

Dengue Vaccines: Expectations and Reality

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Dengue is now one of the most rapidly-spreading mosquito-borne viral infectious diseases. It is endemic in tropical and subtropical countries and areas. Half of the world's population is now at risk of dengue, with an estimated 100 - 400 million infections occurring each year.¹ Over the previous two decades, dengue has become established as endemic in Bangladesh and in the year 2023, as of September 27, a total of 2,64,062 cases and 1,317 deaths have been recorded from all 64 districts of the country.² Along with optimum treatment and other public health measures, vaccines are showing lights in reducing clinical cases, morbidity and mortality.

Two vaccines are currently commercially available in some countries. Chimeric yellow fever virus-dengue virus (DENV) tetravalent dengue vaccine (CYD-TDV) (Denvaxia made by Sanofi Pasteur) is a live attenuated, tetravalent vaccine, which was approved by the European authorities and recommended by the World Health Organization (WHO) in 2018 for people aged 9 to 45 years with confirmed previous dengue virus infection and for those who live in endemic regions.³⁻⁵ United States Food and Drug Administration (FDA) approved CYD-TDV in 2019 and the Advisory Committee on Immunization Practices (ACIP) of the United States Centers for Disease Control and Prevention (CDC) officially recommended it for children between 9 and 16 years with past dengue virus infections and children residing in endemic areas.^{6,7} It is not recommended for travellers from non-endemic areas and those without a past infection, as subsequent infections may produce severe disease, probably through antibody-dependent enhancement. It is administered in three doses, 6 months apart. CYD-TDV was found effective in 57-61% against virologically confirmed dengue of any severity and in 80-95% against dengue haemorrhagic fever or dengue virus infection requiring

hospitalization. Takeda's candidate dengue vaccine (TAK-003) (Qdenga made by Takeda) is a tetravalent vaccine administered in two doses, three months apart, among people irrespective of past dengue virus infection. In August 2022, the Indonesian FDA approved TAK-003 for use in individuals six years to 45 years of age; TAK-003 was approved in the European Union in December 2022.⁸⁻¹⁰ Phase 3 trials revealed its overall efficacy in 73.3% cases at 18 months.

Tetravalent vaccine TV-003/005 is an admixture of monovalent vaccines, those were developed by National Institute of Allergy and Infectious Diseases (NIAID), tested separately for safety and immunogenicity. The vaccine passed phase I trials and phase II studies in the United States, Thailand, Bangladesh, India and Brazil. With 3 years of follow-up, the single-dose tetravalent dengue vaccine, TV005, was found well tolerated and immunogenic for all four serotypes in Bangladeshi children to adults, including individuals with no previous dengue exposure.¹¹ Tetravalent dengue virus purified inactivated vaccine (TDENV PIV) is undergoing phase I trials as part of a collaboration between GlaxoSmithKline (GSK) and the Walter Reed Army Institute of Research (WRAIR). Merck is studying recombinant subunit vaccines expressed in *Drosophila* cells. In 2011, the Naval Medical Research Center attempted to develop a monovalent deoxy-rhyboneucleic acid (DNA) plasmid vaccine but early results showed it to be only moderately immunogenic.

In spite of efficacy and safety, the types and quantity of dengue vaccines are lagging far behind the global requirements. Till date, none of the approved vaccines are commercially available in Bangladesh. Along with proper treatment, importance of aborting transmission of dengue virus infection by strengthening other general public health measures remain important.

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