

## DBSQC/OCBQ ANALYTICAL METHOD REVIEW MEMO

**To:** The file [STN 125770/0]

**From:**

Reviewer	Role	Date finalized	Stamp	Supervisor	Stamp
Hsiaoling Wang, Ph.D.	Lead Reviewer	9/18/2023		Kenneth Phillips, Ph.D.	
Tao Pan Ph.D.	Reviewer	9/18/2023			
Anil Choudhary Ph.D.	Reviewer	10/3/2023		Muhammad Shahabuddin, Ph.D.	
Yen Phan MLS(ASCP) <sup>CM</sup>	Reviewer	9/25/2023		James L. Kenney, D.Sc.	

**Through:** Maryna Eichelberger, Ph.D.  
Division Director, DBSQC/OCBQ

**Applicant:** Pfizer, Inc.

**Subject:** Review of Analytical Methods used for PENBRAYA (b) (4) Drug Product Lot Release

**Recommendation:** Approval

### Executive Summary:

The following analytical methods used for lot release of PENBRAYA and the associated analytic method validations or qualifications, were reviewed:

- (b) (4) for (b) (4) MenA-TT, MenC-TT, MenW-TT and MenY-TT (Hsiaoling Wang)
- (b) (4) MenA-TT, MenC-TT, MenW-TT and MenY-TT (Hsiaoling Wang)
- (b) (4) MenA-TT, MenC-TT, MenW-TT and MenY-TT (Hsiaoling Wang)
- (b) (4) MenA-TT, MenC-TT, MenW-TT and MenY-TT (Hsiaoling Wang)
- (b) (4) for MenACWY-TT DP component (Hsiaoling Wang)

6. (b) (4) for subfamily A and subfamily B for DP MenABCWY (Hsiaoling Wang)
7. (b) (4) I Assays (Hsiaoling Wang)
  - a. Appearance for (b) (4) MenA-TT, MenC-TT, MenW-TT and MenY-TT (Clarity and Color), for MenACWY-TT DP component (before and after Reconstitution) and for DP MenABCWY (after Reconstitution)
  - b. pH for (b) (4) MenACWY-TT DP component
  - c. (b) (4) for MenACWY-TT DP component
  - d. Reconstitution Time for MenACWY DP component
  - e. Extractable Volume for MenB-fHBP DP component and Volume of Injection for DP MenABCWY
8. MenA-TT (b) (4) (Tao Pan)
9. MenC-TT (b) (4) (Tao Pan)
10. MenW-TT & MenY-TT (b) (4) (Tao Pan)
11. Polysaccharide A content (DP) (Tao Pan)
12. MenW-TT, MenY-TT (b) (4) MenC-TT, MenW-TT and MenY-TT (b) (4) (DP) (Tao Pan)
13. (b) (4) (DP) (Tao Pan)
14. Visible Particulates (DP) (Tao Pan)
15. (b) (4) (DP) (Tao Pan)
16. Bacterial Endotoxin (b) (4) (Yen Phan)
17. Sterility (b) (4) DP (Yen Phan)
18. (b) (4) Identity of (b) (4) DP (Anil Choudhary)
19. (b) (4) of MnB (b) (4) (Anil Choudhary)
20. (b) (4) of MnB (b) (4) (Anil Choudhary)
21. (b) (4) of MnB (b) (4) (Anil Choudhary)
22. Polysaccharide Content of MenC in DP Component MenACWY-TT (Anil Choudhary)

Analytical procedures of (b) (4) MnB (b) (4) subfamily A and subfamily B proteins and the MenB-fHBP DP component are the same as those approved for Trumenba® and were reviewed in BLA 125549 and therefore most of them are not covered in this memo. Their associated testing laboratories are qualified to perform these tests under STN 125549.

**Conclusion:** The analytical methods and their validations and/or qualifications reviewed for the PENBRAYA drug substances, drug product components and drug product were found to be adequate for their intended use.

**Abbreviations:**

PS: polysaccharide

PSA: polysaccharide A

PSC: polysaccharide C

PSW: polysaccharide W

PSY: polysaccharide Y

TT: tetanus toxoid

MenA: *Neisseria meningitidis* serogroup A

MnB or MenB: *Neisseria meningitidis* serogroup B

MenC: *Neisseria meningitidis* serogroup C

MenW: *Neisseria meningitidis* serogroup W-135

MenY: *Neisseria meningitidis* serogroup Y

MenA-TT or MenA<sub>AH</sub>-TT: *Neisseria meningitidis* serogroup A - tetanus toxoid conjugate

MenC-TT or MenC<sub>AH</sub>-TT: *Neisseria meningitidis* serogroup C - tetanus toxoid conjugate

MenW-TT: *Neisseria meningitidis* serogroup W - tetanus toxoid conjugate

MenY-TT: *Neisseria meningitidis* serogroup Y - tetanus toxoid conjugate

MnB (b) (4) *Neisseria meningitidis* serogroup B recombinant (b) (4) proteins

MenB-fHbp: Meningococcal group B factor H binding protein

MenACWY-TT: Meningococcal Groups A, C, W-135, Y conjugated to tetanus toxoid

(b) (4)

#### Documents Reviewed:

Information in sections of the original submission that describe control of (b) (4) DP (3.2.S.4 and 3.2.P.5, respectively), including descriptions of (b) (4) DP specifications, analytical procedures of (b) (4) DP and validation of these analytical procedures were reviewed. Additional information in amendments specified by each reviewer were also reviewed.

#### Background:

Pfizer submitted a BLA, STN 125770/0 for PENBRAYA on October 21, 2022. This product is proposed for active immunization of individuals 10 through 25 years of age to prevent invasive disease caused by *Neisseria meningitidis* groups A, B, C, W, and Y.

The (b) (4) component MnB (b) (4) includes *Neisseria meningitidis* serogroup B recombinant (b) (4) subfamily A and B proteins. The (b) (4) components, MenA-TT, MenC-TT, MenW-TT, and MenY-TT, are purified polysaccharides of *Neisseria meningitidis* serogroups A, C, W-135, and Y, conjugated to tetanus toxoid. The MenACWY vaccine is composed of two drug product components: MenACWY-TT and MenB-fHBP. It is a suspension for intramuscular injection after the reconstitution of a single-dose vial of lyophilized MenACWY-TT with the accompanying prefilled syringe of MenB-fHBP. The MenACWY-TT DP component is marketed outside of the US as Nimenrix. Nimenrix was first approved in the European Union on April 20, 2012 for GlaxoSmithKline Biologicals (GSK) and acquired by Pfizer in 2015. The MenB-fHBP DP component is identical to Trumenba vaccine, approved by FDA on October 29, 2014 under BLA 125549 for US market, (b) (4)

1. (b) (4) for (b) (4) MenA-TT, MenC-TT, Men W-TT and MenY-TT (Hsiaoling Wang)

4 pages have been determined to be not releasable: (b)(4)

(b) (4)

Conclusion

Based on the information provided in the original BLA and amendment 12, the methods have been validated for their intended purposes.

2. (b) (4) for (b) (4) MenA-TT, MenC-TT, MenW-TT and MenY-TT  
(Hsiaoling Wang)

(b) (4)

1 page has been determined to be not releasable: (b)(4)

(b) (4)

Conclusion

Based on the information provided in the original BLA and the amendment 12, the method has been validated for its intended purpose.

3. (b) (4) (b) (4) for (b) (4) MenA-TT, MenC-TT, MenW-TT and MenY-TT  
(Hsiaoling Wang)

(b) (4)

4. (b) (4) for (b) (4) MenA-TT, MenC-TT, MenW-TT and MenY-TT  
(Hsiaoling Wang)

(b) (4)

3 pages have been determined to be not releasable: (b)(4)



(b) (4)

Conclusion

Based on the information provided in the original BLA and amendment 12, the method has been validated for its intended purpose.

5. (b) (4) for DP component MenACWY-TT (Hsiaoling Wang)

(b) (4)

2 pages have been determined to be not releasable: (b)(4)

(b) (4)

Conclusion

Based on the information provided in the original BLA and the amendment 12, the method has been validated for its intended purpose.

6. (b) (4) for subfamily A and subfamily B for DP MenABCWY (Hsiaoling Wang)

Introduction

(b) (4)

1 page has been determined to be not releasable: (b)(4)

(b) (4)

Conclusion

Based on the information provided in the original BLA, the method has been validated for its intended purpose.

7. (b) (4) **Assays (Hsiaoling Wang)**

a. Appearance for (b) (4)

MenACWY-TT DP component (before and after reconstitution) and for DP MenABCWY (after reconstitution)

(b) (4)

2 pages have been determined to be not releasable: (b)(4)

(b) (4)

In DP MenABCWY-TT batch analyses, appearance results were all homogeneous white suspension after reconstitution for 1 clinical lot and 6 specification evaluation lots, which were in compliance with the proposed specification.

b. pH for (b) (4) MenACWY-TT DP component

The specifications of pH are (b) (4)

The specification of pH is (b) (4) for MenACWY-TT DP component.

#### Method

(b) (4)

(b) (4)

c. (b) (4) for MenACWY-TT DP component

The specification of (b) (4) of MenACWY-TT DP component is (b) (4)

Method

(b) (4)

d. Reconstitution Time for DP MenACWY

The specification of reconstitution time is (b) (4) sec for MenACWY-TT DP component.

Method

(b) (4)



No method verification report was provided in the submission.

(b) (4)

e. Extractable Volume for MenB-fHBP DP component and Volume of Injection for DP MenABCWY

i) Extractable Volume for MenB-fHBP DP component

The specification for extractable volume for MenB-fHBP DP component is (b) (4)

Method

(b) (4)

ii) Volume of Injection for DP MenABCWY

The specification of volume of injection for DP MenABCWY is (b) (4) 0.5 mL.

Method

(b) (4)

(b) (4)

Conclusion

Based on the information provided in the original BLA and amendment 12, these (b) (4) methods have been verified for their intended purposes.

**8. MenA-TT (b) (4)**

**(Tao Pan)**

(b) (4)

12 pages have been determined to be not releasable: (b)(4)

(b) (4)

## 11. Polysaccharide A Content (DP) (Tao Pan)

### Introduction

PSA content in lyophilized MenACWY-TT DP is determined using an (b) (4) method. The specifications are (b) (4) of the target value (b) (4) for both release and stability.

### Method

(b) (4)

### Method Validation

(b) (4)

4 pages has been determined to be not releasable: (b)(4)

(b) (4)

Method Verification

(b) (4)

#### **14. Visible Particulates (DP) (Tao Pan)**

##### Introduction

The visible particulates of MenACWY-TT DP are determined by visual inspection of the reconstituted final container; the same specification, “Essentially Free of Visible Particles”, applies to both release and stability.

Method

(b) (4)

Method Verification

(b) (4)

Conclusion

Based on information provided, the visible particulate method has been verified at (b) (4) (b) (4) for lot release testing of MenACWY-TT DP.

**15. (b) (4) (DP) (Tao Pan)**

Introduction

The (b) (4) of lyophilized MenACWY-TT DP is determined by (b) (4) (b) (4) The same specification, (b) (4) applies to both release and stability.

Method

(b) (4)

Method Validation

(b) (4)

(b) (4)

**16. Bacterial Endotoxin (b) (4) DP) (Yen Phan)**

Introduction

This test is performed at (b) (4)

for DP

component, MenACWY-TT. Specification of (b) (4)

(b) (4) for MenACWY-TT DP component must be met for the lot release.



1 page has been determined to be not releasable: (b)(4)

(b) (4)

**17. Sterility (b) (4) DP (Yen Phan)**

Introduction

This test is performed at (b) (4)

for MenACWY-TT DP component. Acceptance criteria of 'No Growth' must be met.

1 page has been determined to be not releasable: (b)(4)

(b) (4)

**18. Identity (b) (4) DP (Anil Choudhary)**

**A. MnB (b) (4) Identity (b) (4)/DP)**

Method

The purpose of the method is to confirm the identity of the (b) (4)

(b) (4) DP using a (b) (4) The test method was approved in a previous submission for STN125549, Trumenba™.

Method Validation

(b) (4)

12 pages have been determined to be not releasable: (b)(4)

(b) (4)

**22. Polysaccharide MenC Content of DP Component MenACWY-TT (Anil Choudhary)**

Method

(b) (4)

1 page has been determined to be not releasable: (b)(4)

(b) (4)

Conclusion

The method for determination of polysaccharide MenC content was validated at (b) (4) (b) (4) (b) (4) The results met the predefined acceptance criteria and demonstrated that the assay performed at each site are suitable for their intended purpose.