



HIV VACCINE  
TRIALS NETWORK

# The CAB Bulletin

## HIV Vaccines and the Community



*(Left to Right: Dr. Glenda Gray, Dr. Carolyn Williamson, Dr. Atom Dilraj, Dr. Nelson Mandela, CAB member Winnie Serobe, Dr. Tim Tucker, and Dr. Andrew Robinson)*

### **Mandela Supports HIV Vaccine Trials**

Nelson Mandela, eager to support South Africa's effort in finding an HIV vaccine, was briefed on the status of HIV vaccines in South Africa by Soweto CAB member Winnie Serobe as well as by HVTN and the South African AIDS Vaccine Initiative (SAAVI) Principal Investigators. The briefing was held a few days prior to the beginning of HVTN 040, the first HIV vaccine trial to ever be conducted in the country.

**Congratulations to the Durban and Soweto HVTUs for beginning their first ever HIV vaccine trial!**

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# HVTN to Provide Treatment to HIV-infected Trial Participants

Should volunteers in developing countries who become infected with HIV during the course of an HIV vaccine trial be provided with antiretroviral therapy (ART)? While the issue has been hotly debated, the HVTN announced this year that participants who become HIV infected will receive long-term ART. The decision was based on three arguments.

- (1) The provision of ART is now more feasible for a variety of reasons. Some reasons for this phenomenon include a substantial decrease in price, guidelines issued by the World Health Organization for provision of ART in resource-poor settings, and the development of the Global Fund to Fight AIDS, Tuberculosis, and Malaria. Furthermore, the National Institute of Allergy and Infectious Diseases (NIAID) and other sponsors of international HIV vaccine trials have increased clinical capabilities by building and equipping facilities and training clinicians and laboratory staff.
- (2) Ethics guidelines are more supportive of providing ART. The 2002 Council for International Organizations of Medical Sciences (CIOMS) guidelines state that while provision of treatment beyond that necessary for research is not required, it is reasonable. UNAIDS advises that sponsors should seek “at a minimum” to ensure access to the highest level of care and treatment attainable in the host country. Both sets of guidelines encourage the development of a consensus on a standard of care package, which may include ART, before the research begins.
- (3) Many of the current HIV vaccines being tested, or those in the pipeline, may not completely prevent HIV infection but rather may control the amount of virus in the body or delay the progression to AIDS in large-scale efficacy trials (Phase III). Therefore, ART will be used as a comparison of the effect of a vaccine on disease progression. The time at which one begins taking ART may become a trial endpoint. Extending ART to volunteers in Phase I and II trials ensures that participants are treated equally in all stages of research.

The mechanism that will provide ART for persons who may not need drugs until years later is still being

worked out. The HVTN trial site in Port-au-Prince, Haiti has demonstrated one way to accomplish this task. Before a trial starts, private donors are identified and money is put into a fund specifically to pay for treatment of those who become infected during the trial. The amount of money is based on the number of participants, anticipated infection rates, the current price of the medication, and the estimated length of time an HIV-infected person receiving treatment will be alive. The fund is overseen by investigators, a local institutional review board, and community leaders. Additionally, counseling has been enhanced to prevent volunteers from thinking that antiretroviral treatment is a cure for HIV or from increasing risky behavior. Similar strategies may be developed for other sites.

The HVTN recognizes that one organization cannot reverse global inequities in HIV care, but does believe that researchers from developed countries who work in resource-poor settings have an obligation to try to narrow this equity gap. ☞



*Community Educator, Mireille Peck (above), and Haiti HVTU Principal Investigator, Dr. Jean Pape, have helped to develop strategies for the provision of antiretrovirals to those who become infected during the trial.*

*This article is based on an article published in the September 20, 2003 (Volume 362) edition of The Lancet written by Drs. Daniel W. Fitzgerald, Jean William Pape, Judith N. Wasserheit, George W. Counts, and Lawrence Corey.*

# CAB Ethics Working Group Provides Community Ethics Training

By Robert Hood, PhD, Chair of Ethics Training Subcommittee

The Ethics Training Subcommittee, a group within the CAB Ethics Working Group, organized a workshop addressing basic issues in research ethics for the HVTN Full Group Meeting in October. The goal of the training was to provide information on ethical issues in HIV vaccine research to CAB members, Community Educators, and Recruiters. The training, facilitated by David Borasky of Family Health International (FHI), explored basic ethical values, the role of ethics review boards or Institutional Review Boards (IRBs), and the role a community can play in assuring protection of research participants. The workshop assisted attendees in developing a common framework and vocabulary to talk about ethics and introduced some ethical issues unique to HIV vaccine research.

There is agreement among bioethicists that, at a minimum, healthcare providers and researchers should uphold three values: respect for persons, beneficence, and justice. These three values were articulated in the influential Belmont Report.<sup>1</sup> The first of these, respect for persons, is understood both in terms of choice—individuals should have a say about how their lives should unfold—and in terms of the idea that individuals are intrinsically valuable. Researchers demonstrate and uphold the value of respect for persons by providing adequate information to research participants, by making sure they have an opportunity to ask questions, and by ensuring that they have fully understood the information to give their informed consent.

Beneficence means doing good, and requires that researchers balance possible benefits and risks of research. This includes not putting participants in situations without a potential benefit. The idea that healthcare providers have an obligation to do good and avoid causing harm is not a new concept; in fact, it is a core element of various professional ethical codes and can be found in international policies (e.g., UN-

AIDS guidance document).<sup>2</sup> Researchers demonstrate a commitment to beneficence by testing vaccines in animals prior to humans.



CAB members Margaret Wright (Trinidad) and Stephen Reynolds (Seattle) think about which corner of the room to go to during an exercise that required participants to choose the ethical standard they believed most important: respect for persons, beneficence, or justice.

Justice refers to fair treatment of research participants. This requires that research participants reflect the global diversity of the epidemic, and that participants from underserved populations are not singled out. Researchers show a commitment to justice by recruiting diverse populations, by including people from around the world both in the development and testing of HIV vaccines, and by seeking advice from community members.

The training helped attendees understand that there are many safeguards that ensure protection of research participants. The training reassured community members that researchers are well aware of the ethical issues and, in addition, IRBs review vaccine research to ensure that researchers are following certain ethical guidelines. Apart from this supervision, Community Advisory Boards are critical to the management of participant protection. **Knowledgeable CABs can help researchers understand the values, history, and concerns of the local community and help articulate and advocate for community issues.** For those interested in reading more on ethics, there are several handbooks and guidelines available (please see bibliography below).

<sup>1</sup>“Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research,” a report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, April 18, 1979. Online at <http://ohsr.od.nih.gov/mpa/belmont.php3>

<sup>2</sup>The UNAIDS report, “Ethical Considerations in HIV Preventive Vaccine Research” can be found at: [www.unaids.org/publications/documents/vaccines/index.html](http://www.unaids.org/publications/documents/vaccines/index.html). ☞

# Scientific Highlights from the Full Group Meeting

By Lisabeth Bull, HVTN Community Education Unit

A recurring theme on how to maximize our learning from vaccine trials was heard during the science talks of the HVTN Fall Full Group Meeting. Evaluating the implications of a trial is not straightforward work. Many decisions need to be made about which **assays** to do, how to conduct statistical analyses, what indicates certain levels of protection, etc.

Dr. Julie McElrath spoke about HVTN laboratory efforts to develop improved assays that more accurately measure cell-mediated, or **CTL**, responses. She also spoke about the work being done to determine which CTL responses serve as appropriate indicators of relevant immune response. Statistician Tony Rossini presented on the degree to which a Phase I trial may or may not predict immune response. He led attendees through multiple exercises to help them understand the process of statistical analysis. Other presenters discussed research on understanding the link between **memory cell** levels and disease progression, and the ability of *in vitro* studies to predict *in vivo* results.

As scientists design a vaccine, they use the structure of HIV to guide them. However, there are many variations of the HIV virus, so a researcher must decide which variation to use as a model. Some researchers use a single circulating strain, while others develop a hypothetical model applicable to all strains. There are two approaches used to develop this hypothetical model. The first option is a 'consensus sequence' of the virus. The goal of a consensus sequence is to create an image of an "average" HIV virus by looking at the variations of HIV and finding the most common characteristics of each part of the virus' structure. The second possible model is the common ancestor, in which analyses of data about HIV are used to produce a picture of what the ancestor of current HIV strains may have looked like. This model would theoretically then be common to all current strains.

Presentations on the second day covered four vaccine approaches being used outside of the HVTN. Dr. Peter Lilejstrom's group is working with the Semliki Forest virus, which has been used successfully in vaccines against measles, mumps, and rubella. This **replicon** vector is easy to manipulate and can reproduce in large quantities. Dr. Tomas Hanke discussed the International AIDS Vaccine Initiative (IAVI) trials that are testing a DNA prime and an MVA (modified vaccinia Ankara) boost. Their current focus is on understanding CD8+ cells and developing new assays. Dr. Julia Hurwitz's group developed a vaccine that recreates the entire envelope of HIV. This would allow the immune system to learn and recognize the virus in three dimensions. Lastly, Dr. Scott Thomson spoke about an approach called SAVINE, a concept in which researchers cut up the HIV virus and reassemble it in a scrambled order. By doing this, the body is introduced to all of the various parts of HIV, yet this reconstructed virus can no longer cause HIV.

The final day included a series of presentations about working with the injection drug user (IDU) community. The speakers covered a range of topics, from the importance of including IDUs in HIV vaccine trials to profiles of successful programs that reach out to IDUs. Dr. Punnee Pitisuttitham spoke about IDU involvement in the recent VaxGen Thai trial, from which preliminary results were recently announced. Dr. David Metzger indicated that, excluding Africa, where sexual contact is the primary mode of transmission, HIV is most commonly transmitted by injection drug use.

Dr. Rick Klausner concluded the conference by speaking about the Global Enterprise. This summer, 24 leading HIV vaccine researchers and policy experts, including Drs. Larry Corey and Judy Wasserheit, published an article calling for coordinated efforts to streamline HIV vaccine research. Work continues on building the infrastructure to support this effort, and a plan may be introduced as early as next summer. ☞

## Definitions

Assays – Laboratory tests

CTL – cytotoxic lymphocytes, otherwise known as killer T-cells. These are a key part of the immune system response.

Memory cells – CD4+ and helper T-cells are also known as 'memory cells.' They are the part of the immune system that 'remembers' an antigen, or invading force, from one encounter to the next. Vaccines depend on memory cells to function so lessons learned from the vaccine can be applied to the real virus or disease.

In vivo and in vitro – *In vitro* is Latin for 'in glass' and refers to laboratory research done in petri dishes and test tubes. *In vivo* is Latin for 'in life' and refers to just that: research done in a living being.

Replicons – viruses modified so that instead of replicating themselves, they produce genes that have been inserted into their structure.

# Community Highlights from the Full Group Meeting



*(Left to Right) CAB members Parrish Marcenaro (Lima, Peru), Tessie Caballero (Santo Domingo, Dominican Republic), and Jacqueline Montero (Santo Domingo, Dominican Republic) take part in the Saturday morning CAB meeting. During the meeting, Parrish was elected as the new Global CAB co-chair. He will replace Homero Gomes da Silva (Sao Paulo, Brazil), who has served as a co-chair for two years. The meeting consisted primarily of updates from CAB members who participate on other Network committees. Reviewing the 2003 GCAB goals and setting new goals for 2004 will take place on the November and December GCAB conference calls.*



*(Left to Right) Cathy Bunce, Clinic Coordinator at the Rochester HVTU, describes to Josh Barnes (Nashville HVTU), Scott Johnson and Toby Clark (Saint Louis CAB), and John Bonelli (New York CAB) how sites can use local events to advertise their own work. She mentioned that the Rochester site hosted a screening of an HIV/AIDS documentary at a local film festival. Cathy presented at a new Full Group Meeting workshop called the Site Procedure Sharing Session. The workshop consisted of 12 different presentations divided into two 45-minute sections, and provided an opportunity to learn from other sites about some of their successful systems and approaches.*



*(Left to Right) CAB members Malumbo Simwaka (Blantyre, Malawi) and Boyce Mgcina (Soweto, South Africa) participate in the Layperson's Lunch: Plenary Science Explained sessions. A two-hour block during lunch was set aside for scientific presenters to give their talks in a format more understandable for those without extensive scientific backgrounds. These sessions enabled attendees to better comprehend the science as well as provided them the opportunity to speak directly with some of the world's top scientists.*



*(Left to Right) CAB members Bill Snow (San Francisco) and Isaac Lesole (Jwaneng, Botswana) help brainstorm potential goals for the Ethics Working Group (EWG). The list developed will be discussed and reduced to a few main goals on the next EWG conference call. The session included a visit by Dr. Alan Fix, Division of AIDS, who updated the group on issues around providing care for research-related injury. The group was also informed about a survey regarding the use of the Participant's Bill of Rights and Responsibilities (PBORR).*

# HVTN Protocols in the Field

Protocol	Description	CAB Rep	Sites
HVTN 026 (Phase II)	A Phase II trial to evaluate the safety, immune response, and dose response of two HIV vaccines (ALVAC vCP1452 and MN rgp120).  <i>Status: Vaccinations have been completed.</i>	Monica Barbosa	Port-au-Prince, Haiti Rio de Janeiro, Brazil Lima, Peru Port of Spain, Trinidad
HVTN 039 (Phase I)	A Phase I trial to evaluate the safety, immune response, and dose response of two HIV vaccines (ALVAC vCP1452 and MN rgp120). This trial tests whether higher doses give stronger immune responses.  <i>Status: Vaccinations have been completed.</i>	Paul O'Malley	Baltimore Birmingham Boston Nashville New York Rhode Island Saint Louis San Francisco Seattle
HVTN 040 (Phase I)	A Phase I trial testing for safety and immune response using a replicon vector product generated from HIV subtype C (the clade most commonly found in sub-Saharan Africa).  <i>Status: Vaccinations have begun in the United States and South Africa.</i>	MC Mkhize Rose McCullough	Baltimore Durban, RSA Soweto, RSA Rochester Hopkins New York
HVTN 041 (Phase I)	A Phase I trial of a combination vaccine with <i>nef</i> , <i>tat</i> , and gp120 formulated with ASO2A from partner GlaxoSmithKline Biologicals.  <i>Status: Vaccinations have been completed and the dissemination of results is being planned.</i>	Rose McCullough	All U.S. Sites
HVTN 045 (Phase I)	A Phase I trial to evaluate the safety and immune response of the DNA plasmid pGA2/JS2 vaccine produced by Emory University.  <i>Status: Vaccinations have been completed.</i>	Michele Newball	Birmingham San Francisco Seattle
HVTN 048 (Phase I)	A Phase I trial to evaluate the safety and immune response of the Epimune HIV-1090 DNA vaccine at varying dose levels.  <i>Status: Vaccinations have begun in the United States and Botswana.</i>	Nthabi Phaladze Paul Williams	Gaborone, Botswana Boston Rhode Island Saint Louis
HVTN 050 (Phase I/II)	A Phase I trial study of the safety, tolerability, and immune response of an adenovirus HIV vaccine produced by Merck and Co.  <i>Status: U.S. sites and Lima, Peru have begun vaccinations and other sites should begin enrollment soon.</i>	Katherine Soars-Thompson Robert Reinhard	All U.S. Sites Blantyre, Malawi Chiang Mai, Thailand Durban, RSA Lima, Peru Port-au-Prince, Haiti Rio de Janeiro, Brazil Sao Paulo, Brazil Soweto, RSA
HVTN 203 (Phase II)	A Phase II trial to evaluate the immune response of a combination of the ALVAC vector vCP1452 and AIDSVAX B/B using new lab tests.  <i>Status: Vaccinations have been completed.</i>	Hamilton Richardson	All U.S. Sites
HVTN 403	A rollover, natural history study of participants enrolled in Phase I and Phase II vaccine trials who become HIV-infected during the trial.  <i>Status: Participants are currently being followed for safety data.</i>	Paul Williams John Bunting	All HVTN sites Former AVEG sites Subset of HIVNET sites
HVTN 903	This study is to planned determine the preparedness of new HVTN sites to recruit and retain people at-risk for HIV infection (Phase III populations) for potential future HIV vaccine research studies.  <i>Status: Iquitos, Peru began enrollment and other sites will begin soon.</i>	<b>VACANT (TWO CAB MEMBERS FROM THESE SITES NEEDED)</b>	Gaborone, Botswana Iquitos, Peru Jwaneng, Botswana Port-au-Prince, Haiti San Juan, Puerto Rico Santo Domingo, DR

There are currently a few positions that need community representation. Protocol HVTN 903 needs two CAB representatives from the countries conducting the trial. HVTN 204 needs a non-U.S. community representative. Non-U.S. CAB reps are also needed for all five Phase III Subcommittees: Adolescents, Behavior, Efficacy Trial Design, Intercurrent Infection, and Community Preparedness. There is also a list of those interested in serving as community representatives on future protocol teams. Those interested in participating or those who want more information about participation requirements, please contact Gail Broder at [gbroder@hvtn.org](mailto:gbroder@hvtn.org). Any CAB members active at the local level are encouraged to increase their involvement on Network committees. ☞

# Community Protocol Team Members Share Their Experiences

By Robert Reinhard, CAB Member

The scientists and staff who design protocols are legally required to monitor the health and welfare of trial participants. However, the CAB representative on a protocol team has the responsibility of speaking on behalf of the participant from the initial development of the protocol through the implementation and results dissemination process. The only effective way to learn about the issues facing trial participants is to maintain contact with local CAB members from each trial site. As the CAB rep on HVTN 050, I am in continuous dialogue with CABs from all over the world to ensure that I appropriately raise their concerns to the team.

Part of my responsibility on the protocol team is to be informed on the issues so that I can contribute to the conversation. Therefore, there is no topic that should not be reviewed from a community perspective. Concerns such as care for volunteers, inclusion/exclusion criteria, ethical issues, and trial design all must be considered for their acceptability to the communities where the trials will take place. Working on a protocol that is being tested on four continents, I have quickly learned that the issues facing participants vary according to language and culture.

While protocol team involvement is something I thoroughly enjoy, it does bring along some responsibilities. Those include: reading the protocol and informed consent, participating on regular team calls or meetings to revise/explain documents, reporting to the CAB Protocol Working Group and the Global CAB, monitoring trial safety and ethical concerns, as well as applying community lessons learned from other trials.

While scientists may see trials as data-producing machines, a community representative ensures that a human element is added to the scientific agenda. The only way that a vaccine will be accepted by the general public is if they feel that they were a part of the development process. ☘

*Robert Reinhard (San Francisco) has been a CAB member for three years. Previously the CAB rep for HVTN 903, Robert now serves as the CAB rep for HVTN 050 and the Phase III Efficacy Subcommittee.*



By Leonard Jackson, CAB Member

My excitement of being selected to my first protocol team, protocol HVTN 053, was soon elevated to panic and apprehension when I received the draft protocol prior to the protocol face-to-face meeting in Seattle, WA. The title included phrases like “Heat Killed Recombinant *Saccharomyces cerevisiae*,” I quickly began searching the Internet, trying to learn more about these complex words. I also had a chance to speak with HVTN staff, and they answered many of my questions. The information that I gained from my research and phone conversations was invaluable for my confidence and, ultimately, my ability to contribute.



*Lenny Jackson (Hopkins and Baltimore) has been a CAB member for over one year. Lenny serves on the Global CAB, Protocol Working Group, and the Ethics Working Group.*

Due to snowstorms at home, I did not arrive at the face-to-face meeting until shortly after it had begun. Still a bit concerned about what I would be doing, I entered the room and immediately was asked to join the Informed Consent team, the group that would focus their energy on developing an appropriate draft informed consent document. Listening to all of the educated suggestions, I wondered what I was doing in this group and if my voice would even matter.

When the group suddenly turned their attention to my issues, like that ray of light that breaks through the clouds (and mine was not all that bright either), it all seemed to come together and I was suddenly spewing out my newfound knowledge and heads around me where nodding in signs of approval. I had something to contribute. When I spoke they listened, and when I raised questions they answered.

Looking around the room, it was evident that I was a part of a small group of dedicated individuals who yearned to learn from one another’s experiences and assist in finding an HIV vaccine. As I left the meeting, an old African saying came to mind: “I felt good about myself and I felt good about the people around me, and if we are to succeed, then it is up to we.” ☘

## NIAID Awards \$81 Million for HIV Vaccine Development

The National Institute of Allergy and Infectious Diseases (NIAID) has committed about \$81 million over the next five years to four new contracts to support the development of novel HIV vaccines. The awards are part of NIAID's HIV Vaccine Design and Development Teams (HVDDT) program, a public-private partnership that seeks to accelerate HIV vaccine development.

Each team is pursuing a unique vaccine strategy, and these strategies include DNA vaccines, virus vector vaccines, subunit vaccines, and virus-like particle vaccines. None of the vaccines contain the genetic information to make a complete virus, and therefore they cannot cause HIV infection in study participants.

"A safe and effective HIV vaccine is critical to the control of HIV globally," says NIAID director Tony Fauci, M.D. "These new awards will speed the development of promising HIV vaccine candidates that are based on recent advances in HIV vaccine design and on the latest discoveries in HIV virology and immunology." ❧

## In Memory of Bonginkosi Sakhile

Bonginkosi Sakhile, CAB member from Durban, South Africa, passed away November 6. Bonginkosi was the community representative on protocol HVTN 204 and the Informed Consent Working Group. Bonginkosi is survived by his wife and children.

Below is a letter of condolence written by the Durban HVTU Principal Investigator, Dr. Andrew Robinson.

"This sad news of Bonginkosi's passing is quite painful to come to terms with, particularly with the knowledge that he would still be with us with antiretroviral therapy. Our Department of Health continues to drag its feet in providing this medication. When I first met him, it was clear that he was a vibrant, bright character, with a serious dedication to contribute toward finding solutions to control the HIV epidemic. He did this by actively and sagely contributing to the CAB's establishment and development.

"At the May Full Group Meeting in DC, he was steadfast in his determination to attend community meetings so that he could bring back any new knowledge to strengthen his CAB.

"Go well, Bonginkosi, and thank you so much." ❧



## Calendar of Events



**CAB PROTOCOL WORKING GROUP CONFERENCE CALL:**  
Friday, December 5, 2003, 11 a.m. E.T./ 8 a.m. P.T.

Friday, January 2, 2004, 11 a.m. E.T./ 8 a.m. P.T.

**GLOBAL CAB CONFERENCE CALL:**

Thursday, December 11, 2003, 11 a.m. E.T./ 8 a.m. P.T.

Thursday, January 18, 2004, 11 a.m. E.T./ 8 a.m. P.T.

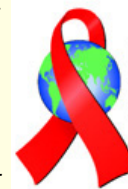
**COMMUNITY EDUCATION/RECRUITMENT COORDINATION CALL:**  
Tuesday, December 16, 2003, 12 p.m. E.T./ 9 a.m. P.T.

Tuesday, January 13, 2004, 12 p.m. E.T./ 9 a.m. P.T.

## World AIDS Day—December 1, 2003

"Live and let live" is the slogan of the two-year World AIDS Campaign 2002-2003, which focuses on eliminating stigma and discrimination.

Stigma and discrimination are the major obstacles to effective HIV/AIDS prevention and care. Fear of discrimination may prevent people from seeking treatment for AIDS or from acknowledging their HIV status publicly. For more information, please visit [www.unaids.org](http://www.unaids.org).



**Live and let live**  
World AIDS Campaign  
2002-2003

Although World AIDS Day is not an HVTN-sponsored event, the Network believes it is an excellent opportunity to talk to communities about the epidemic and the importance of voluntary testing. Eliminating stigma will be crucial as we continue to educate communities about the need for HIV vaccine trials. ❧

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

*Send suggestions, questions, and article submissions to:*  
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