

Safety of CD-JEV: A proven tool for JE prevention

There is no cure for Japanese encephalitis (JE), and vaccination is the only way to prevent the disease. Introducing JE vaccines into routine immunization programs in endemic countries is the most effective way to protect children from JE. The live attenuated CD-JEV vaccine is safe, efficacious, and the most affordable JE vaccine available. CD-JEV was prequalified by the World Health Organization (WHO) in 2013, passing rigorous manufacturing and safety standards. The WHO's 2015 position paper on JE vaccines states that very few serious adverse events following immunization (AEFIs) have been reported following CD-JEV vaccination, and CD-JEV is considered safer than older, mouse brain-derived vaccines.¹

CD-JEV OVERVIEW

CD-JEV is a live attenuated JE vaccine manufactured by the Chengdu Institute of Biological Products in China. It is given via subcutaneous injection in a single dose of 0.5 mL to adults and children 8 months of age and older.

As of early 2018, more than 400 million doses of CD-JEV have been administered. China first introduced CD-JEV in 1988, followed by India in 2006. Today, the vaccine is used in 12 countries.

SAFETY IN CLINICAL TRIALS

As of early 2018, there have been no vaccine-related serious AEFIs in 14 clinical trials assessing the safety of CD-JEV in over 350,000 children. Six early trials were done in China among children 6 months to 6 years of age.²⁻⁷ Two studies were conducted in South Korea among children 1 to 6 years of age and children under 1 year, respectively.^{8,9} One study among children 9 to 15 months of age was conducted in Thailand.¹⁰

PATH conducted five other safety trials in the Philippines, Sri Lanka, and Bangladesh. The results of many of these trials helped inform the WHO prequalification of CD-JEV.

In 2005, PATH sponsored a Phase 3 study of co-administering measles vaccine and CD-JEV to infants in the Philippines. Not only did the study find CD-JEV to be safe

CD-JEV: SAFETY BY THE NUMBERS

- Years of use in immunization programs: **30**
- Countries using CD-JEV: **12**
- Doses administered: **>400 million**
- Earliest age for administration: **8 months**
- Children vaccinated in 14 clinical safety trials: **>350,000**
- Vaccine-related serious adverse events in clinical safety trials: **0**
- Year of WHO prequalification: **2013**

and immunogenic, but it also showed that co-administration did not reduce the effectiveness of measles vaccine.¹¹

PATH also sponsored a Phase 4 study in the Philippines in 2015. While not yet published, early results from this study confirm the safety of CD-JEV when given concurrently with measles-mumps-rubella vaccine at 9 months of age. The results of these two studies show that CD-JEV can be safely given alongside other vaccines as part of countries' national immunization programs.

In Sri Lanka, PATH conducted two Phase 4 CD-JEV clinical trials in 2007. One corroborated the results from the Philippines study that CD-JEV is safe and immunogenic when given concurrently with measles vaccine.¹² The other found that CD-JEV is safe and immunogenic for older children who had previously received two or three doses of the inactivated mouse brain-derived JE vaccine.¹³

In Bangladesh, PATH sponsored a Phase 4 study of lot-to-lot variation in 2012, which found CD-JEV to be consistently safe and immunogenic.¹⁴

A PROVEN RECORD IN ROUTINE USE

Due to its long history and widespread use, CD-JEV has a large safety database.¹⁵ The most commonly observed reactions are minor, such as fever or injection site pain. In a 2014 review of population-based AEFI surveillance in Guangdong Province, China, only 36 serious AEFIs were



A child in Laos receives CD-JEV as part of a national JE vaccination campaign in 2014. PATH/Aaron Joel Santos

reported among 23.3 million infants vaccinated with CD-JEV.¹⁶ In addition, in a 2016 AEFI review in India, only 53 AEFI deaths were reported among over 145 million children under 15 who have been immunized with CD-JEV in 20 Indian states between 2006 and mid-2016, and none of them were caused by the vaccine.¹⁷

While passive surveillance systems can result in underreporting of AEFIs, WHO has reviewed both population-based and clinical trial safety data for CD-JEV on multiple occasions and has confirmed the vaccine's excellent safety profile.¹

A WHO-RECOMMENDED VACCINE

The WHO Strategic Advisory Group of Experts on Immunization reviewed CD-JEV safety data in 2013 and concluded that CD-JEV is well tolerated across a wide range of ages and can be safely given to children as young as 8 months of age.¹⁸ Additionally, the WHO Global Advisory Committee on Vaccine Safety has consistently given CD-JEV an excellent safety rating.¹⁹

Given CD-JEV's proven record of safety, efficacy, and public health impact in JE-endemic settings, WHO recommends its use in all countries suspected to have a JE burden.¹ There are no contraindications for CD-JEV among children without previous JE infection, and the vaccine has maintained prequalification since 2013.

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