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Detailed Results from RV 144 HIV Vaccine Trial Published Today in *The New England Journal of Medicine* and Presented at the AIDS Vaccine 2009 Conference Provide Insight for Future Research

20 October 2009 (Paris, France) – Detailed results from the Prime-Boost HIV Vaccine Clinical Trial involving more than 16,000 adult volunteers in Thailand show that an investigational HIV vaccine regimen was safe and modestly effective at reducing the rate of HIV infection compared to placebo. These results were presented today by the trial collaborators to researchers gathered at the AIDS Vaccine 2009 Conference in Paris, France and published online by *The New England Journal of Medicine*.

“This is the first evidence that a prime-boost HIV vaccine regimen may prevent infection and represents a significant step forward for vaccine research,” said Colonel Nelson Michael, Director, Division of Retrovirology, Walter Reed Army Institute of Research and Director, U.S. Military HIV Research Program (MHRP). “While it will not likely have any immediate public health benefit, we are hopeful that the findings will guide additional studies and accelerate research efforts toward a more effective vaccine.”

According to the collaborating partners, the prime-boost combination of ALVAC[®] HIV and AIDSVAX[®] B/E appeared to lower the rate of HIV infection by 31.2 percent compared to placebo based on the modified intent-to-treat (mITT) population (n=51 vs. n=74, respectively; p=0.04). There was no effect on the amount of virus in the blood of the study volunteers who received either vaccine or placebo and subsequently became infected with HIV.

“Experts are interpreting the results and planning additional studies to maximize the knowledge gained from this study. Our first step is to see if we are able to determine correlates of protection,” said Colonel Jerome Kim, Deputy Director (Science), MHRP and the HIV vaccines product manager for the U.S. Army.

“Observations will inform future basic research, non-human primate and clinical studies to build on the RV144 result.”

“All of this together emphasizes the opportunities these trial results afford – a new vantage point to examine what we understand about vaccine design, immunogenicity testing and animal models,” added Colonel Kim. “Further research is required to determine if immunological mechanisms mediating protection against HIV may be different from those that control viral replication.”

The trial results, first announced by trial collaborators on September 24, 2009, are based on the mITT population, which is the most clinically relevant analysis for this proof-of-concept study. Data from the mITT population, which was monitored by the independent Data and Safety Monitoring Board during its periodic review of the study, include all volunteers who entered the study less seven individuals who were already HIV infected on the first day of vaccination. "Given that you cannot protect someone from an infection that they already have acquired, the modified intent-to-treat analysis excluded these individuals," said Michael.

The detailed study data, which were embargoed for release before the AIDS Vaccine 2009 Conference and *The New England Journal of Medicine* publication, provide analyses of multiple data subgroups including ITT and per protocol (PP), their definitions and results. Data from the PP population show similar trends (26.2 percent reduction in HIV infection compared to placebo; n=36 vs. n= 50 respectively; p=0.16), though the results did not reach statistical significance due to the exclusion of nearly one-third of volunteers from the analysis and the associated loss of statistical power. For the ITT population, the vaccine regimen reduced infection rates by 26.4 percent compared to placebo (n=56 vs. n=76 respectively; p=0.08).

The U.S. Army would like to thank the more than 16,000 Thai men and women who consented to participate in this trial and the efforts of the Thai Ministry of Public Health. Trial collaborators include the U.S. Army, the Thai Ministry of Public Health, Mahidol University, the Armed Forces Research Institute of Medical Sciences – U.S. and Thai components, the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health, sanofi pasteur, Global Solutions for Infectious Diseases and the Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc.

RV144 Trial Background

RV144 tested a prime-boost vaccine strategy that combined two vaccines based on strains (subtypes) of HIV that circulate in Thailand. The first, or "prime" vaccine, known as ALVAC HIV, was developed by sanofi pasteur and the booster vaccine, AIDSVAX B/E, was originally developed by VaxGen and is now licensed to Global Solutions for Infectious Diseases.

The proof-of-concept study, which began in 2003, was designed to evaluate the vaccine strategy's ability to prevent HIV infection, as well as its ability to reduce the amount of HIV in the blood of those who became infected after they enrolled in the study.

More than 16,000 HIV-negative men and women between the ages of 18 to 30 years participated in the study; half of these participants received the prime-boost vaccine regimen and half received placebo. Volunteers received vaccinations over the course of six-months and were followed for an additional three-year period. Before agreeing to participate, all volunteers were informed of the potential risks associated with receiving the experimental vaccine regimen used and consented to participate in the study. Volunteers continued to receive an HIV test every six-months for three-years following vaccination, in addition to counseling on how to prevent becoming infected with HIV.