

From: Polo, Stephanie
Sent: Friday, November 30, 2018 12:15 PM
To: 'Patrick.O'Neil@sanofi.com' <Patrick.O'Neil@sanofi.com>
Cc: Prutzman, Kirk C <Kirk.Prutzman@fda.hhs.gov>; Naik, Ramachandra <Ramachandra.Naik@fda.hhs.gov>
Subject: STN 125682-Information Request

Dear Mr. O'Neil,

We have the following request for additional information regarding STN 125682 (Dengue Tetravalent Vaccine [Live, Attenuated]):

1. In the Risk Management Plan, v 5.0, submitted on September 28, 2018, in Amendment 3, reference is made to a Guide for Health Care Providers (HCPs) and a survey to assess the effectiveness of the HCP guide. Reference is also made to a “synopsis of the effectiveness survey [to] be provided at a later date.” Please provide details of each of the components of the planned HCP guide, including a sample guide, if available, as well as the synopsis of the effectiveness survey. Please also provide details regarding the planned method of distributing both the guide and the survey to HCPs.
2. Please clarify the following items regarding the document, “Safety Information Amendment,” which was submitted in Module 1.11.2 on October 19, 2018, in Amendment 8:
 - a. Reference is made to a document from the Philippines Department of Health at http://home2.doh.gov.ph/ais_public/aopdf/ao2018-0004.pdf. The document cannot be accessed via the link provided. Please submit the document in its entirety.
 - b. The total number of adverse events (AE) for vaccinees listed does not equal the total of Deaths, Non-fatal Serious and Non-serious AEs for vaccinees
 - i. aged ≥ 9 to <18 years
 - ii. age unreportedPlease clarify.

Age of vaccinee (yr)	Death (n)	Non-fatal Serious (n)	Non-serious (n)	Total (n)
<9†	1	3	55	59
≥ 9 to <18	28	281	1283	1593
≥ 18 to ≤ 45	5	89	533	627
>45	0	4	107	111
Age unreported	17	59	305	380
All ages	51	436	2283	2770

3. The following comments pertain to SOP Q_0144050, “Titration of Infectious Particles and Identification of CYD Dengue Vaccine on (b) (4) by CCID₅₀,” which was submitted in Amendment 10 on November 1, 2018:

- a. The SOP does not specify when (b) (4) . Please include this information in the SOP.
- b. The validity criteria in the SOP (page 62) include the following criteria among several others:
 - i. “for each validity control, the titer is within the control limits of the control card.” And the corresponding criteria listed in section 3.2.S.2.4 (subsection 3.1.8) states, “The titer of the validity control sample is within the confidence limits of the control chart.” Please identify the confidence limits in the control card or chart, include them in the SOP, and provide a justification or explanation for the limits.
 - ii. “the statistical calculation indicates that the values obtained are homogeneous.” Please explain how this statistical calculation is performed and include this information in the SOP.
- c. Please submit a revised SOP Q_0144050 to include the changes indicated above.

Please submit your response as an amendment to STN 125682 by Monday, December 10, 2018.

If you have any questions about this communication, please contact Kirk Prutzman, Stephanie Polo or Ramachandra Naik at (301) 796-2640.

Best regards,

Stephanie Polo

Primary Reviewer/Regulatory Project Manager

Center for Biologics Evaluation and Research
Office of Vaccines Research and Review
U.S. Food and Drug Administration
Tel: 301-796-2640
stephanie.polo@fda.hhs.gov



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