INFORMATION PAPER

Military Vaccine Agency
21 December 2011

SUBJECT: Japanese Encephalitis and Japanese Encephalitis Vaccine

1. Purpose. To describe Japanese Encephalitis Virus and the vaccine to prevent it.

2. Facts.

a. Microbiology. Japanese Encephalitis Virus (JEV) is a single-stranded RNA virus that belongs to the genus Flavivirus, and is closely related to West Nile and St. Louis encephalitis viruses. Four genotypes of JEV have been identified.

b. Disease. JEV may result in an acute infection of the brain, spinal cord, and lining of the brain (meninges) with high rates of complications, chronic disability, and death. Less than 1% of individuals infected with JEV develop clinical disease. Incubation is on average 5-15 days and begins with acute onset of fever, headache, and vomiting. Additional neurologic symptoms may begin to develop as well. Japanese encephalitis (JE) has a case-fatality ratio of approximately 20-30% with 30-50% of JE survivors having neurologic or psychiatric sequelae even years later.

c. Epidemiology. JEV is an arthropod-borne virus transmitted by the bite of various species of Culex mosquitoes. The disease is most common in rural, agricultural areas of Asia, as well as, certain western Pacific Islands, where mosquito larvae are found in flooded rice fields and marshes. Transmission is highest in the summer and fall. Domestic pigs are the most important source of infection for mosquitoes that transmit JEV to humans

d. Vaccine.

1) IXIARO® Japanese Encephalitis Virus vaccine (absorbed) is manufactured in the United Kingdom by Intercell Biomedical. IXIARO® is a sterile purified vero cell-cultured inactivated vaccine. The formulation does not include preservatives, stabilizers or antibiotics. IXIARO® is a clear liquid with white precipitate and when shaken before use, a white/cloudy suspension forms

2) JE-VAX® was manufactured in Japan by the Research Foundation for Microbial Disease of Osaka University (known as “Biken”) and distributed by Sanofi Pasteur. JE-VAX® is an inactivated mouse brain-derived whole-virus vaccine licensed in December 1992. In 2006, production of JE-VAX® was discontinued and remaining supplies of vaccine expired in May of 2011.

e. Cautions. Those that should not receive the JEV vaccinations include, people with known hypersensitivity to either vaccine, its components or those with multiple allergies especially a history of urticaria (i.e. hives) or angioedema. Defer vaccination if the person has a moderate to severe acute illness.

IXIARO® does contain protamine sulfate, a compound known to cause hypersensitivity reactions in some individuals. Individuals who show hypersensitivity reactions after receiving

the first dose of the vaccine should not be given the second dose. IXIARO® should not be administered to individuals who have previously experienced a serious reaction to any JEV vaccine

f. Immunization.

1) IXIARO® is a two dose series administered 28 days apart. Each 0.5mL dose is administered intramuscularly in the deltoid. The vaccine is indicated for individuals 17 years of age and older. Safety and effectiveness has not been established in pregnant women, nursing mothers, or in children and adolescents younger than 17 years of age. The series must be completed a minimum of 1 week prior to potential exposure to JEV. ACIP recommends that if the primary series of IXIARO® was administered greater than 1 year previously, a booster dose may be given before potential JE virus exposure. Data on the response to a booster administered greater than two years after primary series is not available. Vaccine must be stored in a refrigerator at 2° to 8° C (35° to 46° F). Do not freeze vaccine.

2) It is recommended that persons who previously received JE-VAX® and require further vaccination should receive a two dose primary series of IXIARO®.

3) JE-VAX®, the only vaccine for those younger than 17 years of age, is no longer available. ACIP guidelines suggest the following options for obtaining JE vaccine for U.S. children deemed at risk for JE exposure.

a) Enroll children in the ongoing clinical trial. The ongoing pediatric safety and immunogenicity trial with IXIARO® is enrolling children aged 2 months to 17 years of age (trial identifier NCT01047839). The study is open-label, and all enrollees receive two (2) doses of IXIARO® administered 28 days apart. A third study visit is required 56 days after the first dose. Additional information about the clinical trial is available online from the National Institutes of Health at http://clinicaltrials.gov/ct2/show/nct01047839.

b) Administer IXIARO® off-label. A health-care provider may choose to administer the vaccine off-label in children aged <17 years. Additional information about the use of IXIARO® in children is available from Novartis Medical Communications by telephone (877-683-4732) or e-mail (vaccineinfo.us@novartis.com).

c) Receive JE vaccine at an international travelers' health clinic in Asia. Several pediatric JE vaccines are licensed for use in Asia but not in the United States. Vaccines available at international travelers' health clinics in Asia include another inactivated mouse brain--derived JE vaccine manufactured in South Korea, live attenuated SA 14-14-2 vaccine manufactured in China, or another Vero cell culture-derived JE vaccine manufactured in Japan. The recommended number of doses and schedule varies by vaccine and country. A partial list of international travelers' health clinics in Asia that administer JE vaccines to children is available online from CDC at http://www.cdc.gov/ncidod/dvbid/jencephalitis/children.htm.

g. Adverse events. The most common systemic effects observed after immunization with IXIARO® are headache and myalgia and local injection site reactions include pain and tenderness. Vaccine recipients should be observed for 30 minutes after immunization and warned about the possibility of delayed allergic reactions. All serious adverse events should be reported to the Vaccine Adverse Events Reporting System (VAERS).

h. DoD policy. Administer Japanese-Encephalitis Virus vaccine to personnel who are or who will be stationed in rural areas of Asia in which the disease is endemic and where they have substantial risk of exposure to the virus, especially during prolonged field operations at night. The groups recommended to receive the Japanese-Encephalitis Virus immunization are designated special-operation units, Navy mobile construction battalions, Marine expeditionary units operating in the Western Pacific, and troops assigned or deploying to Okinawa with extended field exposure. For other travelers, vaccinate those who will spend 1 month or longer with extensive outdoor activities in rural areas, such as where rice cultivation or pig farming is common.

3. References.

a. Centers for Disease Control and Prevention. Japanese Encephalitis Vaccines – Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2010;59(No. RR-1):1-32

b. Centers for Disease Control and Prevention. Recommendations for Use of a Booster Dose of Inactivated Vero Cell Culture-Derived Japanese Encephalitis Vaccine– Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 27 May 2011: 60(20); 661-663

c. Centers for Disease Control and Prevention. Update on Japanese Encephalitis Vaccine for Children United States – Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 27 May 2011: 60(20); 664-665

d. Centers for Disease Control and Prevention. CDC Health Information for International Travel 2012. Atlanta: U.S. Department of Health and Human Services, Public Health Service, 2011

e. Multiple resources (e.g., product insert, Vaccine Information Statements) assembled by the Military Vaccine Agency: www.vaccines.mil/Japaneseencephalitis

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