



MEMORANDUM

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Center for Biologics Evaluation and Research (CBER)
Food and Drug Administration (FDA)

To: **Biologics License Application Submission Tracking Number # 125546/0**

Subject: **Review of Analytical Procedures for Drug Substance and Drug Product of**
Biologics License Application for Meningococcal Group B Vaccine
[Identity test for DP; Identity tests for -----(b)(4)-----
-----]

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Applicant: Novartis Vaccines and Diagnostics, Inc.

Product: Bexsero - Meningococcal Group B Vaccine

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1 General Information

1.1 CMC Review Identifiers and Dates

1.1.1 Biologics License Application (BLA) Submission Tracking Number (STN) #: 125546

1.1.2 Submission received by CBER: June 16, 2014

1.1.3 Review completed: October 21, 2014

1.1.4 Material Reviewed

Original BLA: Amendment 1 submitted on July 9, 2014, comprised the rolling BLA submissions.

The following general module sections of the BLA were reviewed: M3 CMC, Quality-Analytical Procedures

1.1.5 Related Master File, INDs and BLAs:

- IND (b)(4): **Recombinant Meningococcal B Vaccine**

2 Executive Summary:

The assay method SOP228563 is properly validated for its intended use for Identity Test of drug product by ---(b)(4)----- . Also, the assay method SOP 63.473 (MenB 961) , SOP 63.474 (MenB 287-953) and SOP 63.475 (MenB 936) are properly validated for their intended use for Identity of - -----(b)(4)----- . The assay method SOP202148 is properly validated for intended use for Identity Test of -----(b)(4)----- . The assay method SOP238751 is properly validated for its intended use for -----(b)(4)----- .

3 Review

3.1 Documents Reviewed

1. Validation Protocol and Report for determination of (b)(4) and Identity of MnB
----- (b)(4)----- (Section 3.2.S.4.2.3) by --- (b)(4)----.
2. Validation Protocol and Report for determination of (b)(4) and Identity of MnB
----- (b)(4)----- (Section 3.2.S.4.2.3) by --- (b)(4)----.
3. Validation Protocol and Report for determination of (b)(4) and Identity of MnB
----- (b)(4)----- (Section 3.2.S.4.2.3) by --- (b)(4)----.
4. Validation Protocol and Report for determination of MnB -----
----- (b)(4)----- (Section 3.2.S.4.2.3) by ----- (b)(4)-----.
5. Validation Protocol and Report (SOP 228563) of the identity test of the
following MenB trivalent and MenB tetraivalent NZ vaccine phases:

----- (b)(4)-----
----- (Section 3.2.P.5.3).
6. Assay Method SOP228563: Identity of Tetraivalent Recombinant Vaccine (287-
953, 936-741, 961c and NZ-OMV) against Meningococcus serogroup B Final
(b)(4), Product in vials and Packaged Product.
7. Validation Protocol and Reports for SOP 238751: -----
----- (b)(4)-----
-----.

3.2 Method Overview

3.2.1 Identity:

The SOP 228563 (DP), SOP 63.473---(b)(4)--, SOP 63.474 ----- (b)(4)-----
-----, SOP 63.475 --- (b)(4)-- and SOP202148 (b)(4) describe the methods for
identification of the MenB antigen and ----- (b)(4)----- final
container of the Meningococcal B group vaccine by --- (b)(4)----- method. This
method is an-----

----- (b)(4)-----

-----.

3.2.2 ----- (b)(4)-----:

----- (b)(4)-----

(b)(4)

3.3 Review of Validation of Identity (ID) Assay of MenB ----(b)(4)----- (Section 3.2.S.4.3)

The validation of the -----
----- (b)(4) -----, was performed in
conformance with ICH Q2(R1) guidelines, for establishing the “Identity” of the MenB
----- (b)(4) -----.

(b)(4)

(b)(4)

----- (b)(4) -----

----- (b)(4) -----

----- (b)(4) -----

3.4 Review of Validation of Identity (ID) Assay of MenB for DP (Section 3.2.P.5.3)

SOP 228563 was validated for the **identity** test of the following MenB trivalent and MenB tetravalent NZ vaccine phases: -----

----- (b)(4) -----

----- (Section 3.2.P.5.3). This SOP describes the method for identification of the MenB antigen components in final

container by --(b)(4)-- method. The SOP was performed in conformance with ICH Q2(R1) guidelines, for establishing the “Identity” of the MenB in the DP.

-(b)(4).

-(b)(4).

3.5 Review of Validation of test method for ----(b)(4)----- (SOP 238751) with respect to -----(b)(4)----- (Section 3.2.S.4.3)

The validation of the assay method SOP 238751 for -----(b)(4)-----
was performed in conformance with ICH Q2(R1) guidelines (Section 3.2.S.4.3). The
method is used for -----

-(b)(4).

-(b)(4)-

[(b)(4)]

[(b)(4)]

The results show that all the validation parameters assessed in the three validation reports (315663.02, 238751VR2, 315685-01) meet the pre-set specifications for repeatability, intermediate precision, accuracy, linearity, specificity, range, LOD and LOQ. The results summarized in the table above demonstrate that the SOP238751 used by the sponsor for -----(b)(4)----- has been properly and fully validated. Also, based on data collected for a number of -----(b)(4)----- considering that there is 50 µg of each of the MenB recombinant protein per 0.5 ml dose. The specification corresponds to --- (b)(4) ---, which is within the Limit of Detection of the test method. The test method is suitable to serve its intended purpose.

3.6 Conclusions

The methods SOP 63.473, SOP 63.474, SOP 63.475 and SOP202148 have been validated for demonstrating the ID of the ----- (b)(4) ----- method, respectively. The method SOP 228563 has been validated for demonstrating the Identity of the four components of MenB recombinant proteins in tetravalent vaccine drug product by --- (b)(4) --- method. The transfer of the assay method SOP 228563 to the --- (b)(4) --- lab was also validated satisfactorily, for testing the ID on MenB component in tetravalent vaccine DP. The specificity parameter was evaluated and all the specifications were met satisfactorily. The method is suitable for the intended purpose and the results are acceptable. The validation of method SOP

238751 for the -----(b)(4)----- has been validated properly and all the parameters of validation- repeatability, intermediate precision, accuracy, linearity, specificity, range, LOD and LOQ met the pre-specified criteria. The assay for -----
---(b)(4)----- has been validated satisfactorily.

These assay methods are approvable.