

Japanese Encephalitis (JE) Vaccine

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Overview of key issues

- **Inactivated Vero cell culture-derived JE vaccine (JE-VC) is the only JE vaccine licensed and available in the U.S.**
- **In 2009, JE-VC licensed for use in adults ≥ 17 years of age**
- **On May 17, 2013, FDA licensed JE-VC for use in children 2 months through 16 years of age**
- **We will present the evidence review, GRADE evaluation, and proposed recommendations for use of JE-VC in children**

JE-VC (Ixiaro)

- **Manufactured by Intercell Biomedical**
- **Distributed in U.S. private market by Novartis Vaccines**
- **Indicated for active immunization to prevent disease caused by JE virus**
- **Dosage and administration**
 - **0.25 mL dose for children 2 months through 2 years of age**
 - **0.5 mL dose for children ≥ 3 years of age and adults**
 - **Primary series: 2 doses administered 28 days apart**

JE-VC efficacy and correlate of protection

- **No efficacy data for JE-VC**
 - Availability of several effective JE vaccines in Asia make a comparative efficacy trial difficult to perform
- **Established immunologic correlate of protection**
 - JE virus 50% plaque reduction neutralization test (PRNT₅₀) titer ≥ 10 *

*Hombach. Vaccine 2005; Markoff. Vaccine 2000.

JE-VC licensure in adults

- **Non-inferiority of neutralizing antibody response compared to licensed mouse brain-derived JE vaccine (JE-MB)**
 - **Proportion of JE-VC recipients who achieved JE virus PRNT₅₀ titer ≥ 10 as a correlate of protection**
 - **JE-MB had 91% efficacy in a randomized controlled trial in >65,000 children in Thailand in 1984–86**
- **Safety evaluations in ~5,000 adults in clinical trials**
- **Since licensure, >300,000 doses distributed in U.S.**

ACIP recommendations for JE vaccine

- **In June 2009, ACIP approved recommendations for use of JE vaccines in U.S. travelers, including**
 - **JE-VC in adults ≥ 17 years of age**
 - **Inactivated mouse brain-derived JE vaccine (JE-MB) for adults and children ≥ 1 year of age**
- **In February 2011, ACIP approved recommendations for a booster dose of JE-VC**
- **JE-MB is no longer manufactured or available**
 - **Estimated 2,000-3,000 doses distributed to pediatric providers from 2002-2009**
 - **Options for obtaining JE vaccine for U.S. children were published in MMWR in May 2011**

ACIP JE Vaccine Workgroup activities

- **Reactivated the workgroup in October 2012**
- **Met 13 times to discuss JE-VC in children**
 - **Reviewed epidemiology of JE in travelers**
 - **Reviewed JE-VC safety and immunogenicity data**
 - **Performed GRADE evaluation**
 - **Developed proposed recommendations**
- **Two previous presentations to ACIP on this topic**
 - **October 2012: Workgroup charge and plans**
 - **February 2013: JE and JE vaccine for travelers**

ACIP JE Vaccine Workgroup members

ACIP members

Joseph Bocchini (Chair)

Lorry Rubin

Designated federal officer (CDC)

Marc Fischer (NCEZID/DVBD)

Liaison representatives

Cody Meissner (AAP)

Robert Schechter (AIM)

Patsy Stinchfield (NAPNAP)

Ex Officio members

Jorge Carrillo (DoD)

Doran Fink (FDA)

Jesse Geibe (DoD)

Lewis Markoff (FDA)

Pat Repik (NIH)

Invited consultants

Elizabeth Barnett

Lin Chen

Paul Cieslak

David Shlim

Agenda for JE vaccine session

**Safety and immunogenicity of JE-VC
in children**

**Katrin Dubischar-Kastner
(Intercell Biomedical)**

GRADE evidence for JE-VC in children

Marc Fischer (CDC)

**Recommendations for use of JE-VC
in children (vote; no VFC vote)**

Marc Fischer (CDC)