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Merck Plans to Test AIDS Vaccines in Humans

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As the AIDS pandemic spreads largely unabated outside the U.S., public-health officials have been waiting hopefully for a breakthrough in the development of a vaccine.

Now Merck & Co., after numerous

DRUGS

years of effort and failed attempts, appears to have made one.

Merck scientists are laying plans to begin the first human tests of two promising experimental vaccines developed as part of an intense top-secret research effort.

Merck's top vaccine-research executive, in a telephone interview this week, confirmed the vaccines' existence and the company's plans to begin administering them in a small number of healthy, uninfected volunteers by year's end.

The official, Emilio Emini, said he didn't want to raise undue expectations. He said the human tests will be undertaken simply to help Merck scientists determine if the vaccines can produce in people the kind of immune-system reaction generated in animal studies. Those studies themselves are so preliminary that the company hasn't completed their analysis, or presented their results to the AIDS-vaccine research community, Dr. Emini noted.

Still, researchers familiar with the project say that if Merck's vaccines produce a powerful immune reaction, the company is capable of swiftly embarking upon larger trials. Merck, based in Whitehouse Station, N.J., is one of the world's premier commercial vaccine makers.

"The studies are designed to help us quickly see if we are on the right track," said Dr. Emini, director of Merck's infectious-disease research operations. He added: "We are at the point in our research where we need to know if they will trigger the response in people we've seen in animals. And the only way to learn that is by giving them to people." Still, Merck is uncertain if the immune response it has gen-

erated in animals is of the type that will protect people against infection.

Several other companies are testing prototype vaccines in large and small trials in the U.S. and abroad. But one of the Merck vaccines will be among the first of a class of so-called "naked DNA" vaccines for HIV to go into humans. These are vaccines composed of a gene or genes extracted from the virus. No naked DNA vaccines yet exist, and Merck and others have to date been unsuccessful in testing such agents against the flu and other microbes.

Merck declined to provide much detail about the AIDS vaccines. Rumors of the company's testing plans have surfaced in

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Merck Set to Test AIDS Vaccines

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the last week or so, and "mitted information about them has been shared with some research groups and research physicians who will help conduct the small trials. Information from scientists familiar with the company's program suggests that Merck's efforts incorporate the latest technology and knowledge emerging in recent months about what's needed to produce a protective response in people.

"What's exciting and important is that Merck believes it's far enough along to test something," says Margaret Johnston, assistant director for AIDS-vaccine research at the federal government's National Institute of Allergies and Infectious Diseases. "It's good to see Merck involved, and testing an approach that is right now thought to be on the cutting edge."

Specifically, Merck wants to see if its DNA vaccine can stimulate the immune sys-

said that in monkey studies, the altered DNA induced a stronger and longer T-cell response than other test vaccines. Dr. Emini confirmed Mr. Gold's account.

Recent research, however, suggests that a DNA vaccine alone likely won't be powerful enough to fully protect against infection. As a result, Merck confirms that it also will test a vaccine in which bits of the virus are inserted into a defused animal or human virus. The company declined to identify the composition of its virus-based vaccine. "The current sense is that a vaccine against AIDS will require a combination of a DNA vaccine to prime the immune system followed by a booster of a vaccine involving another virus," says Dr. Johnston of the government's NIAID.

Indeed, several weeks ago Pasteur Merieux Connaught, the vaccine-making unit of the French drug company Rhone-Poulenc SA, reported results of a phase-two test of vaccine in which parts of the AIDS virus are inserted into a weakened virus that causes canarypox, a bird virus. Michel Klein, who directs Pasteur Merieux's HIV-vaccine effort, says the company's test vaccine produced some T-cell response, and it expects to test the vaccine further. The company also is developing a DNA vaccine, Dr. Klein says.

Emilio Emini, Merck's top vaccine-research executive, says he doesn't want to raise undue expectations.

tem to release white blood cells often referred to as killer or cytotoxic T-cells. Recent studies by several other research groups show that people exposed to HIV, the virus that causes AIDS, who produce large amounts of killer T-cells and other so-called helper T-cells are able to keep the disease in check. Additional recent studies in monkeys show that triggering such T-cells can also keep the virus at bay for limited periods.

Dr. Emini says animal studies Merck is conducting show that the company has been able to make a DNA vaccine that can prompt a killer and helper T-cell response. The company's trials are designed to see if the same biological response occurs in humans, a test that could be accomplished within a few months.

The human trial will be watched closely by AIDS-vaccine researchers because it will provide a critical test of whether DNA vaccines are useful. Most other experimental vaccines have produced antibodies against HIV that, while able to neutralize the virus outside of infected cells, don't appear to be powerful enough to overcome infection. Scientists are hopeful about the DNA approach because such vaccines also stimulate a cascade of T-cells that are able to target and destroy virus particles that enter the cells during a viral infection.

The trick in making a DNA vaccine, however, is identifying which genes from HIV to put into the vaccine. While Merck declined to disclose the gene or genes it is using, Dr. Emini confirmed that the company is using genetic material from the virus that it has altered in an effort to elicit a desired response.

Information about Merck's efforts will appear in the soon-to-be-published August newsletter of the International AIDS Vaccine Initiative, a private New York organization that promotes vaccine development. David Gold, who monitors AIDS-vaccine research for the organization, will report that Merck has been able to "humanize" the genes, making the DNA produce a more powerful immune response than has been produced in any previous efforts by Merck or others.

Mr. Gold will also report that at a recent meeting of vaccine researchers, Merck