The network “recompetition” - what is it and what does it mean for Community Advisory Boards?

By Genevieve Meyer, HVTN Community Engagement Unit

It is believed that every 7 years humans go through a complete physical change; others say life’s great events come in 7 year cycles. There are 7 days in a week, 7 years between sabbaticals, and in baseball, after the 7th inning, everyone gets up and stretches. For others 7 is simply a lucky number. Here at the HVTN, 7 is an important number because it represents the term limit for our funding agreement from NIAID, which sets the priorities for DAIDS. Every 7 years, NIAID reassesses and reconfigures its HIV clinical trials networks with the goal of increasing efficiency, effectiveness and outcomes.

Earlier this year NIAID released a Funding Opportunity Announcement (FOA) which describes what the new networks (or Leadership Groups [LG]) would look like, and includes a request for applications (RFA) from groups who would like to serve as the Leadership and Operations Centers (LOC) for those networks. In its application, HVTN will propose that the current HVTN Core remain the LOC of the DAIDS network dedicated to Vaccines to Prevent HIV Infection for the next 7 year funding cycle. Applications are due September 29, 2012. The applications will go through a scientific merit review starting in March 2013, followed by a review by the NIAID Advisory Council in October 2013. The earliest possible start date for the new LGs is December 2013. NIAID is committed to supporting the work of the current networks between the end of the current award cycle (May 2013) and the beginning of the next.

Following the announcement of the network reorganization, often called the “re-competition,” NIAID released a separate FOA for sites to apply to be part of these networks. These applications are due to NIAID by January 29, 2013 and awards should be announced in early 2014. The funding for sites begins approximately one year after the networks’ funding cycle begins.

On the road to vaccine licensure, a curvy but clear path emerges

By Genevieve Meyer, HVTN Community Engagement Unit

In late 2009, the results of the Thai Trial (RV144) were released, causing great excitement around the world. (See CAB Bulletin, Dec 2009). The trial showed that a vaccine regimen made from an ALVAC vaccine with an AIDSVAX clade B/E DNA vaccine was 31.2% effective in preventing HIV. This effectiveness, or efficacy as it is called in a clinical trial setting, was too low to license a vaccine, but it represented a much-needed step forward in HIV vaccine research. More recent analysis of the data showed that earlier in the trial, at 12 months post vaccination, the efficacy actually reached closer to 60%.

Due to these findings from RV144, the HVTN has joined a new partnership to help re-create and expand on the efficacy of that trial. The group — called the Pox-Protein Public-Private Partnership, but better known as P5 — is a collaboration of the HVTN, The Bill and Melinda Gates Foundation, NIAID, and the World Health Organization (WHO).
The Dallas CAB...we have a heart on

By Bradley Roschyk, Dallas CAB Vice Chair

The Dallas CAB was formed in August 2010 to support the HVTN 505 HIV Vaccine Trial and the research team at the University of Texas (UT) Southwestern Clinical Research Unit. Since our inception in 2010, the membership of the Dallas CAB has grown to 14 members.

Who makes up the Dallas CAB? Our CAB consists of all men; each volunteering and striving towards an end to HIV infection and transmission for a different reason. Some members are current trial participants, some are volunteers that were not eligible to participate in the study, some are here because the spread of HIV in our ethnic or socio-economic communities is rarely discussed and often ignored, and some members have been living with HIV for many years.

As a new CAB we have felt plenty of growing pains relating to our contribution to the site and CAB leadership. Our original CAB chair was reluctant to have others participate. He eventually resigned and our vice-chair Jason Mooney became chair. Early on we felt some push back on ideas we offered to the site staff. However, through good communication, we have worked through the issues that have arisen. Recently we realized we were missing a female perspective so we have been working diligently to recruit women to join the CAB. We have a pool of volunteers, including women who help at events, our challenge is getting them to join the CAB.

What have we accomplished? The Dallas CAB has participated in numerous educational and volunteer training sessions that are offered during our monthly meetings, and participated in training sessions geared towards helping the site staff recruit at 505 promotional events. Most recently, we had a great HIV 101 refresher by the site’s Community Educator Deneen Robinson. As a CAB and with the assistance of our on-site recruitment team we have participated in the Dallas Gay Pride Parade, Lifewalk Dallas, the South Dallas AIDS Walk, and numerous events in our community on a yearly basis.

Recently we worked with the site staff on marketing all around Dallas for our HIV Vaccine Awareness Event on May 18th. Our hope was to attract potential volunteers for HVTN 505, and individuals from the general public to serve on the CAB or as event volunteers. Since Facebook has brought many contacts into the study in Dallas a facebook event was set up to promote the date to our many Facebook friends. http://www.facebook.com/#!/events/371735422870147/. Apparently it worked because attendance was more than double what it was last year. In addition to our site staff and volunteers, representatives from the Dallas Health Department and Infectious Disease doctors from the University of Texas, Southwestern showed up to help with the event, which we felt was a great turnout!

We became volunteers because it’s time to stop the spread of HIV by finding a vaccine that works and because we want to educate our community on “Safer Sex” and HIV prevention. We continue to participate in the CAB and volunteer events because our staff at the clinical research site listens, participates and cares!
A fond farewell and thank you to Gloria Malindi

By Phineas Malahlela, Soweto CAB, and Carrie Schonwald, Community Engagement Unit

We would like to ask the global community of the HVTN CAB to join together for a moment to say good luck and thank you to the formidable Gloria Malindi, who is leaving the GCAB as well as her local CAB. Gloria joined the PHRU (Soweto) CAB in 2002 and served as co-chair from 2005-2008. At the Network level she has served as co-chair of the Ethics Working Group as well as co-chair of the Global CAB and is a current HVTN representative on Community Partners. Her work has always demonstrated a commitment to ensuring that all voices are heard and she has never turned down a request to be on a call, speak at a conference or co-chair a committee.

In addition to the many network CAB leadership positions she has held, she has also provided tireless leadership to her own community. Gloria has been a professional nurse for over twenty years, as well as both a counselor and trainer on HIV/AIDS education in addition to being involved in orphanage care with the Methodist church. She has resigned from research activity due to a very full schedule within the church, having just become an ordained priest.

We at the HVTN know that Gloria contributes her compassion, intelligence and humor to all that she does; those who come into contact with her on her new path will be lucky to do so. Thanks so much, Gloria, for your dedicated and passionate service all of these years!

Soweto CAB member Gloria Malindi retires this year after more than a decade serving on the local and global HIV vaccine CABs.

---

continued from page 1

The network “recompetition”

Currently DAIDS has 5 research priority areas which are carried out through 6 distinct HIV/AIDS Clinical Trials Networks. This current configuration resulted in multiple networks serving one particular research area. (See image on p.7) The new FOA proposes 6 new research areas, each corresponding to one distinct network. The new LGs are as follows:

- HIV/AIDS and HIV-associated Infections in Pediatric and Maternal Populations
- Integrated Strategies to Prevent HIV Infection
- Microbicides to Prevent HIV Infection
- Therapeutics for HIV/AIDS and HIV-associated Infections in Adults
- Vaccines to Prevent HIV Infection (this is what the HVTN is applying for!)
- Antibacterial Resistance (not related to HIV, but will draw from the expertise of the HIV/AIDS sites to further explore this crucial research area).

In addition to trying to increase efficiency across the networks, DAIDS also hopes to increase efficiency at a site level and is proposing changes to site organization within and across networks. Within this restructuring it will be essential that “[a] priority is placed on reaching populations severely impacted by the HIV/AIDS epidemic whose participation will help address priorities for NIAID HIV/AIDS research. These populations include, but are not limited to women, adolescents and minorities in the United States as well as populations in low and middle-income countries.”

This statement within the FOA will be a factor in how research units and sites are selected. In order to better understand the site process, there are 2 important terms to understand.

A Clinical Trials Unit (CTU) is an organizational structure that oversees the administrative, laboratory and regulatory elements of Clinical Research Sites (CRS). A CRS is the location where the studies are actually conducted. The CRS may be within the same organization as the CTU, or it may be in a different city, county, province or country. Currently there are 72 CTUs across the DAIDS networks, which oversee approximately 160 CRSs. The CTU is responsible for determining the method for CAB involvement, and may choose to facilitate CABs at the CRS level if the community needs differ from CTU to CRS, or among different CRSs.


…continues on page 7
Conference highlights

Editor’s note: While there were many informative presentations and engaging discussions during the HVTN Conference last month, the following section highlights only a few. Several of the conference plenary sessions, such as “Laying Out Our Path Forward” and the “HVTN South Africa Strategy Post RV144,” include topics that are touched on in The network “recompetition”… and On the path to vaccine licensure… (respectively), while plenaries such as “Behavioral Data in Vaccine Trials: Why is it important?” and “HVTN Digital and Social Media Marketing” provided insightful perspectives that can be more easily understood on their own. All plenary and Layperson presentations can be viewed here: [http://hvtn.org/meeting/may2012.html](http://hvtn.org/meeting/may2012.html) (no password required)

Transgender awareness and cultural responsiveness

By Gail Broder, Community Engagement Unit, HVTN Core

When the HVTN first included transgender women as a target population in HVTN 505, it began holding sessions at Network meetings and workshops to raise awareness about this population. Since that first panel discussion held at the May 2009 Full Group Meeting, we have continued to hear requests for more transgender training, both from CAB members and site staff members. The requests have been similar — “We need more transgender training” — but no one has been able to put their finger on specific topics to cover. So the HVTN decided to organize a workshop for the May HVTN Full Group Meeting to address some key aspects of understanding and working with transgender individuals.

A workshop planning committee was formed, co-chaired by Danna Flood, the HVTN’s Associate Director for Training, and Michele Peake Andrasik, the HVTN’s Social Scientist. The planning committee included several members from the HVTN Transgender Working Group and several site staff members. Together, they sketched out an agenda intended to cover the basic, foundational information that the group felt was important for attendees to understand. These topics included definitions of transgender-related terms, data and epidemiology about the transgender community, and the difference between gender identity and sexual orientation (separating “LGB” and “T”). Other areas that the group felt were important to address were raising awareness about how gender identity is formed, and the privileges of gender
What we can learn from monkeys

By Genevieve Meyer, Community Engagement Unit

The start of Thursday’s Layperson’s Lunch was an eye-opening presentation on *HIV/SIV Pathogenesis in the Penile Mucosa* by Dr. Wendy Yeh. Dr. Yeh, of Harvard Medical School, was one of 4 presenters in that afternoon’s plenary session on Non-Human Primate Models for HIV Vaccines. The focus of her research is on better understanding exactly how HIV enters the male reproductive tract. Until now there was not a good animal model to study this route of transmission. Dr. Yeh’s research addressed this need by developing a new technique using SIV (the monkey form of HIV) in rhesus monkeys, which have similar penile anatomy and tissue to humans. Specifically her research focused on a protein called TRIM5α in the penile mucosal tissue of the rhesus monkeys and analyzing how the strength of these genes affects whether the SIV gets blocked or causes infection. Results from this study and similar research will have direct implications for designing vaccines that block HIV infection in men, while other non-human primate studies contribute models for studying HIV prevention in humans overall.

Biosequences and their role in HIV vaccine development

By Genevieve Meyer, Community Engagement Unit

Wrapping up the Layperson’s Lunch on Thursday, Paul T. Edlefsen, PhD, Director of the new HVTN Computational Biology Core and its Biosequence Analysis unit, gave an excellent introduction to what biosequence analysis is and why it’s important for HIV vaccine research. His presentation was meant to provide a preview and explanation for his plenary talk the following day, which outlined the scope, structure and significance of this new department within the HVTN’s Statistical and Data Management Center (SDMC). He explained that biosequence analysis is essential to determining which part of the HIV virus needs to be used to create an effective vaccine.

Biosequences provide a language to understand and describe genes. Both humans and viruses like HIV are composed of biosequences. There are three types of biosequences: DNA, RNA and proteins. The first two are made of words (genes) using only 4 letters (nucleotides); the proteins are made of 20 letters (amino acids). Choosing the right biosequence is essential to vaccine design because it is the part of the vaccine that is introduced into your body for your immune system to recognize and (ideally) fight off the virus. One way that scientists look to identify the best biosequence is by studying the specific viruses that caused infections in HIV vaccine trial participants. Analyzing and tracking viral makeup from past vaccine studies such as the Step Study, Phambili and RV144 (The Thai Trial) is one particular area of focus that keeps this Unit busy. Other projects include collecting and analyzing HIV sequences from around the world (not just from HIV vaccine studies), trying to identify weaknesses in HIV, and collaborating with other bioinformatics experts in an effort to improve this technology and accelerate the development of a safe and effective HIV vaccine.
Transgender awareness and cultural responsiveness

that are enjoyed by the majority of people who are “cisgender” (those whose sex at birth and current gender identity match).

Attendees at the workshop noted that the interactive exercises designed to raise awareness of gender privilege were very effective, helping to illustrate the experiences of transgender people. One participant noted, “The gender privilege exercise was eye opening. I appreciate the opportunity to have more awareness within myself.” Other attendees noted that the mix of different presentation formats was particularly helpful, using interactive exercises, a film, didactic presentations of data, and sharing stories and personal experiences. Many participants commented on the terrific presenters (Michele Andrasik, HVTN Core; Ro Yoon, Seattle; Jess Pinder, San Francisco; Jim Carey, Chicago).

As one of the members of the planning committee, the experience of developing this workshop was very rewarding. I was particularly gratified to see such great attendance and full participation, and to see how receptive everyone was to ideas about transgender inclusion. We are all on a learning journey when it comes to issues of gender identity, and I am so grateful that community members and site staff can support each other as we continue to learn and grow.

More information on the HVTN’s efforts to provide awareness about transgender populations and their inclusion in HVTN trials can be found here:


Ro Yoon (CER, Seattle HVTU) presenting “Definitions” during the Transgender Awareness and Cultural Responsiveness Training.

Eduviges Cuello, CAB member from the Dominican Republic, was recognized with the Volunteer Service Award honoring her numerous contributions to her site and the Network.
In gratitude

Carrie Schonwald, Community Engagement Unit

The HVTN could not advance the search for an HIV vaccine without the collaboration of its numerous clinical trial sites around the world. These sites, located at university research centers, hospitals and clinics, are essential to the success of our studies. At HVTN Core we are grateful for the critical contributions of the staff, CAB members and trial participants at each HVTN site. It is with this gratitude that we would like to acknowledge the University of Puerto Rico, Maternal Infant Studies Center (CEMI) and the Unidad de Vacunas IDCP-COIN-DIGECITSS in the Dominican Republic for their many years of service to the network and to the field of HIV vaccine research. While these sites are no longer conducting HVTN studies, we know they will continue doing phenomenal work within their communities and in the global fight against HIV.

With deepest thanks and admiration for our Puerto Rican and Dominican colleagues, University of Puerto Rico, Maternal Infant Studies Center (CEMI) and at the Unidad de Vacunas IDCP-COIN-DIGECITSS (Dominican Republic)

HVTN Core

continued from page 3

The network “recompetition”

The FOA for the next funding cycle outlines DAIDS’ expectation to fund no fewer than 25 CTUs, each overseeing 1-8 separate CRSs. This represents a significant reduction of CTUs from the current grant cycle. This will also entail a greater level of collaboration within CTU leadership because each CTU will be required to be part of a minimum of 2 NIAID/DAIDS networks. CTUs will be able to oversee anywhere from 1-8 CRSs and have the option of bringing on protocol specific sites. A protocol specific site will work with a network on a particular study, but not become an official part of the CTU. This is similar to what the HVTN did when engaging the expansion sites to work on HVTN 505.

Outlined in the FOA is a continued obligation for community involvement. It states that “Each CTU must develop and implement a plan for forming and maintaining a productive partnership in the communities in which clinical research will be conducted. This partnership may be facilitated through a CAB.” A CAB is only one method of obtaining this community input; a CTU may also choose to conduct an alternate consultative process, as long as it is representative of the communities where studies are conducted. For example, a CTU located in Boston, with a CRS in that city, could not rely on its local CAB to provide community consultation for a study conducted at its CRS in Haiti, but rather would need a CAB in Haiti to provide that consultation.

So what should CABs be doing now? This is a perfect time to ask your PI about the plans for your site in the next grant cycle. Ask if there is advice that your PI needs, letters of support or other kinds of assistance that your CAB can provide during the application process. You could offer to provide suggestions about the structure for community involvement, or perhaps prepare a summary of your CAB’s activities and the support they have provided to the site during the current grant cycle. Each site will be unique, so it is important to ask your PI about what is needed.

Regardless of the structure, DAIDS is committed to ensuring that the voices of those who are affected or infected by HIV/AIDS are brought in as collaborative

...continues on page 8
On the road to vaccine licensure

Foundation, DAIDS, the US Military HIV Research Program (USMHRP), Sanofi and Novartis.

The focus of this group is to develop an HIV vaccine that could ultimately be licensed for public use. In order to license a vaccine, a product must show efficacy in clinical trials first. P5 is proposing several trials that use a similar vaccine regimen to the Thai Trial, with several important modifications. The Thai trial used an ALVAC pox-protein vaccine created by Sanofi, with an AIDSVAX clade B/E DNA vaccine, originally created by VaxGen. P5 collaborators hope to improve the efficacy by making a few modifications to the regimen. The first is to add an adjuvant to the ALVAC vaccine. An adjuvant is a product added to vaccines to help improve the body’s ability to react to the vaccine. In this case the adjuvant would be MF59, developed by Novartis. The other change is to use a clade C HIV insert (instead of B/E) so that the vaccine could be tested in South Africa, where clade C is the most common type of HIV. The HVTN would ideally conduct a phase 3 trial in South Africa, while the USMHRP would conduct another trial in Thailand using the clade B/E inserts. The goal of both trials would be to obtain a minimum of 50% efficacy, and ideally up to 70% efficacy, at 24 months post vaccination. Both studies would contribute essential results for the vaccine licensure path.

While the plans for conducting such trials are still early in the planning phases, the P5 represents an exciting new step in vaccine development and collaboration. We look forward to sharing the progress of this partnership in the months and years to come.

The network “recompetition”

members in the research process. It is because of the contributions of committed CAB members throughout the years that this requirement is in the grant application and that it holds a prominent place in the Site Structure and Function requirements. CAB members provide and will continue to provide critical insight to all aspects of HIV/AIDS clinical trials. We could not do this work without you!

For more information on the network application process, visit: http://www.niaid.nih.gov/labsandresources/restructuring/pages/default.aspx

For information on the application for Vaccines to Prevent HIV Infection, visit: http://grants.nih.gov/grants/guide/rfa-files/RFA-AI-12-012.html

For information on the CTU application process, visit: http://grants.nih.gov/grants/guide/rfa-files/RFA-AI-12-018.html