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JE vaccines at a glance

There are two types of JE vaccines widely available in Asia and several others that will become available in the region over the next few years. Some countries have conducted routine immunization with an inactivated, mouse brain-derived JE vaccine for many years. The live, attenuated SA 14-14-2 vaccine has been used in China for almost 20 years and more recently in several other countries. The table below provides an overview of the JE vaccines currently available in Asia, and information on new vaccines in development follows beneath the table.

	Live, attenuated SA 14-14-2 vaccine	**Inactivated, mouse brain–derived vaccine**
Presentation	• 5-dose or single-dose vial. • Lyophilized powder requiring reconstitution with supplied diluent.	• 10-dose or single-dose vial. • Lyophilized or liquid.
Primary series	• Single dose	• Two doses given at an interval of 1–4 weeks
Timing of primary series	• Aim is to provide protection as early as needed according to local JE epidemiology and to ensure ease of administration. • Can be co-administered with measles vaccine; therefore, the scheduled EPI visit at nine months of age provides an ideal opportunity for immunization.	• Schedules vary from country to country, but primary series commonly commences at 12 months of age. • May be co-administered with measles, DPT, and polio vaccines.
Boosters	• Boosters are unlikely to be required in countries with ongoing JE virus transmission, but this must be confirmed by monitoring of long-term efficacy. • Studies have already documented ongoing protection from a single dose for a minimum of five years in a JE-endemic area.	• First booster dose required after one year. • Repeated boosters are required. Schedules vary from country to country.
Administration	• 0.5 mL dose given by subcutaneous injection.	• 1 mL dose (0.5 mL for children <3 years) (Nakayama strain vaccine), given by subcutaneous injection. • For Beijing strain vaccine, equivalent doses are 0.5 mL or 0.25 mL.
Storage and use after reconstitution	• Stored and transported between 2°C and 8°C. • Manufacturer recommendations suggest that vaccine should be used within one hour of reconstitution, but data exist on reconstituted vaccine stability for longer periods and local recommendations may apply.	• Stored and transported between 2°C and 8°C. • Should be used within six hours of reconstitution.
Manufacturers	• Chengdu Institute of Biological Products (CDIBP) is the only manufacturer authorized to export this vaccine from China.	• BIKEN, Japan has been the largest manufacturer and international distributor but has ceased production. • Other manufacturers are found in South Korea, Taiwan, Thailand, and Vietnam.
Availability of supply	• Guaranteed supply for 20 years to meet market needs.	• The primary producer (BIKEN, Japan) has stopped production. India has also stopped production. • Increasing supply problems are expected in the coming years as manufacturers scale back production with the availability of new and improved JE vaccines.
Countries with experience using vaccine	• Public sector: China (since 1988), Nepal (since 1999), India (since 2006); Private sector: South Korea (since 2001), Thailand (since 2007).	• India, Japan, Malaysia, South Korea, Sri Lanka, Taiwan, Thailand, and Vietnam (used for up to 20 years in some countries).

Cost	• CDIBP established a maximum public sector price to allow import and introduction in lower-income endemic countries in Asia (Gross National Income per capita <US$1,000) for use in the public health system through 2026. • The price per dose for eligible countries is comparable to the EPI measles vaccine.	• The price can vary widely and fluctuate annually, due to production by many manufacturers in several countries. Currently, countries in Asia report paying up to US$4.50 per dose. • Price is also compounded due to this vaccine's multi-dose schedule.
Safety	• WHO's Global Advisory Committee on Vaccine Safety acknowledged the vaccine's excellent safety and efficacy profile.[1] • Transient fever may occur in 5–10% of recipients; and local reactions, rash, or irritability in 1–3%. • Neither acute encephalitis nor hypersensitivity reactions have been associated with this vaccine.	• Approximately 20% of recipients experience local reactions or mild systemic symptoms, including headache, myalgia, gastrointestinal symptoms, and fever. • Rare allergic reactions or hypersensitivity (about 1 in 10,000). • Although extremely rare, severe adverse events following vaccination have been recognized, including demyelinating neurologic events, such as acute disseminated encephalomyelitis.
Efficacy	• Studies in an endemic area of Nepal reported efficacy of a single dose of 99.3% in the same year and 98.5% one year later.[2, 3] At 5 years the protective efficacy was 96.2%.[4] • Although one early case control study in China found 80% vaccine efficacy in children receiving a single dose, other field trials in China have yielded protective efficacy rates above 95%.	• Efficacy of 80–91% after a 2-dose primary series and ongoing protective efficacy over 90% following a booster dose[5].
WHO prequalification and licensure	• Not prequalified, but file is in preparation for submission. • Licensed in several Asian countries: China, India, Laos, Nepal, South Korea, Sri Lanka, and Thailand.	• Not prequalified and no plans for prequalification. • Licensed in many Asian countries, including India, Japan, Malaysia, South Korea, Sri Lanka, Taiwan, and Thailand.

The current status of other JE vaccines is listed below. None are yet licensed for use in children, the primary target population for JE immunization in Asia, but licensure is likely in the next few years.

ChimeriVax-JE vaccine (Sanofi Pasteur/Acambis)

- Live, recombinant vaccine (uses Yellow Fever 17D as backbone and SA 14-14-2 JE vaccine strain).
- Late-stage development; possible adult licensure in 2009–2010.
- Pediatric clinical trials in progress in India, Thailand, and Philippines; possible pediatric licensure 2010.

IC51 JE vaccine (Intercell/Novartis/Biological E.)

- Inactivated vaccine derived from the attenuated SA-14-14-2 JE virus strain grown on Vero cells.
- Licensed for adults in early 2009 in Australia, Europe, and United States.
- One pediatric clinical trial completed in India and other trials planned; possible pediatric availability in 2011.
- Intercell established a partnership with Biological E. for production of the vaccine in India for distribution to countries of south and southeast Asia.

Inactivated, Vero–cell derived JE vaccine (BIKEN and Kaketsuken, Japan)

- Inactivated vaccines derived from the Beijing JE virus strain grown on Vero cells.
- Both companies have vaccine in late-stage development; possible pediatric licensure of at least one vaccine in Japan in 2009.

[1] World Health Organization. Global Advisory Committee on Vaccine Safety, 9-10 June 2005. *Weekly Epidemiological Record.* 2005;80(28):242–243.
[2] Bista M, et al. Efficacy of single-dose SA 14-14-2 vaccine against Japanese encephalitis: a case control study. *Lancet.* 2001;358(9284):791–795.
[3] Ohrr H, et al. Effect of single dose of SA 14-14-2 vaccine 1 year after immunization in Nepalese children with Japanese encephalitis: a case-control study. *Lancet.* 2005;366(9494):1375–1378.
[4] Tandan J, et al. Single dose of SA 14-14-2 vaccine provides long-term protection against Japanese encephalitis: a case-control study in Nepalese children 5 years after immunization. Vaccine. 2007; 25(27):5041–5045.
[5] Halstead SB, Tsai TF. Japanese Encephalitis Vaccines. In: Plotkin SA, Orenstein WA *Vaccines, 4th ed.* Philadelphia: Saunders; 2004.