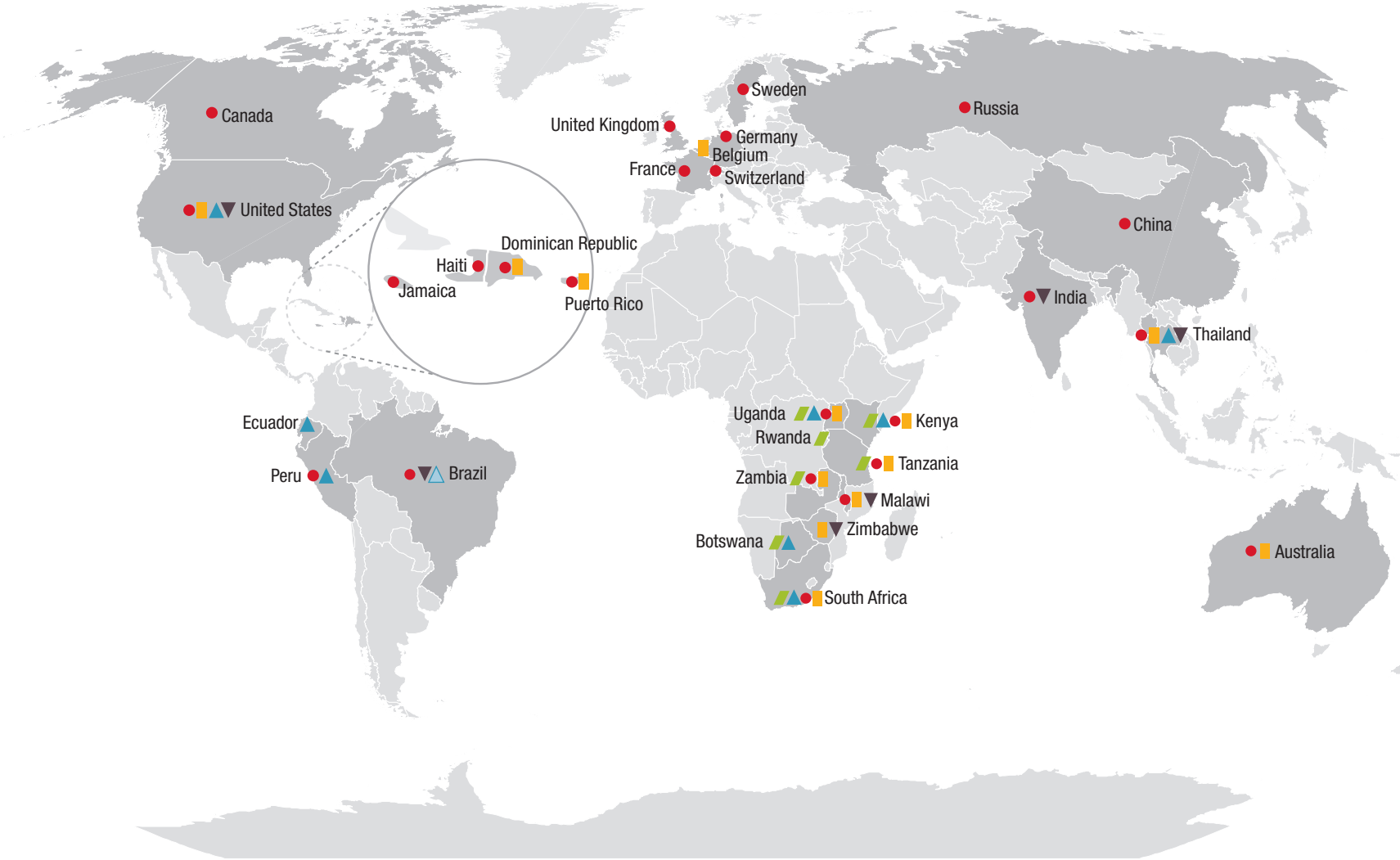
ONGOING TRIALS OF NEW PREVENTION OPTIONS WORLDWIDE



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- Rwanda
- South Africa
- Sweden
- Switzerland
- Tanzania
- Thailand
- Uganda
- United Kingdom
- United States
- Zambia
- Zimbabwe

VACCINES	MICROBICIDES	PRE-EXPOSURE PROPHYLAXIS	HSV-2 TREATMENT	PARTNER TREATMENT
New	New	New	New	New

HIV PREVENTION RESEARCH: A COMPREHENSIVE TIMELINE OF EFFICACY TRIALS*

To view this timeline online with trial details please visit www.avac.org/timeline-website/.

* *The trial end-dates listed in this table are estimates. Due to the nature of clinical trials the actual dates may change. AVAC will continue to monitor the trials' progress and will update the timeline accordingly.*

If you have any questions or comments regarding the information presented here please email avac@avac.org.

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of reducing viral load set point or the risk of HIV infection. The vaccine also appeared to increase the risk of acquiring HIV in a subset of male volunteers with very specific characteristics (uncircumcised, and having previous exposure to Ad5 as measured by antibodies to Ad5). The reasons for this increased risk are still not well understood. However, the interaction between volunteers' pre-existing antibodies to Ad5 (acquired through exposure to the Ad5 cold virus prior to getting the vaccine), and the Ad5 vector in the vaccine may have played a role. This raises safety issues for any future Ad5-vectored vaccine.

Understanding who was—and was not—at increased risk in Step is of the utmost importance in understanding the proposed HVTN 505 study. In Step, men who were circumcised and did not have any previous exposure to Ad5 had equal rates of infections in the vaccine and placebo arms. This means that while the vaccine did not provide any benefit it also did not increase the risk of HIV infection among men with these specific characteristics.

Based on this finding the HVTN 505 trial would enroll only Ad5-seronegative, circumcised gay men and other men who have sex with men.

The trial protocol is still being developed, and it will have to be reviewed by DAIDS and by the US Food and Drug Administration as part of the approval process. Right now, the design calls for around 1,300 participants in the US. The study will look at whether the vaccine strategy lowers viral load set point (the point that viral load settles at after a peak immediately following infection) in volunteers who get the vaccine and go on to become infected. Measuring the vaccine's ability to prevent infection is not one of the study's primary endpoints.

In late November, the HVTN Legacy Project, the Black Gay Men's Network and AVAC collaborated on a meeting with black gay men to explore HIV prevention research and black gay men's health in the US, and to learn about the HVTN 505 trial. The questions at this meeting underscored that, if the trial goes forward, this may be one of the most complex trials ever conducted. This includes explaining what's known and not known about safety; why the inclusion criteria are so specific; why the study is focused on viral load endpoints instead of HIV infections; and how this vaccine trial relates to broader HIV prevention research goals.

AVAC believes that the scientific question HVTN 505 is asking is a valid one. However, there remains extensive additional work to be done by the trial sponsors to address the aforementioned complexities and to ensure that communities asked to participate in and communicate about the trial are able to do so as full, informed partners. ■

Coming Up: New Trials

- **FEM-PrEP,** a study to assess the effectiveness of a once-daily TDF/FTC pill in preventing HIV in women is slated to begin in February. The phase III trial will enroll 3,900 women at sites in Kenya, Malawi, South Africa and Tanzania and will investigate the safety and effectiveness of this strategy in preventing HIV infection via sexual intercourse.

- **The VOICE study** (MTN 003) is a phase IIb trial to look at the effectiveness of vaginal and oral tenofovir and oral TDF/FTC in preventing sexual transmission of HIV. This trial, which plans to enroll 4,200 women from southern Africa, is on schedule to begin in early 2009. This is the first study to evaluate the effectiveness and acceptability of oral and vaginal forms of PrEP in the same study. ■

Not to be Missed

January 22–25: National African American MSM Leadership Conference on HIV/AIDS, *Atlanta*

February 8–11: CROI 2009, 16th Conference on Retroviruses and Opportunistic Infections, *Montreal*

February 22–24: WHO/UNAIDS HIV Vaccine Initiative Meeting on Developing an Asian Network, *Beijing*

February 23–24: 2009 National Conference on African Americans and AIDS, *Philadelphia*

March 22–27: Keystone: Prevention of HIV/AIDS, *Keystone, Colorado*

March 23–25: Stop TB Partners' Forum, *Rio de Janeiro*

About AVAC

AVAC seeks to create a favorable policy and social environment for accelerated ethical research and eventual global delivery of new HIV prevention options as part of a comprehensive response to the pandemic.

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