HHS NEWS

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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The National Institute of Allergy and Infectious Diseases is initiating clinical trials of a genetically engineered AIDS vaccine made with the virus used to inoculate humans against smallpox. The vaccine will be tested in NIAID-funded Vaccine Evaluation Units at six university medical centers.

Manufactured by Bristol Myers Company, the vaccine is produced by recombinant DNA technology using live vaccinia virus. The recombinant vaccinia virus produces the envelope glycoproteins of HIV-1 (human immunodeficiency virus 1), the cause of AIDS.

HIV infects and destroys the body's immune system, thus causing susceptibility to other life-threatening infections and cancers. While many AIDS-related illnesses can be treated, no known therapy can cure the underlying defects caused by the virus.

The new study is one of numerous AIDS research projects conducted and supported by NIAID in the search for effective drugs to treat HIV-infected persons and effective vaccines to prevent infection. Since January 1988, the Vaccine Evaluation Units have been evaluating a different recombinant product, the first experimental AIDS vaccine to be approved for testing in humans. Scientists in NIAID's intramural program in Bethesda, Md., began the initial studies of that AIDS vaccine in August 1987.

In the new vaccine study, the Vaccine Evaluation Units will recruit a total of 54 volunteers for a Phase I trial to determine the vaccine's safety and ability to produce an

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immune response. Volunteers must be healthy men or women who are not infected with HIV, as determined by blood tests, and who are not engaged in behavior that would place them at high risk of contracting HIV.

At each unit 6 volunteers will receive the AIDS vaccine and 3 will receive vaccinia (smallpox) vaccine alone, as a control. Vaccinia virus was used for many years as a smallpox vaccination. Because smallpox has been eradicated worldwide, vaccinia vaccine is now used only by the armed services.

Volunteers will be randomized and the study will be double-blinded; i.e., neither the volunteers nor the physicians conducting the study will know which vaccine each person is receiving until data are analyzed in the future.

Because the recombinant vaccine contains no live or killed HIV, there is no possibility of contracting AIDS from the vaccine. Volunteers may have side effects that are not uncommon following administration of smallpox vaccine.

Recruitment of volunteers will begin at the individual Vaccine Evaluation Units following approval of the study plan by local institutional review boards.

# # #

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National Institute of Allergy and Infectious Diseases

Backgrounder

NIAID VACCINE EVALUATION UNITS CONDUCTING PHASE I STUDY OF RECOMBINANT AIDS VACCINIA VACCINE

To facilitate the testing of AIDS vaccines, the National Institute of Allergy and Infectious Diseases (NIAID) has called on the experience and resources of NIAID's six Vaccine Evaluation Units (VEUs). The VEUs are located at university medical centers in Huntington, WV, Baltimore, MD (two units), Houston, TX, Rochester, NY, and Nashville, TN.

During the past 20 years, the VEUs have conducted clinical trials to determine the safety and immunogenicity of numerous experimental vaccines for various diseases. In January 1988, the VEUs began evaluation of the first experimental AIDS vaccine to be approved for testing in humans. The VEUs are initiating a new AIDS vaccine study, using a genetically engineered vaccine made with a modified vaccinia virus.

Q. 1. What is the vaccine being tested?

A. The vaccine, called HIVAC-le, is a genetically engineered vaccinia virus, produced by recombinant DNA technology. This recombinant vaccinia virus produces the envelope glycoproteins of HIV-l (human immunodeficiency virus I), the cause of AIDS. The vaccinia virus was used for many years to immunize people against smallpox; because smallpox has been eliminated worldwide, the vaccine is now used only by the armed services.

Q. 2. What company manufactures this product?

A. Bristol Myers Company.

Q. 3. Did NIAID scientists play a role in the development of this vaccine?

A. Bernard Moss, M.D., Chief of the Laboratory of Viral Diseases, NIAID, created the basic recombinant technique for constructing new experimental vaccines by inserting genes from a variety of viruses into live vaccinia virus. Dr. Moss provided Bristol Myers with his vaccinia system.

In his own research, Dr. Moss and his colleagues inserted the HIV envelope gene into live vaccinia virus that, when inoculated into animals, produced HIV envelope proteins that stimulate the formation of antibodies. In collaboration with other scientists at the National Institutes of Health, the investigators showed that animals inoculated with the recombinant product developed antibodies capable of neutralizing, or killing, HIV in the test tube.

Q. 4. What are the results of animal studies using this vaccine?

A. HIVAC-le has been evaluated extensively in animals, including mice, guinea pigs, rabbits, and chimpanzees. These studies have demonstrated that HIVAC-le appears to be safe in doses equivalent to and greater than those planned for human studies. Tests in animals have shown that the vaccine is capable of producing immune responses to HIV.

Q. 5. What is the purpose of the clinical study?

A. The vaccine will be evaluated to determine its safety and ability to produce an immune response in human subjects.

Q. 6. Who will receive the vaccine in this study?

A. Each Vaccine Evaluation Unit will enroll 9 volunteers, for a total of 54 volunteers. At each VEU, six volunteers will receive HIVAC-le and three will receive vaccinia (smallpox) vaccine alone, as a control. Volunteers will be randomized and the study will be double-blinded; i.e., neither the volunteers nor the physicians conducting the study will know which vaccine each person is receiving until data are analyzed in the future.

Volunteers must be healthy men or women who are not infected with HIV, as determined by blood tests. They must not be engaged in behavior that would place them at high risk of contracting HIV. Because the effects of HIVAC-le on an unborn fetus are unknown, women of child-bearing age may not enter the trial unless they do not intend to bear children, and these women must have a pre-trial pregnancy test. All volunteers must agree to remain available for followup during the 14-month duration of the trial.

In addition, volunteers are to be "vaccinia naive;" i.e., they have to have no evidence of previous smallpox vaccination.

Q. 7. Are there any risks or expected side effects to HIVAC-le?

A. There is no possibility of contracting AIDS from receiving HIVAC-le because the vaccine contains no live or killed HIV.

Volunteers may experience side effects that are not uncommon following administration of vaccinia (smallpox) vaccine. A normal response to smallpox vaccination is characterized by the formation of a blister that becomes pustular, forms a scab, and eventually leaves a scar at the site of vaccination. Side effects may include pain, redness, swelling at the vaccination site, fever, and enlarged and tender lymph nodes. These usually resolve without medical treatment.

Rarely, persons receiving smallpox vaccines have experienced abnormal skin reactions or central nervous system disorders, but these nearly always occur only in persons with deficient or suppressed immune systems.

Q. 8. Has HIVAC-le been given to humans before?

A. Yes, there is an on-going study using this vaccine at the University of Washington, Seattle. No results have been reported from that study to date.

Q. 9. Can HIVAC-le protect against AIDS?

A. No one knows. This study is designed only to evaluate the safety and ability to produce an immune response. Even if immune responses develop, it is not known whether they would confer protection against infection with HIV. Therefore, all participants must continue to avoid any high risk behavior that might expose them to HIV.

Q. 10. After vaccination with HIVAC-le, are vaccinees expected to test positive for HIV on standard ELISA and Western blot HIV antibody tests?

A. Individuals may test positive on ELISA. The Western blot test shows antibody responses to specific viral proteins. Because vaccinees will show antibody response to HIV envelope proteins, but not to HIV core proteins, their Western blot tests will be considered "indeterminate."

Q. 11. What documentation will volunteers receive to show that they received HIVAC-le and were not infected with HIV?

A. Each volunteer will receive an identification card that will state his or her participation in the trial, and an 800 number that can be called to further verify participation.

Q. 12. If the vaccine proves to be safe and immunogenic in this Phase I study, what is the next step?

A. Additional, larger studies to evaluate safety, immunogenicity and optimum dosage would be conducted in Phase II.

Q. 13. What does a Phase III vaccine trial involve?

A. A Phase III study of an AIDS vaccine would require large numbers of people who are at high risk of becoming infected with HIV. Such a trial cannot be done until the results of Phase I and Phase II studies are completely evaluated.

Q. 14. How can people volunteer to participate in the studies?

A. They may contact the nearest VEU.

Q. 15. Who are the principal investigators of the Vaccine Evaluation Units?

A. Dr. Robert Belshe, Marshall University School of Medicine, Huntington, WV.
Dr. Mary Lou Clements, The Johns Hopkins University, Baltimore, MD.
Dr. Robert Couch, Baylor College of Medicine, Houston, TX.
Dr. Raphael Dolin, University of Rochester School of Medicine, Rochester, NY.
Dr. Myron Levine, University of Maryland School of Medicine, Baltimore, MD.
Dr. Peter Wright, Vanderbilt University, Nashville, TN.

Q. 16. Why is the study being conducted at several centers?
A. A multicenter trial has several advantages over a single-center trial, including the ability to rapidly obtain scientific data and the ability to draw on a number of geographic areas to recruit sufficient volunteers for a specific study.

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