

The CAB Bulletin

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HIV Vaccines and the Community

The Step Study Issue

This issue of the CAB Bulletin

The last months of 2007 brought with them a series of revelations about the Step Study that were first unexpected and then troubling. Researchers determined that the Adenovirus 5 study vaccine did not protect people from HIV infection or reduce the HIV viral load in those who got infected. Additionally, as researchers looked at the data they saw a trend toward increased susceptibility to HIV among those who received the study vaccine and who had higher levels of antibodies to Adenovirus 5 (Ad5). There is only enough data to indicate that this is a trend, however, which means that it is not certain whether there is a scientific reason truly leading to increased susceptibility or whether it is just chance. There is also no clear explanation for how the study vaccine might have created any increased susceptibility.

Given the complexity and importance of the data, we are devoting much of this issue of the CAB Bulletin to further information on the Step Study results and the impact it is having on related trials. The results from the Step Study mark a significant curve in the path towards an HIV vaccine, and we hope that the following articles outline for you the key issues that the Network is working to understand. ☘

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An overview of the Step Study results

The HVTN has been conducting two Phase 2B trials of a vaccine developed by Merck & Co., Inc. The Step Study, run jointly with Merck & Co., Inc. has been conducted in North and South America, the Caribbean, and Australia. Phambili is a trial in South Africa, conducted by the HVTN working closely with the South African AIDS Vaccine Initiative (SAAVI). At the first planned interim analysis of the Step Study, the Data Safety Monitoring Board (DSMB) found that there was no indication that the study vaccine could be shown to be effective. They recommended stopping vaccinations in the trial. Based on this recommendation, vaccinations were stopped in the Step Study, Phambili, and the third trial using the same study vaccine, HVTN 071, which is a small Phase I trial being run in the U.S. Although the results were disappointing, the trial did exactly what it was supposed to do: we learned that this product is not effective, and we learned this in less than three years.

The initial analysis looked at data from the 1500 participants who had low or no antibodies to Ad5. The data showed that there was no reason to continue the trial, as there was next to no chance that the product would be effective. Researchers call this “meeting the futility criteria.” This was true for both goals of the trial: the study vaccine in Step was neither lowering the likelihood that vaccine recipients would be protected against HIV infection nor reducing viral load in those who did become HIV infected. For all three trials, the Step Study, Phambili and HVTN 071, participants were told of the new information and asked to come in for special discussions of the situation and to come into the study site for their planned study visits.

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CAB involvement in Step Study discussions

The data from the Step Study moved the HVTN into unexpected territory and, with the resulting uncertainty, the Network turned to its community members as a crucial part of the discussion and decision-making process. Efforts were made to ensure that CAB members heard the news as it was announced and had their questions answered so that they would feel able to give their feedback in return. The HVTN and Merck also actively sought community input through CAB representatives on the protocol teams, GCAB-based advisory conference calls, and input at the HVTN Conference. There was also work done at the site level to include CABs in decision making.

The majority of the data that is currently known about the Step Study was presented at the fall HVTN Conference. All sites had community representation at the conference. On the day that the Step data was announced, several community members were asked to sit on a panel that was convened to discuss next steps. This included the CAB representative on the protocol team, DeWayne Mullis, from Atlanta, and Mitchell Warren, Director of the AIDS Vaccines Advocacy Coalition (AVAC). Given the complex nature of the data, there were sessions set aside in which community members could ask questions of key protocol researchers and plenary presenters directly. Com-

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An overview of the Step Study results

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While researchers continued to look at additional data from the Step Study, the decision was made to unblind participants in Phambili, letting them know whether they had received study vaccine or placebo. The Phambili trial had only recently begun, and had enrolled 801 people out of an expected 3000. Only 58 people had received all three planned vaccinations. The decision to unblind the trial was influenced by the fact that it was extremely unlikely that any reliable scientific findings could come from the trial, given its early stage. All Phambili participants will continue to be followed with an altered visit schedule. More about Phambili can be found on page 5.

At the same time the announcement was made about unblinding Phambili participants, researchers announced that ongoing data analysis indicated a possibility that the study vaccine increased the risk that some vaccine recipients could get infected with HIV if they are exposed to the virus. At this point, researchers still did not have enough information to make any claims beyond this statement. Participants were notified of the new development and reminded that, while they could choose to leave the study, their willingness to continue to be followed might help advance HIV vaccine research.

PHASE IIB TRIALS ARE A NEW CONCEPT; BY USING AN INTERMEDIATE TRIAL SIZE AND LENGTH, IT ALLOWS THE HVTN TO IDENTIFY PRODUCTS THAT WORK VERY WELL OR NOT AT ALL EARLIER THAN TRADITIONAL TRIAL STRUCTURES.

At the HVTN Conference on November 7th, researchers from the HVTN and Merck & Co, Inc. announced results from data as of October 17th. This analysis included a larger amount of data from participants with both high and low titers of adenovirus antibodies. As researchers had examined the unblinded data for a greater number of participants, they found that, although 1,150 women were in the trial, only one had become infected and she had received placebo. Additionally, there have been very few in-

fections among heterosexual men, so the implications of this data are unknown for heterosexual men.

When statisticians looked at the trial data as of October 17th, they saw a disturbing trend.

Among male participants who had antibodies against Ad5, more participants who received vaccine had become HIV infected during the trial than participants who received placebo. As statisticians broke down the groups into those who had different amounts of Ad5 antibodies, they noticed that among the groups with higher levels of Ad5 antibodies, it appeared that the likelihood of becoming infected with HIV increased. The numbers of infections in the data are so small that they are not statistically significant, which means that the differences in the number of infections between the two groups could still be due to chance. It is also possible that there is an explanation for the differences that has to do with the population, regional differences, risk levels, or some unknown biological cause. Researchers are considering these other causes, but they are carefully looking to see if there might be a possibility that the study vaccine itself increased the likelihood of a vaccine recipient becoming HIV infected once he was exposed to the virus through sex.

The HVTN and Merck were faced with a question: would it be better to let participants decide whether to remain blinded through their follow up or to make the decision for all participants? Maintaining the blind for as many participants as were willing would have increased the chance that researchers could obtain sufficient data to more thoroughly understand this disturbing trend. Unblinding all participants, however, might enhance the safety of all participants potentially facing an increased risk of HIV.

Partial analysis of Step Study data in men by Ad5 titer

Ad5 titers	Ad5 less than 18	Ad5 between 18 & 200	Ad5 between 200 & 1000	Ad5 above 1000	Total
Trial group					
Vaccine	20	8	14	7	49
Placebo	20	4	7	2	33
Both	40	12	21	9	82

As researchers looked through trial data as of October 17th, they found that the likelihood of becoming HIV infected seemed to increase among groups with higher levels of antibodies to Adenovirus 5. The numbers are too small to be statistically significant. It is still possible that this unexpected finding is due to chance, but the trend is disturbing, and researchers are continuing to try to learn as much as they can from the data they have.

Researchers, clinicians, and community representatives held a series of discussions following the data presentations. Representatives then attended the Scientific Steering Committee meeting at which a vote was taken on attendees' recommendations regarding whether or not to unblind all participants in the Step Study. The prevailing opinion was that this was a very complicated question, and in absence of a clear answer, it was better to err on the side of participant safety and unblind the trial. This recommendation was accepted by the scientists leading the study.

The Step Study raised a number of questions, most of which continue to lack answers. Several factors contribute to this uncertainty: The small number of participants who became HIV infected in the course of the trial as well as the near absence of data concerning women or heterosexual men; the lack of any previous indication that increased susceptibility might be an issue; and the absence of any clear mechanism that might explain all the complicated factors that are seen in the data. Analysis of the data will be ongoing, and current efforts involve identifying sub-studies that are likely to produce the most information. It is possible that we will never fully understand the trend that was indicated in the Step Study. However, it is important for us to learn all that we can to help move the field forward as safely and efficiently as possible. ❧

What this means for Step Study and Phambili participants

The Step Study, Phambili and HVTN 071 are continuing to follow participants. Each participant has been informed of the developments, and is able to withdraw from the trial if they are most comfortable doing so. Significant information can still be gained from these trials, however, and most participants have been willing to continue to be followed.

Most participants in both the Step Study and Phambili have been unblinded (HVTN 071 was planned as an unblinded study). As soon as researchers began to identify a possible difference in HIV incidence among those who received vaccine versus those who received placebo, they began to consider the process of unblinding trial participants. Double-blinded trials like those conducted by the HVTN are trials in which neither trial participants nor their doctor nor the clinical staff knows who receives product and who receives placebo or control. This is done to remove any bias that either the staff or the participant might have.

The discussion about whether or not to unblind raised many complicated issues. The DSMB of the Phambili trial recommended in mid-October that the participants be unblinded. The decision was somewhat more complicated with the Step Study, in which it was possible that researchers could learn more about what happened in the trial if the study remained blinded. Due to the complexity of the many issues, Dr. Larry Corey, PI of the HVTN, together with the protocol team leaders decided that it was best to make the decision at the HVTN Conference, when a large number of those involved in and partners with the Network could gather in person and discuss the issue. It was particularly important to them that this would be a time in which a lot of community members would be gathered together and would be able to provide their thoughts and opinions.

Those who wanted to unblind the trial felt that the safety of the partici-

pants would best be guarded by giving them the full information about the situation. Those who were considering keeping the trial blinded felt that the scientific questions that could be answered by continuing to follow blinded participants would be extremely important. By keeping the blind, the data from the trial would have fewer confounders—in other words, it would be more likely to be meaningful and unbiased. Another argument for keeping the trial blinded was to give the participants the respect of maximizing the knowledge gained from their participation as well as to give the participant the right to make their own decision. Once the participant was given the full information, he or she could decide for themselves whether to stay blinded. There was quite a bit of discussion about whether enough participants would choose to stay blinded to allow for significant data to be gathered. Peter Gilbert of SCHARP presented information about how reliable the data would be based on differing numbers of participants remaining blinded.

In the end, it was felt that the chance of getting meaningful data was not high. Given the uncertainty, there was a strong desire to err on the side of participant safety. While the decision included more complicated issues, in the end the majority of those gathered felt that participant safety was better supported by unblinding. The scientific leadership of the protocol accepted this recommendation at their meeting four days later, and announced that the trial would be unblinded.

Protocol team members, as well as key advisors from NIAID, Merck and the HVTN, are continuing to discuss the changes that will be made to the Step Study and Phambili to adjust to the new data. As soon as these decisions are made, participants will be informed and re-consented. Further visits will involve blood draws and physical

histories, as well as questions about social harms and ongoing risk reduction counseling.

Risk reduction counseling is a key component of all HVTN studies, and it has been conducted with Step and Phambili participants throughout both studies. Knowing that the study vaccine might have increased the likelihood that HIV exposure could lead to infection, the HVTN and Merck are working to make sure that all participants not only receive full unblinding information but also continue to receive the best available risk reduction counseling.

While participants are disappointed, their interest in helping to further the science has not changed, and we applaud them for their dedication! ❁



Sites used their CABs and their creativity to find the best ways to spread the information and answer community questions. In Lima, Peru, site staff held a drag show (pictured above) filled with informational updates. They also held “Casas Afueras,” or “outside houses”—the opposite, in a sense, of an open house. Staff went out into the community to various locations at announced times and did short presentations. Sites also worked creatively to contact participants. In the commercial sex worker population in Chicago, the participant CAB recommended that outreach information not be revealing. The site sent letters to participants letting them know that there was news to share and that open houses would take place at Project WISH at various times.

Looking to the future

Ongoing Analysis

While there is a possibility that we might not ever fully understand the Step Study results, researchers are continuing to try to untangle the answers to our questions. Studies of immune activation, behavioral variation, demographic differences, and viral and genomic analyses are all being initiated or are underway. It will take time for additional results to be available, and the HVTN will share this information as it becomes understood. Participants in HVTN trials are asked to have their blood stored for future research; the Step Study is a perfect example of why this is asked. Only a finite amount of blood is stored, however. While resources are being dedicated to further work, they are also finite. This has led to the formation of a group, chaired by Bruce Walker at Harvard University, that will work to prioritize additional research that is done to clarify the Step Study results.

I HAVE NOT FAILED. I'VE JUST FOUND 10,000 WAYS THAT WON'T WORK.

—THOMAS A. EDISON

Uncertainty

To some degree, we know which questions will likely go unanswered. For instance, since there was only one infection found so far in the women who were enrolled in the trial, it is unlikely that we will ever have enough data to understand how women responded to the vaccine. Since Phambili had only just started, we also will not have information on how the study vaccine may have impacted heterosexual transmission. Most importantly, researchers are telling us that we may never have enough clear information to indicate why vaccinated men with higher levels of Ad5 seem to be more susceptible to HIV.

The big picture--finding a vaccine

There was hope that, somehow, results from the Step Study would show us the way forward as we move toward an effective HIV vaccine. Despite the fact that the results were disappointing, the results are

helping researchers learn a great deal. We learned what didn't work, and researchers are now investigating why this approach did not work. The answers will create important criteria to guide future trials. The results are also leading to a new understanding of animal models. By its nature, there are many disappointments in research, but these are ripe with information. To be a success as a scientist, you must continue to pick yourself up and dust off the frustration, turning back to the challenges that you face. We can expect other products to fail, and we can expect that it will still be some time until we find an effective HIV vaccine. This slow process makes the time and commitment that our trial participants make all the more admirable, appreciated, and valuable. We must continue to give them our thanks and support for their willingness to be a part of something so uncertain, and to honor them for their hope.

Other approaches, other trials

The HIV vaccine field as a whole is sitting back and trying to absorb this new information. Discussions are taking place about what the Step results mean for trial designs and for adenovirus vaccines. The Pave trial, which is a prime-boost trial of DNA and adenovirus vaccines made by the NIH Vaccine Research Center, was planned to start just a few days after vaccinations were stopped in the Step Study. Pave has been put on hold as the protocol team reconsiders the planned protocol; while the adenovirus study vaccine in Pave is different than the one in Step, researchers want to move forward as cautiously as possible. There will be opportunities for community members to give input to the leaders of the Pave protocol team in the coming weeks.

The HVTN has several HIV vaccine approaches that do not involve adenovirus, including one that is planned to move into a Phase II trial. The field will continue to look at new approaches and to move forward with basic science research that will help give vaccine developers more information on which to base new concepts. ❁

CAB involvement

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community members at the Conference then had time to work together and discuss their thoughts. Led in discussion by CAB members Dave Crawford (Chicago) and Tom Gibson (CAB member-at-large), the CAB members discussed their recommendations, outlining their thoughts on flip chart paper. Six CAB members from Step sites represented the community at the Scientific Steering Committee (SSC) dinner, where they shared the community recommendations and read the points detailed on the flip chart sheets. The community representatives were Nancy Anderson (Jamaica), Juan Hernandez (Puerto Rico), Mauro Nunes (Rio de Janeiro), Dwayne Mullis (Atlanta), Ian Maki (Seattle), and Butch McKay (Birmingham, EWG co-chair). Tom Gibson, the SSC representative, was there as well. These CAB members then participated in the subsequent discussion and voting. ❁



Mike Robertson, Merck and Co., Inc. and Susan Buchbinder, HVTN Investigator at the San Francisco Department of Public Health, are Co-Chairs of the Step Study. Over the last few months, they have been on several calls helping to explain new data to the community. Dan Fitzgerald, HVTN Investigator from Haiti, is the third Co-Chair.

Key Messages about the Step Study results

- There is an urgent need worldwide for a vaccine to fight AIDS.
- The Step Study vaccine product did not cause infection, and there is no HIV in the vaccine.
- We care about our participants—their safety and needs. The volunteers are the real heroes. We can't move forward without their commitment.
- The study vaccine in the Step Study did not prevent infection. The study vaccine also did not lower viral load.
- The study vaccine in the Step Study may have made it easier for participants to get HIV infected. We don't know for sure if this is true, or, if it is true, why it might have happened. As soon as we have more information, we will share it with you.
- The Step Study staff is telling all participants whether they received vaccine or placebo and their Ad5 antibody level. The Step Study sites are also continuing to give all participants HIV risk reduction counseling.
- We got the answer to whether the study vaccine worked or not in 33 months—much faster than in the past.
- The Step Study was conducted according to the highest ethical standards, and with participant safety as a priority.

More details about the Phambili trial

The Merck Ad5 study vaccine that was being used in the Step Study was also being used in two other trials. One of these was the Phambili trial, which is being conducted in South Africa. Phambili means “moving forward” in Swahili, and it was the next step in the process of learning about the Merck Ad5 product. Researchers at the HVTN worked closely with the South African AIDS Vaccine Initiative (SAAVI) to undertake Phambili, hoping to learn more about how the study vaccine might work in an area of the world very much in need of a vaccine.

There are several reasons to hold trials in diverse locations. Phambili was planned to learn more about how the vaccine might work in a population with high rates of heterosexual transmission. The study vaccine was based on a subtype of HIV, clade B, that is different from the most common subtype in South Africa, clade C. Researchers still don't know if clade variation will affect how a vaccine works. Finally, researchers want to make sure that any vaccine found to be effective will work in all populations where it is needed, as it is possible that genetic variation or other regional differences may effect the vaccine.

When vaccinations were stopped, the five clinics conducting Phambili had enrolled 801 participants. As vaccinations were ongoing—only 58 participants had received all three vaccinations—Phambili researchers wanted to spread the word quickly. In Soweto, for instance, the clinic held an emergency CAB meeting to get advice on contacting participants and quickly drafted a plan of action. Instant text messages (SMSs) were sent to participants with cell phones alerting them to important news regarding Phambili and announcing a meeting on the fol-

lowing Tuesday. The message also included the cell phone numbers of the PI, a co-PI and the clinic coordinator for any participants who had questions over the three-day weekend. In South Africa, it is possible to send someone's cell phone a message saying “please call me” for free; participants would message researchers, who would then call them back, so that participants had no cost for the call. Approximately 60 participants took advantage of the chance to speak to a staff member prior to the meeting.

Other sites used local radio announcements as well as phone calls. All sites followed up those who could not be reached by cell with calls to land lines and home visits. Sites worked to communicate with CAB members and set up group sessions to inform their participants about the news.

The same systems were put in place a few weeks later when the decision was made to unblind all Phambili participants. Polishing the processes they had drawn on when first notifying participants, the sites were able to reach out to participants and bring them in for unblinding in an incredibly quick, streamlined fashion. Their experience was helpful a few weeks later when Step Study sites began to unblind their own participants.

In general, the reaction among Phambili participants has been quite supportive. Participants understood that this is a scientific process that will have setbacks, and that the only way to move forward is to look ahead to the next step. As in the Step Study, there were many participants who were interested in being unblinded in order to join the next trial, but once they learned how much benefit could come from remaining in Phambili, most have been willing to continue to be followed. ☘

HVTN 071

HVTN 071 was the third, smallest trial using the Merck Ad5 study vaccine. A phase I trial, 071 was planned to investigate in more detail immune responses to the Merck Ad5 product. When the Step Study vaccinations were stopped, researchers stopped vaccinations in HVTN 071 as well, but follow up has been adjusted to help learn as much as possible from willing participants.

HVTN 071 was planned to collect information about correlates of protection, and to determine which lab assays (tests) provide the most useful data to help prioritize assays in future trials. When vaccinations were stopped, only 55 participants had been vaccinated, and it was clear that it would not be possible to fulfill the original goals of the study. However, HVTN 071 was planned to include leukapheresis, a complicated process in which a significant number of peripheral blood mononuclear cells, or PBMCs, can be collected--many more than through a typical blood draw. In addition to being a long, complicated process, only a few sites have the capacity to do leukapheresis.

When HVTN 071 began, only participants at the Seattle site were asked to consider giving their consent for leukapheresis. Given the Step Study results, however, researchers are now very interested in doing significant analysis of PBMCs, and the trial is being amended. Sites are asking participants in HVTN 071 if they are willing to consent to leukapheresis in order to help researchers try to understand more about the Step results. Participants who decide to give full informed consent to the process are being flown to Seattle or Rochester, as these are the only sites currently prepared to do leukapheresis. Researchers will use this information to help understand more about the Step Study data. ❀

The process of unblinding

Listed below are some brief updates on how unblinding is proceeding at some of the Step Study sites, from Rio to Rochester, current as of the end of November:

Rio de Janeiro: Participants have been coming in regularly and unblinding is proceeding smoothly. So far, all participants have agreed to stay in the study.

Rochester: The majority of volunteers have been contacted, which has gone mostly well.

Philadelphia: They've unblinded 90/126. They have been trying to unblind at a rate of 12 per day. Their CAB has been helpful in the process. They have submitted a request to the IRB to do unblinding visits for their 8 incarcerated women. This will be reviewed by the full IRB in mid-December, and the process will include a prison representative. They expect that the last 25 participants on their list will be the most difficult to locate and bring in for discussions.

Alabama: All participants have been contacted, and all have opted to continue in the trial. Their main concern has been about details of follow up.

New York (NYU Merck): As of late November, 103 volunteers had been unblinded, and it was expected that the remaining 55 participants would be unblinded within 1-2 weeks. Most participants have received the news calmly, but a few have been upset by the information. As of November, all participants who were being followed at the time of the announcement, even those who were upset by the news, have agreed that they are willing to continue to be followed.

Seattle: By the end of November, 30 of 119 participants had been unblinded, and a participant forum was held in early December. While some participants have had anxiety about the news, all 30 unblinded so far have agreed to stay in the study.

San Francisco: They have been averaging about 20 unblinding visits per week, with each visit taking up to 1.5 hours. They had a participant forum with about 25 in attendance.

Dominican Republic: As of December 10th, they had unblinded 70 out of 77 participants, and it had been going very well, with good questions being asked and a general willingness for participants to continue in follow-up.

Boston: They have only unblinded a small percentage of the participants, but they did hold a participant forum. So far, there has been more disappointment about the lack of efficacy of the study vaccine rather than anxiety about possible increased risk.

Montreal: All participants have been contacted, and all are willing to continue to be followed. They met with significant others when this was requested, and participants have very much appreciated this gesture.

Sydney: They have unblinded 13/19, and have found the participants to have appreciated the support and clear communications that they have received.

As of the end of November, some sites had either just received their IRB approval, or were still waiting for it. Many sites noted that participants were willing and interested in staying in the trial, and were appreciative of the communication from the sites. ❀

A basic Q&A concerning the Step Study

What is the Step Study?

The Step Study is a double-blinded, placebo controlled, clinical trial testing an HIV study vaccine. It was conducted in South America, the Caribbean, Canada, Australia, and the United States. There is also a sister trial, called Phambili, which tested the same product at sites in South Africa. Both studies are “test of concept” trials, also known as Phase IIB trials.

The trial began in 2005 with the goal of enrolling 3000 participants. The Step Study was fully enrolled by March of 2007. On September 18th, an independent review board that periodically reviewed data from the trial, called the Data and Safety Monitoring Board (DSMB), determined that the product was not effective at preventing HIV or at lowering viral loads of anyone who did become HIV infected. The DSMB recommended stopping vaccinations, and the protocol team agreed. Vaccinations were also stopped in Phambili. Later, participants in both trials were unblinded, although both trials are continuing with scheduled clinic visits to monitor participants. Participants are also given risk-reduction counseling, as they have been throughout the trial.

What is Ad5 immunity?

The trial was testing a study vaccine developed by Merck which used a common cold virus, known as Adenovirus 5 (Ad5), as a vector (delivery method) that introduced several pieces of a man-made copy of the HIV virus into the body. The Step Study measured participants’ immunity to the Ad5 virus at the beginning of the trial. Immunity means whether or not your body has seen a virus before and has the means to fight it. Some people in the Step Study had a high level of immunity to Ad5 because they had gotten this particular cold before, and some had a low level or none.

After the study vaccine was found to not work, researchers began a very intense analysis of all of the data gathered during the trial so far. They found that more men who have sex with men who had gotten the vaccine became HIV positive than those who had received the placebo. This was even more noticeable among men who had high levels of immunity to Ad5.

Researchers are still trying to find the answer to the question of why there was this difference. It may be due to the vaccine, it may be due to differences between the groups of people with high and low levels of immunity, or it may be due to chance. Hopefully, researchers will understand this at some point, which is what they are now working very hard to do.

Did the trial “fail”?

No! The trial had an unexpected and disappointing result, but that does not mean it failed. The STEP trial was called a “test of concept” trial/Phase IIB, because that is exactly what it was meant to do- to determine if the concept behind the product actually did what everyone hoped it would do. Also, this type of trial was planned to find an answer with fewer participants and

less time and money than Phase III trials.

So, while the hope of the product as a potential vaccine was not realized, the goal of testing the concept was met.

Did the study vaccine give people HIV?

No! The Merck product did not contain live HIV, only pieces of a man-made copy. Think of how seeing a steering wheel might help you recognize a car, but a steering wheel alone cannot do the things a car can do.

Why are there more people who received vaccine who became HIV infected?

No one knows for sure. The difference between the number of people who received vaccine and got infected and the number who received placebo and got infected could be due to any of these three things:

1. The study vaccine
2. Differences between the groups
3. Chance

Researchers are trying to answer the question of whether the study vaccine made the immune systems of those with particularly high Ad5 immunity more susceptible to contracting HIV, once they were exposed to it. It is not known right now if that is what happened, and researchers are working tirelessly to try and answer this question.

What kind of follow-up is happening for participants in the Step Study?

A decision was made in mid- November to reveal to participants whether they had received placebo or the vaccine (unblinding). Most of those participants, at US sites as well as international, agreed to remain in the Step Study for follow up. This will allow researchers to continue to try to understand the effects of the study vaccine.

Participants who did contract HIV during or after the time they were in the trial were referred to appropriate services and also have continued to consult with their sites when needed. All participants continue to receive risk reduction counseling as they have throughout the trial.

How can I get more information about the Step Study?

If you would like to read more about the Step Study, please look at the website of the HIV Vaccine Trials Network: www.hvtn.org.

What will happen now with HIV vaccine trials?

While the future of HIV vaccines is not entirely clear, what is clear is that we are all as determined as ever to find a vaccine to stop the spread of this devastating disease. There are potential study vaccines being looked at, and many dedicated people who are truly motivated by the results of STEP to redouble their efforts to develop a vaccine that works! ❄

The CAB Retreat

Every two years we host a CAB Retreat in Seattle, and this year it will be held on February 8, 9 and 10, 2008. The CAB Retreat is an intensive train-the-trainer retreat, in which one CAB member from each site attends and learns key topics regarding the Network and HIV vaccine research. All aspects of the Retreat are paid for by the HVTN; in return, we ask that the local CABs send committed CAB members who are willing to take the trainings and training materials they are given and return home to present at least two of the trainings to their local CABs.

Each local CAB chooses its CAB Retreat representative. It is requested that the CAB member have participated in their CAB for at least a year (when possible). We offer translation and interpretation, so English is not a requirement. No CAB member can attend more than one CAB Retreat.

The train-the-trainer model used in the CAB Retreat puts focus on training the attendees to be ready to lead the sessions they attend when they return home. Attendees get practice teaching each other, and some of the sessions cover tips in giving presentations and working with groups. All attendees will receive the materials used in the trainings, including scripted slide sets and handouts. We will also ask some of the CAB Retreat attendees to help us in leading the Retreat sessions. This allows the sessions to stay in language that retreat attendees will feel comfortable using when they return to present to their own CABs.

We will be working with sites over the remaining weeks to get travel arrangements in place and to prepare our Retreat guests for their trip. Please help us by communicating in your CAB about what information you most want to have your Retreat representative bring back to you. ☘



EDITOR'S NOTE: WE ARE SWITCHING THE CAB BULLETIN TO A QUARTERLY FORMAT, MEANING THAT YOU WILL RECEIVE 4 CAB BULLETINS EACH YEAR.

Conferences and announcements

Conference calls to update the community regarding the Step Study and Phambili will occur as needed. Please stay in touch with your Community Educator regarding announcements concerning upcoming calls.

The HVTN Conferences will take place this year on May 21-23, 2008 and November 18-20, 2008. ☘



Calendar of events



CAB Scientific Working Group conference call:

Friday, February 1st, 8 a.m. PST/11 a.m. EST

Friday, March 7th, 8 a.m. PST/11 a.m. EST

Global GCAB conference call:

Thursday, February 14th, 8 a.m. PST/11 a.m. EST

Thursday, March 13th, 8 a.m. PST/11 a.m. EST

Global Ethics Working Group call:

Thursday, February 28th, 7 a.m. PST/10 a.m. EST

Thursday, March 27th, 7 a.m. PST/10 a.m. EST

Community Education/Recruitment coordination call:

Tuesday, February 19th, 9 a.m. PST/11 a.m. EST

Tuesday, March 18th, 9 a.m. PST/11 a.m. EST

Community Advisory Boards (CABs) are one way that the HVTN involves community 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 has been invaluable to the broad community education efforts, as well as to the development of this bulletin.

Send suggestions, questions, and article submissions to:
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