

USAMMDA INFORMATION PAPER

PRODUCT: HEPATITIS E VIRUS (HEV) VACCINE

DESCRIPTION: The HEV vaccine is designed to provide protection against infection with and disease caused by the HEV. The HEV vaccine is a recombinant vaccine that consists of a purified polypeptide produced in insect cells infected with recombinant baculoviruses. It is formulated with an aluminum salt adjuvant. Hepatitis E is endemic in many regions of the world with U.S. national security strategic interests. The virus is transmitted primarily by the fecal-oral route; drinking fecally contaminated water is the most common mode of transmission. The illness often occurs two to six weeks after infection and results in protracted convalescence lasting several weeks to months. In some cases, infection results in severe rapidly progressing disease that ends in death due to liver failure. The case-fatality rate is approximately two percent in men and non-pregnant women and up to 20 percent during the third trimester of pregnancy. The highest incidence of HEV infection occurs in young adults (of military age). Approximately 97 percent of American adults are susceptible to HEV infection. Outbreaks of HEV infection have been identified in India, Myanmar (Burma), Iran, Bangladesh, Ethiopia, Nepal, Pakistan, central Asian Republics of the former Soviet Union, Algeria, Libya, Somalia, Mexico, Indonesia and China. Non-immune Service members deployed to endemic regions are at high risk, and the resultant disease could seriously disrupt the conduct of a military mission.

PROGRAM RELEVANCE to the ARMY: This product supports both the core mission of the Army and the Army Transformation. Of the Army's core competencies, this product supports: "Shape the Security Environment," "Forcible Entry Operations," "Sustained Land Dominance" and "Support Civil Authorities" by protecting U.S. Forces against infection with the HEV virus. The HEV vaccine will enhance the survivability and sustainability of U.S. Forces in regions of the world where HEV is endemic. In addition, this product supports Future Operational Capability MD97-007 (Preventive Medicine).

ISSUES/ ACTIONS:

- A number of significant protocol amendments were implemented by the investigative team without formal review and approval by cognizant institutional review boards. Though none of the changes increased risk of harm to study volunteers, they did result in extensive protocol deviations. The investigative team continues to document all deviations by memoranda for the site's regulatory file. A protocol amendment (Amendment 9) encompassing all previously unapproved changes to the protocol was approved by the requisite institutional review boards during December 2003-January 2004.
- Since the study Data Safety Monitoring Board certified 79 hepatitis cases in February 2003, an additional 26 cases have accrued that have yet to be certified. A USAMMDA quality assurance monitor will review these additional cases in early June 2004. Statisticians at GlaxoSmithKline Biologics, Inc. will then issue case certificates for review and certification by the DSMB in mid-June 2004. Unblinding of the study data, with the DSMB, will begin in late June 2004.

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MAMP RANK: 14/36**ARMY ORD:** Draft**SCHEDULE:**

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