

AVAC's Take

AVAC is expanding its activities to keep pace with the evolving HIV biomedical prevention field. As part of this effort, we're delighted to introduce our quarterly update, *Px Wire*. Every three months, we'll release a new issue where you'll find an updated prevention trials map and timeline of ongoing prevention efficacy trials around the world. In the "Data Dispatch" and "At a Glance" sections, you'll get a snapshot of recent developments in the field. We will continue to keep you updated through the electronic Advocates' Network—check out <http://aidsvaccineclearinghouse.org/network.htm> for past updates and information about subscribing. We hope this publication serves to keep you informed and engaged as events unfold. Please let us know what you think and what additional information would be helpful—*email us at pxwire@avac.org*.

Data Dispatch: Flurry from the Field

The first quarter of 2008 brought disappointing news from several HIV prevention trials. Much of this news was released in February at the 15th Conference on Retroviruses and Opportunistic Infections (CROI), a major US-based AIDS science conference.

An HPTN phase III trial testing the suppression of herpes simplex virus-2 (HSV-2) to reduce the risk of HIV infection in HIV-negative people with HSV-2 showed no efficacy. However, there is another ongoing trial, known as "Partners in Prevention," looking at suppressive treatment of HSV-2 in people with HIV and their risk of transmission to sexual partners. This large-scale trial, which enrolled roughly 3,000 serodiscordant couples, is expected to be completed in 2009. To learn more about HSV-2 research, look for AVAC's upcoming document on understanding the results of these trials.

The Rakai Health Sciences Project (Uganda) presented data on safety and efficacy of male circumcision in HIV-positive men. The study was designed to determine whether circumcision reduced HIV-positive men's risk of transmitting HIV to their female partners. Data presented at CROI reinforced an earlier observation that circumcision was associated with an increased risk of transmission among men who resumed sex before complete wound healing. While these data are not statistically significant, they do point to a trend with important implications for this prevention strategy. One of AVAC's priorities for the next quarter is to work with a range of advocacy groups and other partners to inform and raise civil society agenda(s) related to male circumcision.

In mid-February, the Population Council announced data from an efficacy trial of its candidate microbicide, Carraguard. More than 6,000 South African women were enrolled in the trial. Women in the experimental arm were asked to insert the seaweed-based gel into their vaginas before having sex; women in the control arm used a placebo gel. There was no significant difference in rates of HIV when comparing the control and intervention arms. For more information about Carraguard and the result, go to http://www.popcouncil.org/mediacenter/newsreleases/Carraguard_Findings.html.

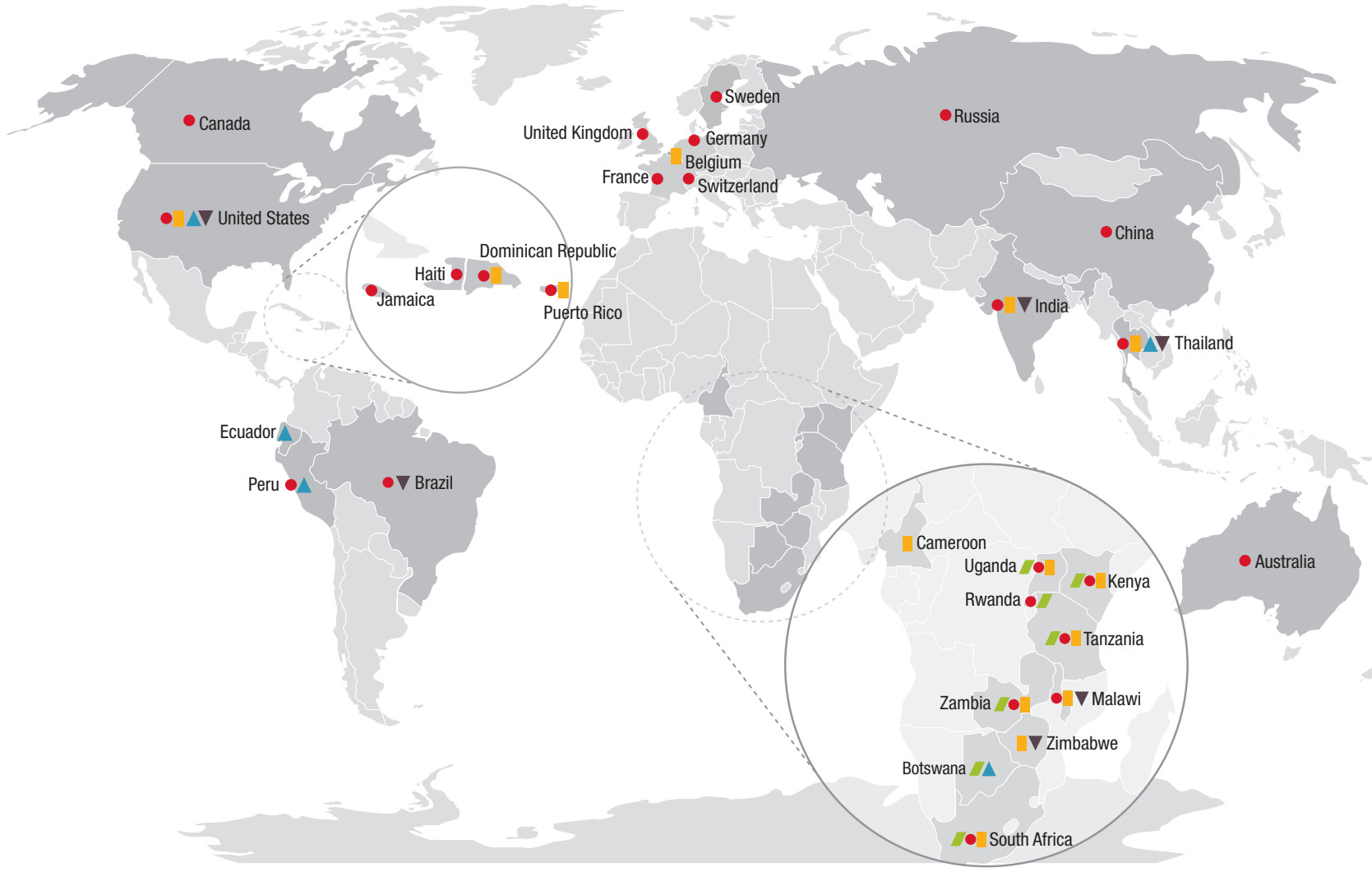
The UK-based Microbicides Development Programme (MDP) announced that an efficacy trial of a candidate called PRO 2000/5 had been scaled back from two experimental arms to one. The trial, which is ongoing in Uganda, Tanzania, South Africa, and Zambia, was testing the microbicide in two different concentrations (2% and 0.5%) alongside a placebo gel. After reviewing interim data, the Data and Safety Monitoring Board (DSMB) recommended discontinuing distribution of the 2% gel. This was because of a futility finding, which means that statistical analysis showed that there

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At a Glance: Ongoing Trials of New HIV Prevention Options

	Safety	Expanded Safety	Safety & Efficacy
Vaccines	26	3	3
Microbicides	14	1	3
Pre-Exposure Prophylaxis (PrEP)	0	1	3
HSV-2	0	0	1
Partner Treatment	0	0	1
Cervical Barriers	0	0	0
TOTAL	40	5	11

ONGOING TRIALS OF NEW PREVENTION OPTIONS WORLDWIDE



- Australia
- Belgium
- ▲ Botswana
- ▼ Brazil
- Cameroon
- Canada
- China
- Dominican Republic
- ▲ Ecuador
- France
- Germany
- Haiti
- India
- Jamaica
- Kenya
- Malawi
- ▲ Peru
- Puerto Rico
- Russia
- Rwanda
- South Africa
- Sweden
- Switzerland
- Tanzania
- ▲ Thailand
- Uganda
- United Kingdom
- ▲ United States
- Zambia
- ▼ Zimbabwe

HIV PREVENTION RESEARCH: A COMPREHENSIVE TIMELINE OF EFFICACY TRIALS*

2007	2008	2009	2010	2011	2013
<p>FHI Phase III trial of the vaginal microbicide Cellulose Sulfate gel for the prevention of HIV infection in women</p> <p>Trial stopped early—January 2007 Results announced July 2007</p>	<p>Phase III trial of acyclovir for the reduction of HIV infection in high-risk, HIV-negative, HSV-2 seropositive individuals</p> <p>Results announced February 2008</p>	<p>Phase III trial of a prime-boost (ALVAC-AIDSVAX) combination preventive HIV vaccine</p>	<p>Large-scale trial of a once-daily dose of tenofovir+emtricitabine to prevent HIV infection in heterosexual men and women</p>	<p>Phase III trial of community mobilization, mobile testing, same-day results, and post-test support for HIV</p>	<p>Phase III trial to determine the effectiveness of two antiretroviral treatment strategies in preventing the sexual transmission of HIV in HIV-serodiscordant couples</p>
<p>CONRAD Phase III trial of the vaginal microbicide Cellulose Sulfate gel for the prevention of HIV infection in women</p> <p>Trial stopped early—January 2007 Results announced July 2007</p>	<p>Large-scale trial to evaluate the safety of male circumcision and its potential protective effect for HIV-negative female partners of HIV-positive circumcised males</p> <p>Trial stopped enrollment and surgeries in December 2006. Results announced February 2008</p>	<p>Phase II/IIb trial of the vaginal microbicides BufferGel and 0.5% PRO 2000/5 gel for the prevention of HIV infection in women</p>	<p>Large-scale trial of a once-daily dose of tenofovir+emtricitabine to prevent HIV infection in high-risk men who have sex with men</p>		
<p>Phase III trial of the female diaphragm to prevent HIV infection in women</p> <p>Results announced July 2007</p>	<p>Phase III trial of the vaginal microbicide Carraguard for the prevention of HIV infection in women</p>	<p>Phase III trial of the vaginal microbicide PRO 2000 for the prevention of HIV infection in women</p>	<p>Phase II trial of the vaginal microbicide tenofovir gel for the prevention of HIV infection in women</p>		
<p>Test-of-concept trial of Merck's adenovirus preventive HIV vaccine candidate (Step study)</p> <p>Trial halted immunizations, September 2007. Follow-up and data collection continue.</p>	<p>Phase III trial of the vaginal microbicide Carraguard for the prevention of HIV infection in women</p> <p>Results announced February 2008</p>	<p>Phase II trial to test the clinical and behavioral safety of a once-daily dose of tenofovir among HIV-negative men who have sex with men</p>			
<p>Test-of-concept trial of Merck's adenovirus preventive HIV vaccine candidate (Phambili)</p> <p>Trial halted enrollment and immunizations, September 2007. Follow-up and data collection continue.</p>	<p>Study of different risk-reduction interventions for HIV vaccine trials (Project UNITY)</p>	<p>Large-scale trial of a once-daily dose of tenofovir to prevent HIV infection in injecting drug users</p>			
		<p>Phase III trial of HSV-2 suppression in serodiscordant couples</p>			

	VACCINE		CERVICAL BARRIER METHOD
	PRE-EXPOSURE PROPHYLAXIS (PrEP)		PARTNER TREATMENT
	HERPES SIMPLEX VIRUS 2 (HSV-2) TREATMENT/SUPPRESSION		BEHAVIORAL
	MICROBICIDE		
	MALE CIRCUMCISION		TRIAL COMPLETED OR STOPPED

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.



was no more than a small chance that the high-dose gel would show protection compared to the placebo gel. The DSMB recommended that the low-dose and placebo arms of the trial should continue in order to evaluate safety and effectiveness of the 0.5% dose. To read the MDP public statement on this development visit <http://www.mrc.ac.uk/consumption/groups/public/documents/content/mrc004378.pdf>.

The Microbicides 2008 conference in late February brought additional updates on the development of antiretroviral-containing compounds, which make up the majority of “next-generation” microbicide candidates. Tenofovir gel, the first microbicide gel containing an ARV as its active ingredient, was shown to be safe for daily use according to data from a six-month phase II safety study.

There continues to be an upsurge in discussions about how to proceed with vaccine research, triggered by last September’s announcement of Merck’s vaccine-candidate failure. There are open questions about whether to proceed with a redesigned PAVE 100 (a proposed efficacy trial that tests a combination prime-boost vaccine approach) and broader questions about how best to proceed with AIDS vaccine research overall. To read more about AVAC’s perspective on these issues, go to <http://avac.org/pave.htm>.

Not to be Missed

March 25: NIAID Summit on Vaccine Research and Development, Bethesda, MD
<http://www3.niaid.nih.gov/news/events/summitHIVVaccine.htm>

March 27–April 1: Keystone Pathogenesis Symposia, Banff, Canada

April 6–9: HPTN and IMPAACT Annual Meetings, Arlington, VA

April 21–23: MTN Annual Meeting, Arlington, VA

May 15: Launch of AVAC Report 2008

May 18: HIV Vaccine Awareness Day

May 21–23: HVTN Full Group Meeting, Washington DC

June 10–11: UN General Assembly High Level Meeting on HIV/AIDS, New York City

Coming Up

Later this year we expect the launch of three new large-scale pre-exposure prophylaxis (PrEP) trials in southern and eastern Africa. The Partners Study will look at serodiscordant couples, comparing tenofovir (TDF) to TDF plus emtricitabine (TDF+FTC). This study is slated to start in the second quarter of 2008 and is sponsored by the Bill & Melinda Gates Foundation. The FEMPrEP trial, planned to start in the third quarter of ’08, will study TDF+FTC in sexually active women. Family Health International and local African sites are implementing this trial, which is funded by USAID. The VOICE Study, to be launched in the fourth quarter of the year, is a five-arm trial—and the first trial to compare an ARV-containing microbicide gel (TDF gel) against oral PrEP (both TDF and TDF+FTC). The VOICE Study will involve African sites in the NIH-funded Microbicide Trials Network (MTN). In addition to these studies, there are four ongoing trials looking at PrEP in heterosexuals, men who have sex with men, and injecting drug users. The expanding array of PrEP trials is needed to provide definitive answers about its safety and efficacy. For more information about these trials and about PrEP generally, visit www.prepwatch.org.

About AVAC



Founded in 1995, the non-profit AIDS Vaccine Advocacy Coalition (AVAC) seeks to create a favorable policy and social environment for accelerated ethical research and eventual global delivery of AIDS vaccines and other prevention options as part of a comprehensive response to the pandemic.

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