continued from page 1

Why GCAB Representatives are Essential!

participate instead. If the alternate is also not available, the site should select another CAB member or the site's CAB liaison staff person to join the call.

Core often asks GCAB representatives to seek input from their local CAB to be shared in later GCAB discussions or activities. This helps keep the GCAB informed of issues or activities that may be of interest to multiple sites. Without the full participation of GCAB representatives, it is very difficult for Core to know what is going on at the site CAB level. We rely on the GCAB representatives to support this flow of information.

4. Following each GCAB conference call, Core sends out call minutes via email. It is expected that the GCAB representative will share these minutes with the local CAB, regardless of whether he or she was able to participate on the call. If members of the local CAB do not have email access, the GCAB representative should request the site's CAB liaison staff person print out the minutes and share them at the next CAB meeting.

5. Regular email communication occurs among GCAB representatives as well as with the staff of the CEU. GCAB representatives are expected to participate in these communications and meet stated deadlines for requested actions. GCAB representatives are also expected to keep their local CAB up to date on GCAB discussions and activities.

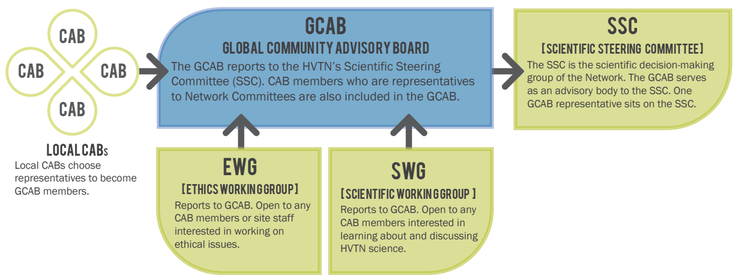
6. Non-English Language Calls and Emails: HVTN provides translation of some printed materials and email communications into Spanish and French whenever possible. The CEU strives to hold regularly scheduled Spanish-language conference calls for GCAB representatives who cannot otherwise participate in the Global CAB due to language barriers.

7. GCAB representatives should always feel comfortable to directly contact either CEU staff at Core or their site liaison if they have a question, whether it is scientific or logistical.

The HVTN could not do its work without the dedication and commitment of community members around the globe. CAB members at the local site level as well as those who serve on Network committees play a crucial role in ensuring that the concerns of their communities are being addressed by the Network. GCAB representatives are an essential link in the communication between their CAB, their site and the HVTN. We hope that the expectations outlined above can keep communication between CAB members and the Network both fruitful and robust.

The list of expectations above has been adapted from the HVTN Manual of Operations (MOP). The MOP also outlines additional aspects of CAB involvement and HVTN Core procedures in general. To view the complete document, please ask your CAB liaison staff person to help you access it through the HVTN website or the Atlas portal.

GCAB STRUCTURE



Helpful Terms for Understanding HIV Clinical Trials

*Indicates terms that are explained on page 6

Adverse Events means things that have gone wrong. For clinical trials, this term usually relates to safety issues or side effects and can go from minor to serious.

ART stands for antiretroviral therapy and includes several classes of drugs typically used to treat HIV. These drugs are now being studied for their effects in preventing HIV. This new use is called PrEP.

DSMB stands for Data Safety Monitoring Board. It is an independent group of professionals who review the safety data from studies that are phase 2 and higher.

Efficacy means effectiveness within the clinical trial setting, which is not the same as the real world. For HIV prevention trials, this means whether the product can prevent new HIV infections, or lower viral load in those who become infected.

Serodiscordant describes two people in a relationship when one person is HIV infected and the other person is not.

Send suggestions, questions, and article submissions for the CAB Bulletin to:

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Thank you to those who helped with this issue: *Jim Maynard, Gail Broder and Erik Schwab.*

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ABOUT CABS

Community Advisory Boards (CABs) are one way that the HVTN involves community members in the research process. CABs consist of volunteers from diverse backgrounds who work with local research units and advise the site from a community perspective. Community input is invaluable to community education efforts, as well as to the development of this bulletin.

MISSED AN ISSUE?

If you have missed an issue of the CAB Bulletin, all of our past issues are archived on the HVTN website community pages (no password required!). View past issues including featured clinical research sites, scientific updates, CAB experiences and much more. *www.hvtn.org/community/bulletin.html*

CAB CONFERENCE CALLS

If you are interested in joining one of these calls, email Genevieve Meyer (gmeyer@hvtn.org)

GLOBAL GCAB CALL*
Second Thursday of every month
Thurs., September 8
8 a.m. PT/11 a.m. ET
Thurs., October 13
8 a.m. PT/11 a.m. ET

GLOBAL ETHICS WORKING GROUP CALL
New time and date to be determined

CAB SCIENTIFIC WORKING GROUP CALL
First Friday of every month
Fri., October 7
8 a.m. PT/11 a.m. ET
Fri., November 4
8 a.m. PT/11 a.m. ET

FRENCH LANGUAGE CAB CALL
Second Wednesday of even months
Wed., October 12
9 a.m. PT/12 p.m. ET
Wed., December 14
9 a.m. PT/12 p.m. ET

SPANISH LANGUAGE CAB CALL
Third Thursday of odd months
Thurs., September 15
9 a.m. PT/12 p.m. ET
Thurs., November 17
9 a.m. PT/12 p.m. ET

AFRICAN REGIONAL CAB CALL
Third Thursday of even months
Thurs., October 20
9 a.m. PT/6 p.m. RSA
Thurs., December 15
9 a.m. PT/6 p.m. RSA

***Please note that the GCAB call is only open to GCAB representatives and alternates at each site. All other CAB calls are open to any and all CAB members.**

HVTN CAB Bulletin

HIV Vaccines and the Community

HIV VACCINE TRIALS NETWORK

From Local CABs to HVTN Core: Why GCAB Representatives Are Essential!

By Carrie Schonwald, International Project Manager, Community Engagement Unit.

The division of the U.S. government that funds the work of the HVTN is the National Institute of Allergy and Infectious Diseases (NIAID). NIAID requires its research sites to have a defined process for consulting with the community. Sites typically call these groups Community Advisory Boards (CABs). A site may call the group a different name, as long as it provides organized and regular input into the site's HVTN research.

The Global Community Advisory Board (GCAB) is a network-level body made up of one or two CAB members from each site. The GCAB reports directly to the Scientific Steering Committee (SSC). The SSC is the Network's scientific leadership decision-making body. One of the primary roles of GCAB representatives is to be the communication bridge between the local CAB, their site and HVTN Core. [See graphic on page 6]

Earlier this year, The Community Engagement Unit (CEU), formerly the Community Education Unit, of the HVTN noticed some weak links in the chain of communication between local CABs, the GCAB and Core. During a CAB breakout session at HVTN's June Full Group Meeting, CAB members and the CEU discussed this topic.

One of the key challenges appears to be that not all GCAB representatives are aware of the expectations that Core has of them. Because of this, the CEU created a list of expectations which was shared and approved on the July GCAB call. Since then, the CEU has more closely examined the HVTN Manual of Operations (MOP) to see what it says about CABs in general and communication more specifically. The list below is a combination of the CEU-created, GCAB-approved list of expectations and language from the MOP.

The HVTN Community Engagement Unit: (from left to right) Associate Director Jim Maynard, Project Managers Gail Broder, Carrie Schonwald and Genevieve Meyer.

HVTN Core's Expectations of GCAB Representatives

1. The Global Community Advisory Board (GCAB) is composed of 1-2 representatives from each local CAB. The Associate Director of the CEU can also select up to 3 at-large Global CAB representatives. The GCAB advises the Network and local CABs advise individual clinical research sites.

2. Each site can determine the process by which its Global CAB representative is selected, and the length of time this individual will serve. Sites are also encouraged to select an alternate representative. The GCAB holds elections every 2 years to select 2 new co-chairs. Ideally one co-chair is from the U.S., and the other from an HVTN site outside the U.S.

3. HVTN Core expects GCAB representatives to bring the concerns and ideas of their local CAB to the GCAB and to bring information from the GCAB back to their local CAB. In order to achieve this, Core expects GCAB representatives to be on all monthly GCAB calls whenever possible. If the GCAB representative is not available, then the alternate should

...continues on page 5

Getting PrEPared: Results and Remaining Questions from Recent Biomedical HIV Prevention Trials

In the past few years the idea of PrEP has taken the HIV biomedical prevention field by storm. With PrEP, which stands for Pre-Exposure Prophylaxis, drugs originally designed to treat HIV infections are used for prevention. Recently the results of multiple PrEP studies have made headlines around the world. In order to keep all of these studies straight, Gail Broder and the HVTN 505 Protocol Team have put together a table summarizing the results. In addition, they have included what these results may mean for HIV vaccine studies. ***This table is meant as a reference tool only.*** *Actual study documents should be referenced for updates. For more information on what PrEP effectiveness may mean for future HVTN studies, see "Planning for PrEP," in the December 2010 CAB Bulletin, hvtn.org/community/bulletins/HVTNCABBulletin_Dec2010.pdf.*

STUDY	STUDY DRUG/INTERVENTION	STUDY POPULATION & SIZE	PARTICIPANT HIV STATUS	LOCATION	STUDY RESULTS	SOME REMAINING QUESTIONS	IMPACT FOR PREVENTIVE VACCINE TRIALS
CDC 4323 *extended safety study*	Once daily Tenofovir (Viread) as PrEP (compared to placebo)	MSM N=400	HIV negative	San Francisco, Atlanta, Boston	Announced July 2010: no significant differences in HIV risk behaviors between study arms; no serious adverse events;* not designed to evaluate efficacy.*	→ Additional safety info needed regarding age, gender, HIV risk, and use in combination with other medicines → What is the safest dose?	→ We will be studying the impact of PrEP on immune system responses to vaccines. → There is no need to advise against PrEP use with Viread on the basis of any safety concerns.
iPrEx *Phase 3 efficacy study*	Once daily tenofovir+FTC (Truvada) as PrEP (compared to placebo)	Men and transgender women who have sex with men N=2499	HIV negative	Brazil, Ecuador, Peru, South Africa, Thailand, US	Announced November 2010: reduced the risk of HIV infection by an average of 43.8%. Participants also received intensive counseling about safer sex, HIV testing, condoms, treatment for STIs and other prevention services monthly; early analysis indicates that adherence is a factor which significantly impacts efficacy.* The Open-Label Extension (iPrEx OLE) began July 2011 and will look at ways to improve adherence now that partial efficacy has been established and will also further assess safety. Results expected in 2013.	→ Can PrEP with Truvada be equally effective when used independently of the other prevention services? → Can PrEP with Truvada be effective when used intermittently rather than daily? → Are there ways to improve adherence to the dosing regimen? → Is there similar efficacy in other populations? → Can this efficacy be replicated in this population, and is such replication necessary?	→ Contributed to the redesign of HVTN 505 v. 3.0, with less restrictive inclusion criteria for PrEP use, educating participants about PrEP, additional counseling messages, and additional exploratory objectives to look at PrEP/vaccine interactions. → The CDC issued preliminary guidelines for use of PrEP in some MSM groups. Consultations continue as analysis from several studies continues, and will provide further guidance for use and any contra-indications. This could change the standard of HIV prevention used in clinical trials.
FEM-PrEP *Phase 3 efficacy study*	Once daily tenofovir+FTC (Truvada) as PrEP (compared to placebo)	Women whose primary risk factor is vaginal sex N=1950	HIV negative	Kenya, Tanzania, South Africa	Announced April 2011: at a scheduled interim review by the DSMB,* it was determined that the trial would not be able to answer the question of whether the study drug decreased risk of HIV infection among HIV-negative women at risk via sexual transmission; study discontinued.	Analysis ongoing – reasons for the results are not yet known.	→ None at this time. → For now, it is unclear if the standard of prevention should change, or if any change should apply only to specific populations, since this trial had negative results, whereas iPrEx and TDF2 had favorable results.
HPTN 052 *Phase 3 efficacy study*	Does early initiation of ART* upon study entry (in the infected partner) reduce the risk of HIV transmission in serodiscordant couples,* as compared to those who do not begin ART until their CD4+ count is below 250 cells/mm3 or who have an AIDS-related illness?	Serodiscordant couples; Infected partner has not started ART and has a CD4 count of 350-550 cells/mm3 at enrollment N=1763 couples	HIV-infected individuals and their uninfected partners (97% were heterosexual)	Botswana, Brazil, India, Kenya, Malawi, South Africa, Thailand, Zimbabwe	Announced May 2011: at a scheduled review by the DSMB,* it was determined that early initiation of ART resulted in a 96% reduction in HIV transmission to the uninfected partner. The DSMB recommended stopping randomization and making treatment immediately available to those in the delayed-initiation study arm. Early initiation of ART also had medical benefit for the infected individual.	→ Is there similar efficacy in other populations? → How should such care be implemented? → In settings where access to ART is limited, how will the decision be made whether to use ARTs for treatment or for prevention?	→ If this use of treatment as prevention is implemented, it could change the size of trials in which participants are in relationships with a HIV+ partner taking ART, thereby changing the way preventive vaccine studies are designed and statistically evaluated.
Partners PrEP *Phase 3 efficacy study*	Comparison of once daily tenofovir (Viread) or tenofovir+FTC (Truvada) as PrEP (compared to placebo)	Serodiscordant couples,* where the HIV uninfected partners were randomly assigned to the 3 study groups N=4758 couples	HIV-infected individuals and their uninfected partners (heterosexual)	Kenya, Uganda	Announced July 2011: at a scheduled review by the DSMB,* it was determined that the tenofovir arm had an average of 62% fewer infections and the Truvada arm had 73% fewer infections than the placebo group. The study is ongoing, but the placebo group is now being offered PrEP. This reduction of risk was seen in men and women. Adherence was very high, with 97% of dispensed doses taken.	Unclear, analysis is just beginning.	→ Pending further study analysis.
TDF2 (also called CDC 4940) *extended safety study*	Once daily tenofovir +FTC (Truvada) as PrEP (compared to placebo)	Heterosexually active young adults. Primary risk factor is vaginal sex. N=1200	HIV negative	Botswana	Announced July 2011: Truvada is safe when taken daily, and though the study was not designed to show efficacy, the data did show a 63% reduction in the risk of acquiring HIV infection. A separate analysis was done to better understand the level of effectiveness among trial participants believed to be taking study medications. It excluded any HIV infections that occurred more than 30 days after a participant's last reported drug dose, because those individuals could not have been taking study pills at the time of infection. These results indicate that Truvada reduced the risk of HIV infection by 78%.	See iPrEx above.	The CDC plans to convene groups to draft guidelines for use of PrEP in heterosexual populations. This could change the standard of HIV prevention used in clinical trials.