
AVAC's Take

In this issue we provide an update on ongoing civil society efforts to influence the targets, priorities and budgets set by the “Country Operating Plans” that guide US Government-funded PEPFAR activities on a yearly basis. Just twelve months ago, this might have seemed an odd focus for a group dedicated to biomedical HIV prevention research. But that was before the results of HPTN 052, the trial that showed that earlier treatment initiation slashed the risk of HIV-positive people transmitting HIV to their HIV-negative long-term partners, while also maintaining health for the HIV-positive individual. It was also before global leaders began to talk about ending the AIDS epidemic in the next generation using combination prevention—including voluntary medical male circumcision (VMMC), earlier treatment and other strategies (see below).

To start ending the AIDS epidemic, it's critical to deliver the strategies that work today, while demonstrating the effectiveness of emerging tools and continuing the discovery effort for tools farther out on the horizon. We'll always have a focus on and commitment to emerging options, but we're also committed to vibrant advocacy to deliver what works today. In this issue we've highlighted some exciting examples of what this looks like on the ground.

Ensuring PEPFAR targets show strategic vision

It's not too late. Since January advocates in a number of countries in sub-Saharan Africa have delivered this message to the US PEPFAR country teams as part of coordinated campaigns to ensure that 2012 PEPFAR activities are optimally geared towards beginning to end the AIDS epidemic. These coalitions, many of which include AVAC partners, are seeking the opportunity to influence the targets and strategy of the Country Operating Plans, or COPs, that help guide PEPFAR's in-country activities for the year ahead.

In December US President Barack Obama announced that PEPFAR would expand its funded treatment slots to ensure that 6 million individuals are on PEPFAR-supported antiretroviral treatment by 2013. To get to “6 by 13”, PEPFAR country teams (which include all of the US agencies working on HIV in those countries) need plans to ensure targets

that are ambitious and strategic. Under the new schedule, revised draft COPs were submitted to the Washington DC-based Office of the Global AIDS Coordinator in March and are currently in a revision process. In the US and developing world, advocates are demanding that PEPFAR funding is not cut and that the program seizes the opportunity to start ending the AIDS epidemic.

Advocates at the country level are asking for the chance to have input during this revision process. These coalitions are also pressuring national governments to set ambitious targets for the components of combination prevention: testing, treatment initiation, VMMC and prevention of vertical transmission, ideally via the WHO-defined “Option B-Plus” which provides pregnant and lactating HIV-positive women antiretroviral treatment for life.

The goal of the COPs-oriented campaign is to ensure that PEPFAR targets match country ambition and also show a clear, strategic vision for implementing combination prevention. As a Zimbabwean-coalition convened by AVAC's 2012 HIV Prevention Research Advocacy Fellows Chamunorwa Mashoko and Memory Makamba wrote to the in-country PEPFAR coordinators: “Simply continuing at the current pace of ART scale-up will mean more costs without halting new HIV infections. Treating more people earlier and faster, will save more lives and will cost less money.”

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At a Glance

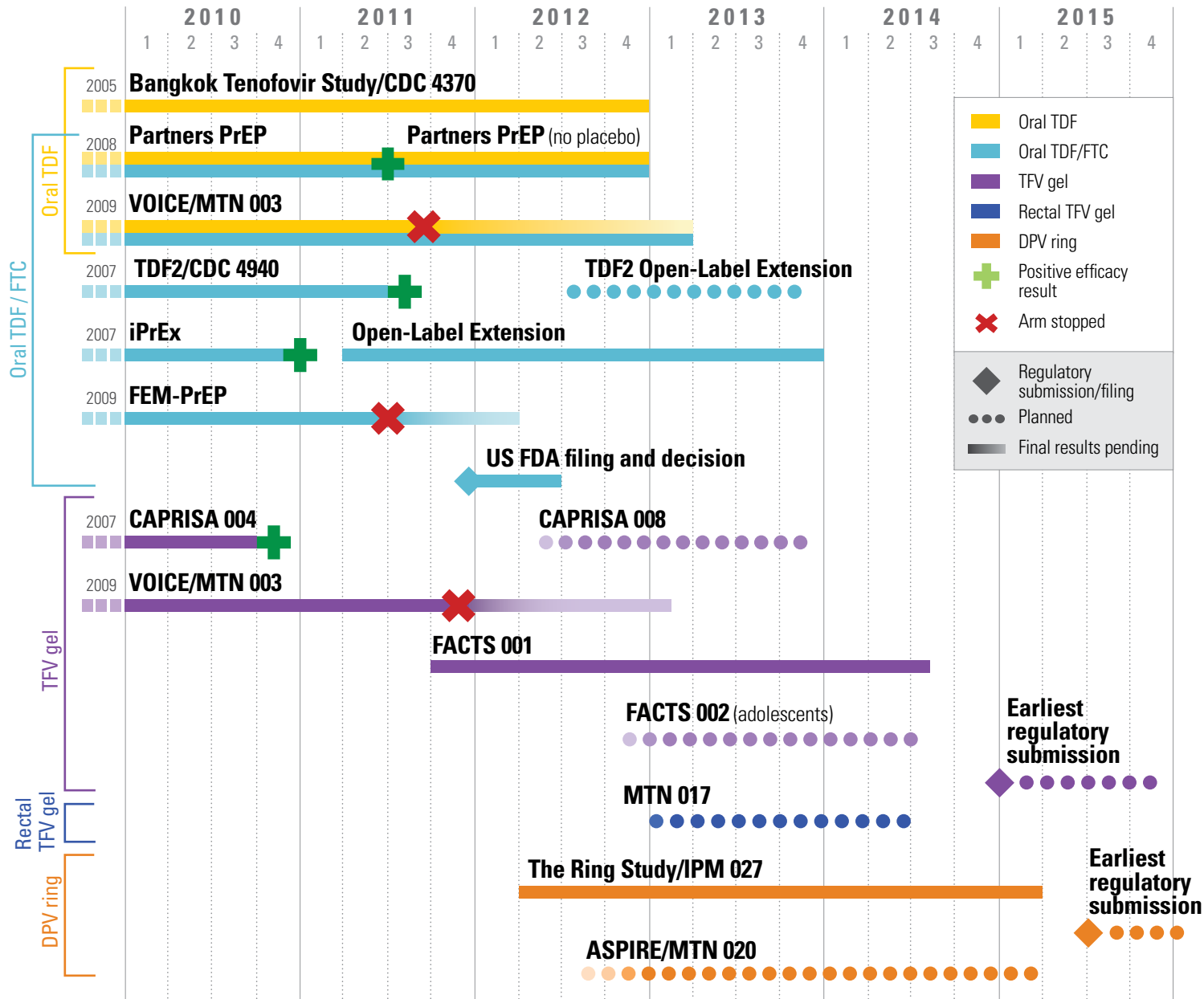
Tell the US FDA what you think about TDF/FTC (Truvada) as PrEP for HIV-negative adults

On May 10 the US Food and Drug Administration (FDA) will convene a public meeting of its Antiviral Drugs Advisory Committee at which officials will discuss and hear public comments on Gilead Science Inc.'s application for an indication for its drug TDF/FTC (Truvada) as pre-exposure prophylaxis (PrEP) for HIV prevention. The FDA will decide in June whether to approve the label change.

AVAC recently convened a webinar and drafted a primer with details on navigating the FDA review process. Both are available at www.avac.org/prep. For more information on the various ways in which you can submit comments, visit www.avac.org/prep/FDAcomments.

ARV-BASED HIV PREVENTION FOR HIV-NEGATIVE ADULTS: A RESEARCH TIMELINE

(April 2012)



Time-to-Approval Trajectory

This timeline shows efficacy trials, related confirmatory studies and dates of possible regulatory submission for a range of ARV-based prevention options. Products include oral PrEP with TDF, oral PrEP with TDF/FTC, vaginal and rectal formulations of tenofovir gel and the dapivirine-containing vaginal ring. See *At a Glance* for an update on the US FDA review of daily oral TDF/FTC as PrEP in HIV-negative adults.

Not included are next-generation candidates or strategies in earlier phase trials. Please note trial end-dates are estimates; due to the nature of clinical trials the actual dates may change. Visit www.avac.org and browse our "By Intervention" section for a range of resources including:

- A complete list of ongoing and planned PrEP and microbicide trials
- A round-up of recent data from PrEP studies
- The *AVAC Playbook* goals for microbicides, PrEP and treatment as prevention
- Basic and in-depth background materials

TRIAL RESULTS: A TIMELINE OF HIV PREVENTION EFFICACY AND FOLLOW-ON TRIALS*

(April 2012)

2011	2012	2013	2014+
<p>FEM-PrEP No evidence of benefit in women using daily oral TDF/FTC. Trial stopped early for futility.</p>	<p>CDC 4370 Phase II/III trial to evaluate the safety and efficacy of daily oral TDF for HIV prevention in injecting drug users (Thailand)</p>	<p>VOICE (MTN 003) Phase IIb trial to evaluate the safety and effectiveness of daily oral TDF/FTC to prevent HIV infection in women; <i>daily oral TDF and 1% tenofovir gel arms were dropped for futility after DSMB reviews in 2011.</i></p>	<p>FACTS 001 Phase III trial to evaluate the safety and effectiveness of 1% tenofovir gel before and after sex to prevent HIV and HSV-2 infection in women (South Africa)</p>
<p>HPTN 052 Early results released based on data from DSMB review showing that in HIV-serodiscordant couples ART initiation at CD4 cell count 350–550 reduced risk of transmitting HIV to the uninfected sexual partner by 96% (CI 73% to 99%; P<0.001).</p>		<p>PARTNERS PrEP Phase III trial to evaluate the safety and efficacy of two different strategies to prevent HIV transmission in HIV-serodiscordant couples: daily oral TDF and daily oral TDF/FTC provided to HIV-negative partners. <i>Since initial results released in July 2011, TDF and TDF/FTC arms will continue and those receiving placebo are being randomized to TDF or TDF/FTC.</i></p>	<p>HPTN 052 Phase III trial to evaluate the effectiveness of two treatment strategies to prevent HIV transmission in HIV-serodiscordant couples: immediate ART (CD4 350-550) and ART as indicated by guidelines. <i>Since initial results released in May 2011, those receiving ART continue and those in the delayed arm offered ART.</i></p>
<p>PARTNERS PrEP Early results released based on data from DSMB review showing that in HIV-serodiscordant couples daily oral TDF reduced risk of HIV in seronegative partners by an average of 67% (95% CI 44 to 81; P=0.0003); daily oral TDF/FTC reduced risk of HIV by an average of 75% (95% CI 55 to 87; P=0.0001).</p>		<p>HVTN 505 Phase IIb test-of-concept trial to evaluate the safety and efficacy of a DNA prime/Ad5-boost vaccine strategy to reduce risk of HIV infection and decrease viral load in participants who later become infected with HIV (US)</p>	<p>ANRS IPERGAY Pilot for a Phase III trial to evaluate the safety and efficacy of intermittent oral TDF/FTC, before and after sex, in MSM and transgender women (Canada, France)</p>
<p>TDF2 (CDC 4940) Daily oral TDF/FTC reduced risk of HIV by an average of 63% in heterosexual men and women (95% CI 21 to 83; P=0.013).</p>		<p>CAPRISA 008 Open-label implementation study to evaluate the effectiveness of 1% tenofovir gel in communities where CAPRISA 004 took place (South Africa) <i>Proposed start date Q2 2012</i></p>	<p>iPrEx OLE (Open-Label Extension) Safety and adherence follow-on trial to evaluate daily oral TDF/FTC in HIV-negative iPrEx trial participants (Brazil, Ecuador, Peru, South Africa, Thailand and the US)</p>
<p>VOICE (MTN 003) No evidence of benefit for women prescribed oral TDF or 1% tenofovir gel; both arms stopped early. Daily oral TDF/FTC arm continues and data are expected in 2013.</p>		<p>ALVAC-AIDSVAX (RV 144) Late-Boost Strategies Phase II trial to evaluate safety, immunogenicity and tolerability of late-boost regimens of AIDSVAX B/E alone, ALVAC-HIV alone, or ALVAC-HIV/AIDSVAX B/E combination in HIV-negative participants from the RV144 trial (Thailand) <i>Proposed start date 2012</i></p>	<p>TasP (ANRS 12249) Phase III trial to assess the acceptability, feasibility and efficacy of regular and widespread HIV testing with immediate ART initiation (South Africa)</p>
		<p>TDF2 Open-Label Extension (CDC 494) Follow-on trial of daily oral TDF/FTC in heterosexual men and women (Botswana) <i>Proposed start date Q3 2012</i></p>	<p>The Ring Study (IPM 027) Phase II trial (with planned continuation as Phase III) to evaluate the safety and efficacy of a long-acting dapivirine vaginal ring, replaced every four weeks (Malawi, Rwanda, South Africa, TBD)</p>
			<p>ASPIRE (MTN 020) Phase III trial to evaluate the safety and efficacy of a long-acting dapivirine vaginal ring, replaced every four weeks (Malawi, South Africa, Uganda, Zambia, Zimbabwe) <i>Proposed start date Q2–Q3 2012</i></p>
			<p>CHOICE (MTN 018) Phase IIIb open-label follow-on study to VOICE to collect additional data if daily oral TDF/FTC proves effective (South Africa, Uganda, Zimbabwe) <i>Proposed start date 2013</i></p>

VACCINE	TREATMENT AS PREVENTION
MICROBICIDE	VAGINAL RING
PRE-EXPOSURE PROPHYLAXIS (PrEP)	
TRIAL COMPLETED OR STOPPED	PROPOSED TRIAL
	INITIAL RESULTS

* The trial end-dates are estimates—due to the nature of clinical trials the actual dates may change. Trials listed here are subject to interim analyses. To view this timeline online with trial details please visit www.avac.org/timeline.

ONGOING TRIALS OF NEW PREVENTION OPTIONS WORLDWIDE

- Botswana
- Brazil
- Canada
- China
- Dominican Republic
- Ecuador
- France
- India
- Italy
- Kenya
- Malawi
- Mozambique
- Peru
- Puerto Rico
- Rwanda
- South Africa
- Sweden
- Switzerland
- Tanzania
- Thailand
- Uganda
- United Kingdom
- United States
- Zambia
- Zimbabwe

VACCINES	PrEP & MICROBICIDE
MICROBICIDES	TREATMENT AS PREVENTION
PRE-EXPOSURE PROPHYLAXIS (PrEP)	VAGINAL RING

Visit www.avac.org/globalmap for an interactive version of this map.



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In Uganda, one of the countries where PEPFAR presented a summary of targets to partners, advocates welcomed what appear to be ambitious targets and urged that these be integrated into a comprehensive country strategy for ending the epidemic.

The Ugandan coalition has noted that the draft COP currently proposes an accelerated treatment initiation with approximately twice as many people starting treatment in 2012-2013 as in 2011-2012. But there is concern that the same draft presents a halving of the testing targets compared with 2011-2012—leading to concerns that the treatment acceleration target might be based on double counting patients directly supported by other funding sources. The same coalition is closely tracking Global Fund and Government of Uganda commitments to ending AIDS.

PEPFAR does not have a formal process for civil society input into the COPs, however the US Global AIDS Coordinator, Ambassador Eric Goosby, has made a firm commitment to involving grassroots constituencies in PEPFAR programs and processes. Advocates are hopeful that, even with the tight deadlines and uncharted territory, there will be a chance for dialogue and meaningful input that affects the final version of 2012 COPs.

Even if some of the coalitions' goals are not met in time, advocates expect to continue working to open and maintain channels of communication with PEPFAR, which has been instrumental in scaling up prevention, treatment and care services at a global level.

“Even if we don't change the COPs before they are finalized, we're going to keep pushing. We know the country plans can be adjusted in real time, and we're going to keep working until the country targets are aligned with ending AIDS,” says Jacque Wambui, an AVAC Fellow working with Health GAP in Kenya and hosted by the National Empowerment Network of People Living with HIV in Kenya.

The focus on whether COPs are aligned with US President Obama's “6 by 13” pledge comes as US-based advocates are rallying against proposed cuts in PEPFAR funding included in the Obama Administration's FY2013 budget. The budget, released in February, proposes a 13 percent cut in the PEPFAR program. Advocates are fighting to restore funding in the version approved by Congress.

Recently Released

PrEP Using Daily Oral TDF/FTC or TDF in Women (and Men): What the science tells us in March 2012, AVAC's new one-page fact sheet summarizes the latest research on PrEP.

www.avac.org/prep/prepinwomen

New Voluntary Medical Male Circumcision Resources, In March, to mark the fifth anniversary of VMMC being recognized as an HIV prevention strategy, AVAC launched an expanded portal on VMMC rollout in priority countries worldwide.

www.avac.org/malecircumcision

Not to be Missed

April 15–18: International Microbicides Conference (M2012), *Sydney, Australia*

April 22–25: International Workshop on HIV Treatment as Prevention (TasP), *Vancouver, Canada*

May 30–June 1: HVTN Full Group Meeting, *Washington, DC*

June 11–12: Controlling the HIV Pandemic with Antiretrovirals, summit convened by IAPAC, *London*

June 22–27: HPTN Annual Meeting, *Washington, DC*

July 21: MSM Pre-Conference to the 2012 International AIDS Conference (registration at www.msmsgf.org/aids2012), *Washington, DC*

July 22–27: International AIDS Conference, *Washington, DC*

About AVAC



Founded in 1995, AVAC is a non-profit organization that uses education, policy analysis, advocacy and a network of global collaborations to accelerate the ethical development and global delivery of AIDS vaccines, voluntary medical male circumcision, PrEP, microbicides, and other emerging HIV prevention options as part of a comprehensive response to the pandemic.

To receive regular updates via email sign up for AVAC's various electronic lists at www.avac.org/maillinglists.

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