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### **USAMRIID Begins Clinical Trial of New Vaccine to Protect Against Ricin Toxin**

A clinical study to evaluate a new vaccine against ricin toxin is underway at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID). The trial is a Phase I study, meaning it will look at the safety of the ricin vaccine and its ability to elicit an immune response in a small number of people. Based on the results of this study, the next step would be to continue to evaluate the product in a larger pool of volunteers.

The first volunteer was vaccinated on April 5 and the second was vaccinated April 11, according to investigators in the Department of Clinical Research within USAMRIID's Division of Medicine. To date, both subjects are doing well.

Currently, there is no vaccine or therapeutic intervention (other than supportive care) available to prevent or treat the effects of ricin, a toxin derived from the castor plant. Grown throughout the world for commercial purposes, approximately one million pounds of castor beans are used each year in the process of manufacturing castor oil.

When inhaled as a small-particle aerosol, ricin produces severe respiratory symptoms followed by respiratory failure within 72 hours. When ingested, ricin can cause severe gastrointestinal symptoms followed by vascular collapse and death.

Given its ready availability and its relatively high levels of toxicity—particularly when delivered as an aerosol—ricin is considered a significant potential agent of biological warfare or terrorism. USAMRIID, the Department of Defense's (DOD) lead laboratory for medical research to counter biological threats, has been working for many years to develop a promising ricin vaccine candidate.

According to Dr. Leonard Smith, senior research scientist, the clinical study marks an important chapter in that effort.

“In the recent past, the DOD acquisition strategy involved USAMRIID's developing medical products to a specified maturity and then handing them off to another

agency for advanced development,” said Smith. “Now, we have been able to do the initial production of the vaccine under clinical Good Manufacturing Practices, as well as the Phase I clinical trials, right here at USAMRIID. This early product evaluation in-house saves both time and money.”

In 2004, a USAMRIID team led by Smith and Dr. Mark Olson published the results of its work—using a combination of molecular modeling and protein engineering—to design a new vaccine called RTA 1-33/44-198. The product was essentially a fragment of the ricin protein called the A-chain, which had been modified to make the protein non-toxic and more stable while retaining its immunogenicity—that is, its ability to elicit a protective immune response.

That vaccine, now known as *RVEc*, was shown to be fully protective in mice exposed to lethal doses of ricin toxin by the aerosol route. Further studies, in both rabbits and nonhuman primates, were conducted to evaluate the vaccine’s safety as well as its immunogenicity. Based on the success of those studies, Smith said, the next step was to evaluate the safety and immunogenicity of the vaccine in humans. An investigational new drug (IND) application was filed and accepted by the Food and Drug Administration (FDA) on 1 December 2010.

The study calls for a total of 30 volunteers to be vaccinated in three groups of 10. Three doses of vaccine will be given over a period of about two months, and the vaccine recipients will receive medical follow-up for 9 to 12 months.

“The clinical trials team is very excited about the launch of this ‘first in humans’ study,” said Dr. Ronald Reisler, a research physician with Ke’aki Technologies, LLC, a USAMRIID contractor. “A great deal of pre-clinical work has preceded the phase I launch and a great deal of work remains to be performed in the path forward to licensure of a prophylactic vaccine.”

Study volunteers are being recruited from the Fort Detrick community and the surrounding area. Among the screening criteria participants must meet are to be in good general health, between 18-50 years of age, weighing at least 110 pounds, and to be non-smokers with no history of lung disease.

To evaluate the vaccine’s safety, investigators will assess local and systemic reactions among the volunteers. Local reactions could include such things as redness or tenderness at the injection site, while systemic reactions might include fever and headache. Other more serious symptoms associated with the original toxin are not expected to occur.

To evaluate the vaccine’s ability to elicit an immune response, participants will give a total of 20 blood samples over a one-year period. The blood samples will then be tested for antibodies to ricin toxin to determine if the levels are consistent with antibody levels that correlate to protection observed in animal models.

"This clinical study is a good example of USAMRIID's capability to take a product all the way from concept to early clinical trials," said COL John P. Skvorak, commander of USAMRIID. "It would not have been possible, however, without the support we've received from the Joint Science and Technology Office for Chemical and Biological Defense."

The IND and clinical study are sponsored by the U.S. Army Medical Materiel Development Activity under the Office of the Surgeon General, Department of the Army, and funded by the JSTO-CBD, part of the Defense Threat Reduction Agency.

USAMRIID, located at Fort Detrick, Maryland, is the lead medical research laboratory for the U.S. Department of Defense's Biological Defense Research Program, and plays a key role in national defense and in infectious disease research. The Institute conducts basic and applied research on biological threats resulting in medical solutions (such as vaccines, drugs and diagnostics) to protect the warfighter. While USAMRIID's primary mission is focused on the military, its research often has applications that benefit society as a whole. USAMRIID is a subordinate laboratory of the U.S. Army Medical Research and Materiel Command.

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For more information: [www.usamriid.army.mil](http://www.usamriid.army.mil)