DOH Dengue Task Force

Summary of the Discussions of the National Expert Panel to Provide Technical Assistance related to the CYD-TDV Vaccine

January 18, 2018

Note: A National Expert Panel was created by the Department of Health (DOH) on January 10, 2018 to provide technical assistance to the DOH Dengue Task Force on scientific/medical concerns related to the live, attenuated, chimeric yellow fever-dengue virus, tetravalent dengue vaccine (CYD-TDV). The report below summarizes the discussions and recommendations of the Expert Panel as of January 17, 2018, based on documents provided by the DOH, Sanofi-Pasteur, dengue vaccine updates from the World Health Organization, and the Expert Panel's own review of existing evidence and the epidemiological context of dengue in the country. Additional questions and information have been requested from Sanofi-Pasteur, and may have a bearing on subsequent assessments by the Expert Panel.

I. Safety and Efficacy of the Dengvaxia Vaccine

a. Dengvaxia may pose an increased risk of dengue (hospitalized and severe virologically confirmed dengue) among seronegative individuals, regardless of age. The sample size involving the sub-cohort of seronegative children was too small to demonstrate a statistically significant increase, but the direction and trend towards harm is cause for serious concern.

b. There were some vaccinated children who were likely to have had DHF III/IV– i.e., “severe” dengue using the 2009 WHO classification.

c. Dengvaxia can improve outcomes in seropositive individuals (reduction in symptomatic, hospitalized, and severe virologically confirmed dengue), probably by a booster effect on pre-existing antibodies.

d. There is no readily available, accurate test to rapidly identify serostatus of individuals prior to vaccination.

II. Use of Dengvaxia Vaccine in a Mass Immunization Program

a. Ethics in public health programs dictates that the following universal principles should be followed:

- Respect for persons (Informed consent)
- Beneficence (Balancing benefits and harm)
- Non-maleficence (Identification and mitigation of risks)
- Justice (Equity, sharing of burden and risks, selection of participants)

b. Given the uncertainties and the potential risks, serologic testing should be done and/or history of dengue illness should be ascertained prior to vaccination. Conditions that are contraindications for Dengvaxia use should be elicited through careful interview, the use of an immunization checklist, and a thorough physical examination. Seronegative individuals or, in the absence of a serologic test, absence of evidence of prior dengue exposure, should not be vaccinated.

c. In seropositive individuals in the targeted pediatric age group, the absolute risk reduction in the incidence of hospitalized and severe dengue from Dengvaxia, as estimated from the Dengvaxia clinical trials, is not big enough to justify the enormous costs for a publicly funded mass immunization program.

III. Recommendations

a. **As a precautionary measure, the Dengvaxia mass immunization program should remain suspended at this time. In view of the sparse information from the clinical trials on the consequences of administration of less than three doses of Dengvaxia, a firm recommendation to complete the schedule of vaccination cannot be given. However, for children with incomplete doses who had been confirmed to have had dengue before Dengvaxia vaccination, completion of doses may be protective.**

b. The development of the dengue anti-NS1 IgG test by indirect ELISA to determine pre-vaccination serostatus of Dengvaxia recipients is urgently needed to identify the children at risk for severe dengue. The presence of dengue NS1 antibodies may differentiate past natural dengue infection from previous exposure to Dengvaxia vaccination.

c. The serostatus of vaccinated individuals should be determined as soon as possible. Pending the availability of the dengue anti-NS1 IgG test, serum should be collected from all vaccinees at the earliest possible time to prevent clouding of results because dengue infections from wild type dengue virus may occur through time. Sera may be stored in a bank while the test is under development.

d. There should be a no-fault compensation scheme for vaccine injuries. The medical needs of vaccine recipients at risk should be provided.

e. An enhanced surveillance and monitoring system for all Dengvaxia recipients must be established at the soonest possible time. (THE FINAL GUIDELINES WILL BE ATTACHED).

f. For vaccinated subjects, the Department of Health should institute mechanisms to provide timely access to appropriate care, including serum samples for further testing, in the event of any illness (as defined in the enhanced surveillance and monitoring guidelines) that the vaccine recipient may experience.

g. The DOH should review its manual of procedures and criteria for adding a new vaccine in the Expanded Program of Immunization and/or mass immunization programs to cover all stages, from decision making to implementation and monitoring.