CDC UPDATE

CENTERS FOR DISEASE CONTROL AND PREVENTION

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CDC-FUNDED STUDY TO EXAMINE CRITICAL QUESTIONS IN HIV VACCINE RESEARCH

The Centers for Disease Control and Prevention (CDC) is conducting a study designed to answer critical questions about the potential impact that enrollment in an HIV vaccine trial has on trial participants' risk behavior, and to provide important guidance for the successful development of future trials. Study participants are now being recruited in six U.S. academic and community health centers located in Boston, Chicago (two sites), San Francisco, Seattle, and Columbus, Ohio.

The 1,600-participant study is a sub-study of the ongoing AIDSVAX trial, sponsored by VaxGen, a biotechnology company based in Brisbane, California. Begun in 1998 at 61 sites in the United States, Canada, and The Netherlands – with a separate trial also ongoing in Thailand – the AIDSVAX trials are the first and only *phase III* efficacy trials (study to determine protection from infection in humans) of an HIV vaccine. CDC is funding six of the U.S. trial sites in order to learn more about implementing a successful HIV vaccine trial, including the principal issue of how enrollment in an HIV vaccine trial is related to changes in participants' risk behavior.

In HIV vaccine trials, it is critical for participants to understand that the vaccine may not protect them from infection, so that they do not increase their risk behavior. As the only HIV vaccine currently in *phase III* trials, AIDSVAX offers a unique opportunity to study behavior and other critical factors that contribute to a successful HIV vaccine trial.

The development of a safe and effective HIV vaccine offers the greatest hope for stopping the HIV epidemic worldwide. However, the development of a safe and effective vaccine will likely require multiple trials. While each trial will lead us closer to an effective vaccine, early vaccine candidates are unlikely to be as effective as vaccines for other infectious diseases and unlikely to be effective against all HIV strains.

Recognizing the need to ensure safe and extensive participation in future trials, CDC, VaxGen, and collaborators designed the study to address key concerns about the risks and benefits of participating in vaccine trials. The study results

will help determine how to minimize potential disincentives to participation in future vaccine trials, mitigate any negative side effects such as stigma or discrimination, and develop effective counseling and prevention programs to prevent increases in risk behavior among trial participants and other individuals at risk for HIV infection.

The six AIDSVAX sites participating in the study are Fenway Community Health Center in Boston, Ohio State University in Columbus, Howard Brown Health Center in Chicago, the University of Washington in Seattle, the San Francisco Department of Health, and the University of Illinois at Chicago. These sites were awarded CDC contracts totaling $2.5 million per year for four years in October 1999 (with the exception of the University of Illinois, whose award was made in May 2000). The sites have worked with CDC and VaxGen since that time to develop and obtain approval of their respective sub-study protocols. The study designs have been approved, and sites have now begun recruiting for the behavioral studies.

Researchers from CDC and the six sites will work together to address the following issues potentially influencing or influenced by HIV vaccine research:

Risk Behavior – To study the principal question of whether vaccine trial participation has an impact on sexual decision-making, researchers will compare the risk behavior of the 800 AIDSVAX trial participants at the six sites with risk behavior among a cohort of 800 non-trial participants that has demographic, behavioral, and attitudinal characteristics comparable to the trial participants. After informed consent and entry into the AIDSVAX trial, all participants in the AIDSVAX trial receive initial counseling as well as follow-up counseling to ensure they understand that participation in the trial may not offer protection against HIV infection – either because they may receive a placebo or because they may receive AIDSVAX, the efficacy of which remains unproven. To determine whether AIDSVAX trial participants are more or less likely to engage in high-risk sexual behavior, researchers will compare risk behavior changes seen among AIDSVAX trial participants to those seen among the comparison cohort of individuals who are not participating in the vaccine trial.

Recruitment and Retention – Researchers will examine various factors in recruiting and retaining large study populations of high-risk participants in HIV vaccine trials, a critical long-term challenge in vaccine research. Researchers will study a number of factors that may influence a trial site's ability to recruit and retain participants, including: demographic characteristics of the targeted participants, attitudes toward HIV in the community, trial-related events such as adverse effects of the vaccine, and fear of discrimination or stigmatization at work or in the community.

Qualitative Assessment – Researchers will undertake an in-depth qualitative assessment to explore participant perceptions of the trial, decision-making

processes, motivations and trial experiences. This assessment will also explore reasons for enrollment and factors related to attrition.

Mucosal Immunity – Researchers are working with two of the six sites to investigate whether the vaccine produces a measurable antibody response at points of sexual exposure, including the penis, vagina and mouth, a response known as "mucosal immunity." An HIV vaccine's ability to fight infection at the point of exposure is potentially an important factor in increasing the vaccine's overall efficacy. The two study sites participating in the sub-study are Fenway in Boston and the University of Illinois at Chicago.

Access to Care – Researchers will also address whether AIDSVAX trial participants who become infected with HIV during the course of the trial are effectively referred to and access medical care, including but not limited to highly active anti-retroviral therapy (HAART). CDC will collect data from all 61 North American and European sites, using a questionnaire to evaluate access to care and to identify factors associated with failure to obtain care. Because the trials have large populations of high-risk participants, a proportion of whom are expected to become infected during the trial, access to care will prove to be a critical issue in future HIV vaccine trials.

Drug Resistance – Researchers will also examine drug resistance in those trial participants who become infected and enter treatment during the course of the trial. The agency will obtain blood samples from all participants at the six sites who become infected during the trial to evaluate the HIV strains for resistance to various HIV treatments.

About the AIDSVAX Trial

Both AIDSVAX trials are double-blinded and placebo-controlled. The trial in the United States, Canada, and The Netherlands includes 5,400 participants at sexual risk for HIV infection; about 5,100 are men who have sex with men and about 300 are high-risk heterosexual women. Trial participants receive seven injections over a 30-month period. At the 61 North American and European trial sites, two-thirds of the participants receive the vaccine and one-third receive a placebo. All participants receive risk-reduction counseling during multiple follow-up visits over the 36-month study.

In Thailand, 2,500 injection drug users are enrolled in the AIDSVAX trial, with an equal number receiving AIDSVAX or a placebo. CDC's role in the Thai trial has included working closely with VaxGen and Thai health officials to develop rigorous informed consent procedures and providing technical assistance to train risk-reduction counselors. In addition, CDC provides various forms of technical support, including performing CD4 and viral load tests on blood samples of trial participants who become infected during the trial. The *phase III* AIDSVAX trial in Thailand has been underway since March 1999.

AIDSVAX is derived from the gp120 protein on the surface of HIV. The vaccine seeks to elicit an immune response by introducing the body to the gp120 antigens, thereby producing antibodies that enable the immune system to clear HIV following exposure. If the vaccine is incapable of producing an antibody response sufficient to neutralize HIV, a secondary goal is to slow the natural course of HIV disease in those infected. The AIDSVAX trial is evaluating the vaccine's effectiveness against HIV-1 subtype B, which is prevalent in the United States, and subtype E, commonly found in southeast Asia. Data on safety and efficacy from the U.S. and Thai trials are reviewed by an independent monitoring board every six months. The U.S. trial is scheduled for completion in late 2002, while the Thai trial will be completed in mid-2003.

CDC's Role in Vaccine Trials

As the United State's lead federal agency for HIV prevention, CDC will be responsible for developing policies and procedures for successfully using effective HIV vaccines, once identified and licensed. By working with public and private partners as vaccine trials progress, CDC can use the information to guide the design and implementation of future trials and ultimately vaccination programs.

CDC also has a responsibility to help maintain progress already made in HIV prevention. Effective behavior change programs have greatly reduced the rate of risk behavior and HIV infection in the U.S. over the past two decades. One of the greatest risks, as vaccine trials progress, is that merely the promise of a future vaccine may lead some individuals to abandon proven prevention strategies. We have the knowledge today to prevent new HIV infections, and we must maintain and expand our focus on proven prevention strategies, as we continue our commitment to search for new ones.

About CDC

The Centers for Disease Control and Prevention protects people's health and safety by preventing and controlling diseases and injuries; enhances health decisions by providing credible information on critical health issues; and promotes healthy living through strong partnerships with local, national and international organizations.

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