Trials of NIH’s AIDS Vaccine Get a Yellow Light

POTOMAC, MARYLAND—In late September, the U.S. National Institutes of Health (NIH) in Bethesda, Maryland, at the last minute scotched a massive $130 million trial of an AIDS vaccine made by its researchers. The reason: Much to the dismay of the field, a test of a similar vaccine made by Merck & Co. found that it may have actually increased some people’s risk of becoming infected with HIV. Last week, NIH’s AIDS Vaccine Research Subcommittee met here to discuss the future of the NIH vaccine. Although no final decision has been made, the consensus was to continue testing the vaccine to see whether it works but in a redesigned study that reduces the chance of doing harm. “Everyone seems to think the products are different enough to warrant further testing,” said Peggy Johnston, who heads AIDS vaccine research at NIH. “The issue becomes, what’s the trial design going to be, and is that design feasible to carry out?”

The Merck vaccine and that made by Gary Nabel’s team at the NIH Vaccine Research Center (VRC) both deliver HIV genes into the body using a cold virus as a vector: The prevalence of this adenovirus 5 (Ad5)—there are more than 50 subtypes—varies greatly, infecting one-third of the population in some locales and nearly everyone in others. In the Merck study, vaccinated people who had high levels of antibody to Ad5 at the trial’s start more readily became infected by HIV. Questions remain about the mechanism and whether the finding is even statistically significant (Science, 16 November, p. 1048). But out of caution, the group last week argued to exclude people with Ad5 antibodies from the VRC test.

Originally, Scott Hammer of Columbia University planned to lead a test of the VRC vaccine in 8500 people in the Americas and Africa. Now, as Magdalena Sobieszczyk from his group explained, they think it’s prudent to enroll only 2000 to 3300 people in the Americas and Africa who are negative for Ad5 antibodies. Sobieszczyk described study designs that would include both heterosexuals and men who have sex with men.

Yet staging a trial of a vaccine that, even if it works, could not be used by people with Ad5 immunity raises ethical quandaries. “It may not be acceptable in regions where two-thirds of people are seropositive [for Ad5],” Hammer conceded. Another option is to change the vector altogether, but that would delay the trial indefinitely.

Some participants argued that the trial should be focused more narrowly—for instance, on men in the United States who have sex with men. Subcommittee member Jeffrey Lifson of SAIC in Frederick, Maryland, cautioned that the Merck results have been befuddling in part because the vaccine was tested in many different populations and locations. “I am really concerned to show that we can do clear studies,” Lifson said.

David Watkins, a primate researcher at the University of Wisconsin, Madison, argued against doing the trial at all, as monkey studies have suggested the VRC vaccine will fail, regardless of the safety issues. “I just don’t get it,” Watkins told Science. “The science seems to be really ignored.” Anthony Fauci, head of the National Institute of Allergy and Infectious Diseases, said he doesn’t think the field has the luxury of waiting for convincing efficacy data from monkey studies, which could take more than a decade. But Fauci did not offer his opinion during the meeting, explaining, “I’m going to have to make the final decision, and I don’t want to preempt anybody.” The Columbia team will present a redesigned study to the same subcommittee in January, then Fauci will announce the fate of the VRC vaccine.

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