

PRESS STATEMENT BY SANOFI PASTEUR PHILIPPINES

Sanofi updates information on dengue vaccine in Philippines

- New analysis of long-term dengue vaccine data from clinical studies found differences in vaccine performance in individuals with or without dengue infection prior to vaccination
- Sanofi is working with Philippines Food and Drug Administration (FDA) to update product label to reflect this new information
- Sanofi has started to share this new data with all stakeholders including private healthcare professionals and is committed to keep on cooperating with Philippines Department of Health (DOH) for its on-going review of the public dengue vaccination program

Manila, Philippines, 4 December, 2017 – Sanofi Pasteur recently released a new supplementary exploratory analysis of the long-term follow-up of its dengue vaccine. This is part of the company's ongoing commitment to evaluate the long-term impact of the dengue vaccine and is also consistent with the recommendation put forward in the World Health Organization (WHO)'s position on the vaccine.

These new findings demonstrate a different profile of the dengue vaccine for those with or without a previous dengue infection. In individuals who have been previously infected by dengue virus, there is a clear and sustained benefit of being vaccinated with the dengue vaccine up to 6 years following the first injection. In individuals who have not been previously infected by dengue virus, there is an increased risk of hospitalization for dengue and severe dengue, predominantly Grade I or II Dengue Hemorrhagic Fever (DHF). Severe dengue can be categorized from milder to more severe forms as DHF I, II, III and IV according to WHO. DHF IV was not seen in those vaccinated. We have shared this new data in full transparency with the Philippine Food and Drug Administration (FDA) and the Department of Health (DOH). Furthermore, the severe dengue observed in vaccinated individuals was not clinically different from that reported in unvaccinated people in the studies. All study participants who got severe dengue, whether vaccinated or not, have fully recovered.

Consequently, we are proposing an update to the current vaccine label to ensure that physicians can make appropriate vaccination decisions with their patients to enhance the impact of the vaccine in the Philippines, where majority have been infected by dengue by the time they reach adolescence.

The Company has also started to inform the new label proposal with private healthcare professionals to help them in the assessment of benefit/risk of vaccination of their patients.

Dengue is highly endemic in the Philippines, and since 2010 there has been a reported average of over 160,000 cases every year, mostly in children and teenagers¹. Studies have shown that in individuals aged 9 to 14 years old, 9 out of 10 of them would have already been infected by

¹ Dengue Cases. Report of the Philippines Epidemiology Bureau, Department of Health. Available at: <http://www.doh.gov.ph/taxonomy/term/119?page=1>

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the dengue virus^{2, 3}. However, not all people who have been infected by the dengue virus are aware, because around 75% of them do not have any symptoms.⁴

About dengue vaccine

The dengue vaccine does not contain viruses that can make people ill with dengue or severe dengue. Severe dengue infections are uncommon complications of dengue disease, occurring in an estimated 0.5% of cases manifesting symptoms of dengue annually.⁵

Sanofi Pasteur's dengue vaccine has been clearly proven to be safe and effective in the prevention of dengue in people 9 years of age and older living in endemic settings. Phase III clinical studies conducted in over 30,000 study participants from 10 countries in Latin America and Asia show a pooled efficacy of 65.6% against all four serotypes of dengue; 80% efficacy against hospitalizations due to dengue and 93% efficacy against severe disease in the study population 9 years of age and older over the 25 month follow up period of the study program.⁶

The continuing long-term safety evaluation of the vaccine shows significantly fewer hospitalizations due to dengue in vaccinated vs. unvaccinated participants 9 years and older.^{7,8,9,10}

About Sanofi

Sanofi is dedicated to supporting people through their health challenges. We are a global biopharmaceutical company focused on human health. We prevent illness with vaccines, provide innovative treatments to fight pain and ease suffering. We stand by the few who suffer from rare diseases and the millions with long-term chronic conditions.

With more than 100,000 people in 100 countries, Sanofi is transforming scientific innovation into healthcare solutions around the globe.

Sanofi, Empowering Life

² Alera MT, Srikiatkachorn A, Velasco JM, Tac-An I a, Lago CB, Clapham HE, et al. Incidence of Dengue Virus Infection in Adults and Children in a Prospective Longitudinal Cohort in the Philippines. *PLoS Negl Trop Dis* [Internet]. 2016 Feb [cited 2016 Feb 5];10(2):e0004337.

³ L'Azou et al. *N.Eng J Med* 2016;374 (12): 1155-66

⁴ Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, et al. The global distribution and burden of dengue. *Nature* [Internet]. 2013 Apr 25 [cited 2013 May 22];496(7446):504–7. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/23563266>

⁵ <http://www.who.int/mediacentre/factsheets/fs117/en/>

⁶ Hadinegoro, S.R. et al. Efficacy and Long-term Safety of a dengue vaccine in regions of endemic disease. *N Engl J Med* 2015;373:1195-206. DOI: 10.1056/NEJMoa1506223

⁷ Gailhardou et al. Safety overview of a recombinant live-attenuated tetravalent dengue vaccine: pooled analysis of data from 18 clinical trials. *PLoS Negl Trop Dis*. 2016 Jul 14;10(7):e0004821. doi: 10.1371/journal.pntd.0004821

⁸ Cortez et al. Long-Term Safety of a CYD-TDV Dengue Vaccine in Latin American Dengue Endemic Countries.– Poster LB-5290 ASTMH, Nov 2016

⁹ Limkittikul, Kriengsak, et al. Long-term (6-year) follow-up in Thai children from phase IIb proof of concept efficacy study of cyd-tdv dengue vaccine. Presentation at ACPID, Bangkok, Thailand, 7 – 10 November 2016.

¹⁰ Maria Rosario Capeding, Carina Frago et al Long-Term Safety (Year 5) of the Recombinant Live-Attenuated Chimeric-Yellow Fever-Dengue Virus Tetravalent Dengue Vaccine (CYD-TDV) in Asian Phase III Efficacy Trial. Presentation at the 20th Annual Conference on Vaccine Research 24 April 2017