PUBLIC ASSESSMENT SUMMARY REPORT – Japanese Encephalitis Vaccine, Live (Human)

What is JEV, Live?

The Japanese Encephalitis (JE) Vaccine, Live, is a preparation of live attenuated Japanese Encephalitis virus (strain SA 14-14-2) grown on monolayers of SPF hamster kidney cell cultures. After cultivation and harvest appropriate stabilizers are added into the virus suspension, which is then lyophilized. The major components of the final vaccine are: live attenuated virus (strain SA 14-14-2), human serum albumin, gelatin, sucrose, lactose and carbamide. After lyophilization, the live Japanese encephalitis vaccine is a powder that looks like a light yellow crisp cake. It is stored and transported at 2- 8°C and protected from light.

JEV, Live is a vaccine with the following composition:

Ingredient	Quantity/vial (1 dose)	Quantity/vial (5 dose)
Live attenuated JE virus strain SA 14-14-2	≥ 5.7 log PFU/mL ≥ 5.4 log PFU/dose	≥ 5.7 log PFU/mL ≥ 5.4 log PFU/dose
Gelatin	*4.8 mg*	*6.4 mg*
Sucrose	*21 mg*	*28 mg*
Lactose	*21 mg*	*28 mg*
Carbamide	*2.4 mg*	*3.2 mg*
Human serum Albumin	*0.9 mg*	*2.4 mg*

Single dose lyophilized should be reconstituted with 0.5mL of sterilized water for injection (WFI).
Five-dose lyophilized should be reconstituted with 2.5mL of phosphate buffered saline (PBS).

Container

JE vaccine, Live is dispensed into 2ml CFDA, YBB00292005-2 (glass containers for pharmaceutical use) glass vials which are sealed with chloride butyl rubber stoppers and capped with flip off aluminium caps (blue 1 dose and green for 5 dose vial).

Real time and accelerated stability review supports the use of a VVM type 14. The VVM is attached to the flip off cap.

The bulk, final vaccine and PBS used as the diluent for 5 dose vaccine are produced by Chengdu in China.

WFI, diluent for 1-dose Japanese encephalitis vaccine is purchased from: Jiangsu Desano Pharmaceutical Co., Ltd

What is JEV, Live used for?

JE vaccine, Live is for active immunization of one dose to healthy children from 8 months of age, as well as for children and adults who intend to enter the endemic area from non-endemic areas.

A case-control study conducted in Nepal in 2005 with 239 subjects showed that a single primary dose from 8 months of age can provide at least 5 years of protection. More data on single dose of JEV, Live are difficult to obtain because, in some countries for programmatic purposes a booster dose at 2 years old is recommended.

How is JEV, Live used?

The recommended use will be the same as other live-attenuated viral vaccine: 4 weeks apart from other viral vaccine injection.

What are the vaccine characteristics?

JEV, Live should be stored at 2-8°C, protected from light. Under these recommended storage conditions, the vaccine is stable for 18months after the date of manufacture.

The vaccine does not contain a preservative.
Multi-dose vials once reconstituted should be used during the immunization session or within 6 hours whichever comes first. The unused doses should be discarded.

Cold chain volume per dose for 1 dose and 5 dose vaccine in the secondary carton are 21.2 cm3 and 4.2 cm3 respectively.

Who is the regulatory authority responsible for its oversight vis a vis WHO?

The first JEV, Live was licensed in 1988 in China, its country of manufacture, by Ministry of Public Health. And the new dedicated production facility was approved by Chinese Food and Drug Administration (CFDA) on 16 November 2011.

The vaccine is also licensed in other countries (India, South Korea, Thailand, Nepal, Sri Lanka, DPRK, Laos, Cambodia, Burma, Malaysia and Vietnam).

How has JEV, Live been studied from the clinical point of view?

Extensive “historical” long-term effectiveness clinical trials, involving around 835,000 subjects, were undertaken in China during the 1980s and 1990s prior to introduction and widespread use. It is estimated that over 400 million doses of CDIBP JE vaccine, Live have been used in China, Korea and India and other registered countries.

Evidence for immunogenicity is extensive with ~90% seroconversion shown in most trials and substantial levels of neutralizing antibody exceeding the agreed protective level of 1:10.
Evidence of rapid and extensive impact on the incidence of disease in areas of vaccine use is provided, supported by case-control studies in Nepal and India.
The submission of the PSF was based on available data of the manufacturing of the vaccine in a new facility which obtained the GMP certification from the National Regulatory Authority (CFDA) on 16 November 2011 and clinical data gathered from the old facility. A bridging clinical study was initiated in January 2012 and the results were considered sufficient to support the consistency of 3 lots manufactured in the new facility and the comparability, in terms of immunogenicity, of the vaccines manufactured in the new and the existing facility.
It should be noted that the applicant has provided no information to show that it has in place a safety surveillance system for gathering and critically reviewing spontaneous AEFI (Adverse Event Following Immunization) reports, especially in routine use as distinct from clinical trials, or to produce Periodic Safety Update Reports.
Chengdu Institute of Biological Products Co., Ltd. agreed as post-prequalification commitment to conduct a phase IV study to assess the safety and immunogenicity of the vaccine in HIV-positive individuals.

Other information about evaluation of JEV, Live:

As part of the prequalification process for JEV, Live, the Product Summary File and the responses provided by manufacturer to observations made by WHO has been reviewed for quality, safety and efficacy by a team of WHO experts, and found to meet WHO requirements of WHO TRS 963, Annex 1.
Manufacturer manufacturing facility was audited by a WHO team of experts in date and found in compliance with WHO GMP requirements [WHO TRS 822, Annex 3; TRS 961, Annexes 2, 3 and 6].

WHO has conducted independent testing of batches of the vaccine for critical release parameters in contracted laboratories qualified by WHO for the purpose, and results obtained were in compliance with the quality specifications of the product.

This summary was last updated and published on 12 Nov 2013