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VaxGen Interim Analysis Draft Talking Points & FAQ's

Scenario A: AIDSVAX is determined to be partially effective

- **How did you determine that AIDSVAX was partially effective?**

We were able to determine that AIDSVAX was partially effective because there was a significant reduction in the number of infections found among trial participants who received the vaccine compared with those who received the placebo.

- **Is it possible that AIDSVAX or any vaccine could be 100% effective?**

No. Unfortunately, there are currently no vaccines for any disease that are 100% effective.

- **Could a partially effective vaccine still have an impact in fighting the epidemic?**

Absolutely, even a moderately effective vaccine could have a major impact on the epidemic. The first polio vaccine that was introduced by Jonas Salk in 1955, for example, was initially only 60% effective. However, six months after its introduction, an improved vaccine was developed. Consequently, the improved Salk vaccine was able to virtually eliminate polio in the United States driving down the number of new infections by more than 96%.

Computer models show that a vaccine that is able to reduce HIV infections by even 30% could dramatically curtail the AIDS epidemic. It's due to a phenomenon called "herd immunity" and it works like this: If you decrease the number of people who are susceptible to infection, those people in turn will not pass the disease on to others. Continue this chain reaction long enough and the disease can be dramatically reduced or even eliminated if enough people are vaccinated.

- **Who made the determination that AIDSVAX was partially effective?**

An independent board known as the Data and Safety Monitoring Board (DSMB) reviewed the confidential data from the trial and determined that AIDSVAX was partially effective. The DSMB, which includes numerous health care experts, was established to periodically monitor data from clinical trials to address safety concerns and recommendations for study continuation, discontinuation or modification due to benefit vs. harm. The board includes clinicians with expertise in relevant safety concerns such as hematologists, epidemiologists, biostatisticians, among others.

- **Now that AIDSVAX has been determined to be partially effective, can the U.S. Food and Drug Administration (U.S.F.D.A.) approve the vaccine?**

Yes. The U.S.F.D.A. has indicated that it will consider approving AIDSVAX if there are 30% fewer HIV infections found among trial volunteers compared to individuals who were in the placebo group.

- **If the vaccine is only 30% effective, won't individuals still be able to become infected with HIV even though they get vaccinated?**

Yes. The effectiveness of the vaccine is determined for a group, not an individual. A 30% efficacy rate means that only 3 out of 10 people will be protected from infection. In other words, everyone who participated in the trials needs to continue practicing safer sex and refrain from participating in high-risk behaviors.

If the FDA approves VaxGen, other vaccines will still continue being developed to supplement the partially effective vaccine. We hope some day there will be a vaccine that nears a 100% efficacy rate. Nonetheless, everyone should always engage in safe behaviors.

- **Will the safety of AIDSVAX continue to be monitored?**

Yes, after a vaccine is approved, its safety is continuously monitored by national and international health agencies such as the FDA, Centers for Disease Control, and the World Health Organization.

- **Now that AIDSVAX is considered to be partially effective, will volunteers be needed for other HIV vaccine trials?**

Yes, because additional vaccines will still need to be tested in order to improve the efficacy rate. While we are very pleased that the efficacy of AIDSVAX is 30%, other vaccines are being tested that we hope will be much more effective.

- **Were trial participants provided with any counseling to promote ongoing safe behaviors?**

All participants in the trial received ongoing pre- and post-test counseling to promote the practice of safe behaviors.

Scenario B: The information from the interim analysis is found to be inconclusive

- **What does an inconclusive interim analysis mean?**

It means that in order to make a determination of the vaccine's efficacy, more data needs to be collected. As a result, the independent Data and Safety Monitoring Board (DSMB) recommends that the trial continue to its scheduled conclusion at the end of 2002.

- **Does an inconclusive interim analysis mean that AIDSVAX is ineffective?**

No. It simply means that additional data from the study is needed to determine the vaccine's effectiveness. As an example, the first Phase III trial for the hepatitis B vaccine had two inconclusive interim analyses before the vaccine was shown to be highly effective.

- **Does an inconclusive interim analysis mean there's a problem?**

No. It simply means that additional data needs to be collected to determine if AIDSVAX is effective.

General VaxGen and AIDSVAX Questions

- **Why is the interim analysis being conducted, shouldn't they wait until Phase III is completed?**

The interim analysis is being conducted primarily for ethical, not scientific reasons. If AIDSVAX were determined to be effective at the interim analysis, ethically, VaxGen would have an obligation to begin the licensure process and distribute the vaccine as soon as possible.

- **Can AIDSVAX or any of the other vaccines being tested cause HIV or AIDS?**

No, all the vaccines being tested in humans are made from synthetic proteins or man made, genetically engineered materials that cannot cause HIV infection.

- **How many vaccines are currently being tested through NIAID?**

Currently NIAID is supporting approximately two dozen vaccine studies that are at different stages of development. Many of these vaccines are being tested through the HIV Vaccine Trials Network (HVTN). This network represents the largest clinical trial studies of HIV vaccines around the world.

(The website for HVTN is http://www.hvtn.org)

- **Can AIDSVAX and the other vaccines being tested both prevent HIV infections and cure AIDS?**

The majority of the HIV vaccines in development are "preventive," designed to protect against HIV infection. Conversely, "therapeutic" vaccines attempt to prevent the disease (AIDS) after HIV infection occurs. Physicians, researchers, foundations and pharmaceutical companies are currently developing vaccines that combine preventive and therapeutic functions into one vaccine.

- **Are there any vaccines being tested that contain the HIV virus?**

No, all the vaccines that are being tested on humans are made from synthetic proteins or man made, genetically engineered materials that cannot cause HIV infection. Researchers and ethicists commonly agree that live viruses or live, weakened viruses should not be tested in humans because the risk of infection is too great.

- **What is a clinical trial?**

A clinical trial is a research study intended to answer questions about vaccines, new therapies or better ways of using known treatments. Clinical trials are used to determine whether new drugs or treatments are both safe and effective. Carefully conducted clinical treatments are the fastest and safest way to find treatments that work.
(Source: *ClinicalTrials.gov: A Service of the NIH)*

- **Why are clinical trials kept so confidential?**

One of the major reasons that clinical trials are kept confidential is because the government has established strict guidelines and safeguards to protect those volunteers who choose to participate in clinical trials. Another reason is to avoid premature research findings from being leaked to the general public.

- **What is a Phase III trial?**

AIDSVAX, which is currently a Phase III trial, is the final phase of a clinical trial. During a Phase III trial, the trials are expanded to include thousands of volunteers and is conducted to test safety and effectiveness. This phase includes participants who are HIV-negative, but at-risk for infection. Both vaccine and placebo groups are monitored for long periods of time to track the vaccines' efficacy level and can last 3-4 years.

- **How many vaccines have reached Phase III?**

To date, VaxGen's AIDSVAX is the only vaccine product that has progressed to Phase III trials.

- **Can someone receive a "false-positive" by participating in the clinical trials?**

Yes, after a volunteer receives the vaccine it's possible for them to test positive for HIV during a standard HIV test (i.e. ELISA or Western Blot test.) The reason a false positive may occur is because the vaccine produces HIV/AIDS antibodies. However, it's important to point out that there are other tests that can be used to show that the positive result is NOT because the person is infected with HIV, but because the person received the test vaccine. At this point, it hasn't been determined how long a volunteer may falsely test positive.

Consequently, it's very rare for volunteers to encounter problems as a result of receiving a "false positive" result, however, volunteers could potentially encounter problems donating blood, getting insurance, traveling to other countries, getting employment, in addition to facing other discrimination issues. As a result, all volunteers will be provided with an identification card showing that they are part of the study. Additionally, designated NIH staff will be available to address any issues that may arise.

Alternative response:

Yes. Because HIV vaccines use HIV/AIDS antibodies, there is a possibility that a person who has received a vaccine may test as "false-positive" from the vaccine. That is, register as being HIV-positive because of the antibodies present in the vaccine, but not actually be sero-positive. There are a number of simple tests to determine differences between a false positive and an actual sero-positive result.

ADDITIONAL QUESTIONS THAT WERE NOT INCLUDED IN TOM'S 9/26/01 VERSION OF THE DOCUMENT

- **What criteria does the FDA use in approving vaccines?**

New vaccines are licensed only after the FDA thoroughly reviews the results of extensive laboratory studies and clinical trials performed by scientists, physicians, and manufacturers to determine the safety and effectiveness of the vaccine. After a vaccine hits the market, the safety monitoring continues, as does FDA oversight to assure the highest levels of quality control in the vaccine production process.

(Source: *"Understanding Vaccine Safety: Immunization Remains Our Best Defense Against Deadly Disease,"* U.S. Food and Drug Administration, FDA Consumer magazine, www.fda.gov/fdac/features/2001/401_vacc.html)

- **Wouldn't it have been more effective to launch an ambitious AIDS prevention campaign than spend money on a vaccine that is only partially effective?**

Since the onset of HIV and AIDS there have been several partially successful prevention campaigns that have been launched, however, new HIV cases continue to be on the rise. In 2000 alone, there were 45,000 newly infected children and adults in the United States.

An HIV vaccine, such as AIDSVAX that is deemed "partially effective" can still make a tremendous impact in decreasing the number of new HIV infections.

- **Were trial participants provided with counseling in order to promote ongoing safe behaviors?**

Prior to joining the study, volunteers received extensive counseling regarding potential benefits and risks of participating in the study. For those volunteers who decided to participate in the study, they were required to read and sign an extensive informed consent form that explained their rights as volunteers and the risks associated with their participation in the study.

Once they agreed to participate in the study, all volunteers received ongoing counseling during each of their study visits. Volunteers were counseled about risk reduction behaviors while also being reminded that the injection that they received may either be a placebo or the vaccine. Regardless of what they received, they were strongly encouraged to refrain from participating in risky behaviors. Additionally, they were reminded that even if they received the vaccine, there is no proof at this point that the vaccine is effective.

- **Do you know approximately what the cost will be for AIDSVAX once it is released to the public?**

The cost for AIDSVAX has not been determined as of yet, however, regardless of the final cost, VaxGen is committed to working with international relief organizations, private foundations, UNAIDS, the World Bank, along with other organizations to make the vaccine available at less expensive prices for poorer countries.

Alternative response:

The cost for AIDSVAX has not been determined as of yet, however, vaccines that have used similar manufacturing processes to the ones that were used in the development of AIDSVAX, have been priced at anywhere between $50 to $300 a dose in industrialized countries. However, VaxGen recognizes that AIDSVAX would have to be priced well below that price point to make the vaccine accessible for poorer countries.

- **Is VaxGen involved with any other activities on the AIDS and HIV front?**

Yes, they received a grant from the NIH to support research and development of a vaccine to combat the subtype C strain of the virus. Subtype C is the most widespread form of the virus and is estimated to be responsible for approximately half of the world's 36 million infections. It is the most common subtype found in Southern Africa, India and China.

Additionally, NIAID is supporting a collaboration between VaxGen and a company called BBI Biotech to collect, process, and store white blood cells and seminal plasma from volunteers who are participating in the North American and European studies. If AIDSVAX proves effective, the funding will support an investigation of cellular immune responses and cellular factors associated with the vaccine in collected human tissue and cell samples.

- **Considering that several people who participated in the AIDSVAX trials became HIV positive during their involvement, weren't the researchers, in a sense, treating the individuals as "test subjects?"**

No, not at all. All the volunteers who participated in the AIDSVAX trials received ongoing counseling on how to avoid getting infected by HIV. Unfortunately, in some cases, counseling is not 100% effective, and as a result, some individuals engaged in some degree of risky behaviors.

It has always been the policy of the NIH that all clinical trials adhere to the most stringent ethical and moral guidelines to ensure the safety of participants and the validity and integrity of all research. That being said, all of the volunteers that have participated in the trials have done so independently and were required to read and sign an informed consent form prior to their participation.

- **There are several individuals that have called for a moratorium on HIV vaccine testing because they feel that once the vaccine is made available, it would be harmful to recipients and would be mandated by public officials. Do you believe they have a valid concern?**

Safety has always been the number one priority throughout the entire trial process. Since the inception of the AIDSVAX trials, the DSMB has met every six months to review the safety of the vaccine. In each of the five separate trials, the DSMB confirmed that the vaccine had an excellent safety profile.

Insofar as a vaccine being mandatory, no one has the jurisdiction to mandate required vaccinations. Immunizations are clearly one of the most important and effective ways that people can be protected against serious, preventable diseases, but nonetheless, we can only strongly encourage individuals to get vaccinated. We can't require anyone to receive the vaccine, it would clearly be a violation of civil liberties.

Additional response regarding the notion of mandatory vaccines:

There has never been mandatory HIV immunization guidelines established at the state, federal, or global level. Eventually, we will be in a position to make recommendations on various vaccines, however, those recommendations would only be made after rigorous safety and ethical reviews of the vaccine have been completed.

- **How has safety been monitored throughout the AIDSVAX trials?**

From the inception of the clinical trials, the safety of AIDSVAX has clearly been a top priority. That being said, the DSMB has met every six months to review the safety of the vaccine. In each of the five separate trials, the DSMB confirmed that the vaccine had an excellent safety profile. In addition to the review board, the USFDA requires rigorous monitoring of the safety of all vaccines once they are approved for general public use.

- **Are there any side effects from being exposed to AIDSVAX?**

Any side effects associated with AIDSVAX are similar to those of any approved vaccine, most commonly soreness or redness at the injection site.

- **Has VaxGen been working in collaboration with other organizations besides NIAID on the development and testing of AIDSVAX?**

Yes, they have worked with numerous organizations including the World Health Organization (WHO), the Centers for Disease Control (CDC), United Nations AIDS Programs (UNAIDS), the Walter Reed Army Institute of Research, HIV/AIDS research consortia, several AIDS Service Organizations (ASOs) and Non-Government Organizations (NGOs).

- **What is the HIV Vaccine Trials Network?**

The HIV Vaccine Trials Network (HVTN) is an international collaboration of scientists and institutions whose goal is to accelerate the search for an HIV vaccine by sharing trial results and facilitating parallel, concurrent testing. The HVTN is a unique hybrid that combines the depth and diversity of the academic community and the flexibility of a commercial drug company. The HVTN is composed of 27 research institutions worldwide, coordinated from its headquarters at the Fred Hutchinson Cancer Research Center.

(Source: HIV Vaccine Trials Network website: http://www.hvtn.org)

- **When and why was it established?**

The HVTN was formed by the Division of AIDS of the National Institute of Allergy and Infectious Diseases (NIAID), a component of the National Institutes of Health (NIH), when the federal government reorganized its HIV vaccine research effort. The creation of the HVTN consolidated NIAID's long-standing research program, which until 1999 was carried out by two distinct groups: the U.S.-based AIDS Vaccine Evaluation Group (AVEG), focused on early-stage testing of vaccine candidates, and the HIV Network for Prevention Trials (HIVNET), focused on domestic and international trials of HIV vaccines and other prevention strategies. The mission of the HVTN is to develop and test preventative HIV vaccines.

(Source: HIV Vaccine Trials Network website: http://www.hvtn.org)

- **Is all the research undertaken by HVTN funded by the US government or is their privately funded research as well?**

HIV vaccine research conducted by HVTN member institutions is funded by public and private sources. Collaborators also participate in the cost of conducting actual trials. This includes academic research institutions, foundations, vaccine inventors, and other government agencies.

(Source: HIV Vaccine Trials Network website: http://www.hvtn.org)

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