



MEMORANDUM

Date: April 22, 2019

To: Administrative file for STN 125682

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Applicant: Sanofi Pasteur

Subject: Review of Analytical Methods used for determining (b) (4), potency and identity for Dengue tetravalent vaccine (live, attenuated) DENG VAXIA

Recommendation: Based on the data reviewed in this submission and its amendments, the analytical methods and their validations are acceptable.

Summary:

This document constitutes the Primary Review Memo from DBSQC for the following analytical methods and their validation, as used for lot release of DENG VAXIA.

1. (b) (4) test for potency and identity of (b) (4) Drug Product
2. (b) (4) test for (b) (4)

Conclusion: Based on the review of the original submissions and amendments, the assays for potency and identity as well as that for (b) (4) are approvable for use in quality control testing for this vaccine.

Background:

Sanofi Pasteur submitted a BLA (STN 125682) for a tetravalent Dengue vaccine on August 31, 2018. The Drug Product (DP) is comprised of four live attenuated virus strains. The constructs used in this vaccine are a chimera of yellow fever and dengue virus. The Chimera Yellow Fever Dengue (CYD) virus was constructed by replacing the pre-membrane and envelope protein genes in yellow fever 17D virus by homologous sequences from dengue virus. Chimeras for dengue virus serotypes 1, 2, 3 and 4 were each constructed. The constructs are expressed separately in Vero cells. The four virus strains are combined and freeze-dried for a single dose in a sterile vial. This vial is reconstituted in 0.4%

sodium chloride and administered by subcutaneous injection. This product is proposed for use against dengue virus serotypes 1,2,3 and 4 in persons 9 to 16 years old who have previously been infected by dengue as confirmed by laboratory results.

Since the viruses are expressed in Vero cells, the presence of (b) (4) is monitored in the (b) (4) prior to release. The potency (b) (4) of the (b) (4) DP are determined prior to release by a Cell Culture Infectious Dose 50% (CCID₅₀) assay. This review is focused on the methods used to determine potency and identity for (b) (4) DP and (b) (4) in the (b) (4).

Documents Reviewed

This is an electronic submission. Information submitted and reviewed includes:


- 125682/0 - 3.2.P.5.2 - Analytical Procedures
- 125682/0 - 3.2.S.4.2 - Analytical Procedures
- 125682/0 - 3.2.P.5.3 - Validation of Analytical Procedures
- 125682/0 - 3.2.S.4.3 - Validation of Analytical Procedures
- 125682/0 - 2.3.P.5 - Control of Drug Product
- 125682/0 - 2.3.S.4 - Control of Drug Substance
- 125682/0 - 3.2.P.5.1 - Specification(s)
- 125682/0 - 3.2.S.4.1- Specification(s)
- 125682/10 - 3.2.5.2 -Analytical Procedures - Q_0144050
- 125682/14 -1.11.4 - Multiple Module Information Amendment
- 125682/20 - 1.11.1 - Quality Information Amendment
- 125682/27- 3.2.P.5.2- Analytical Procedures
- 125682/27- 3.2.P.5.3- Validation of Analytical Procedures

1. Potency (b) (4) by CCID₅₀

Review of Method:


Analysis of potency (b) (4) in the DP (b) (4) is performed using the assay described in document (b) (4)

(b) (4)



Identification of dengue serotype components of the final packaged product (FPP) is performed using

(b) (4)



Information Request and Review

The following Information Request (IR) was submitted to the Sponsor on November 29, 2018,

CBER IR: The following comments pertain to SOP Q_0144050 for Titration of infectious particles and identification of CYD:

The SOP does not specify (b) (4) . Please include this information in the SOP.

Response and Review

