Supplementary Digital Content 1. Methods

Additional exclusion criteria.

Exclusion criteria included self-reported Hepatitis B or Hepatitis C infection; known or suspected congenital or acquired immunodeficiency; receipt of immunosuppressive therapy within the preceding six months; long-term systemic corticosteroid therapy within the preceding three months; a previous severe reaction to pertussis, diphtheria or tetanus vaccine including immediate anaphylaxis, encephalopathy within seven days or seizure within three days of receiving the vaccine; known systemic hypersensitivity to any of the vaccine components, or history of a life-threatening reaction to CYD-TDV; and history of Guillain-Barré syndrome.

Study protocol amendment

During the course of this study, an exploratory analysis of data from CYD-TDV clinical trials revealed a difference in the efficacy and safety profile of CYD-TDV in recipients who were dengue seropositive before vaccination compared with those who were dengue seronegative (1). Sanofi Pasteur presented this analysis to the IDMC in an *ad hoc* meeting held in November 2017. The IDMC concluded that the exploratory study provided strong evidence that merited protocol amendments, so that only baseline dengue seropositive participants would be further vaccinated with CYD-TDV. Based on the IDMC recommendation, this trial was paused to allow for amendment of the protocol, and so that the baseline samples from all vaccinated participants could be tested for dengue antibodies. Participants were then informed of their baseline dengue serostatus. This protocol amendment was approved by an independent ethics committee; however, no response on the amendment was received from the regulatory heath authorities in the Philippines. As a consequence, the vaccination schedule was substantially delayed and the decision was made to prematurely terminate the study after an 18-month pause, at which point most participants had received two doses of the CYD-TDV. No study participant received the third dose of CYD-TDV.

**References**

1. Sridhar S, Luedtke A, Langevin E, et al. Effect of Dengue Serostatus on Dengue Vaccine Safety and Efficacy. The New England journal of medicine. 2018;379:327–340