



Food & Drug Administration
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DBSQ/OCBQ ANALYTICAL METHOD REVIEW MEMO

To: Biologics License Application, STN 125814/0

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Sponsor: Merck Sharp & Dohme (MSD) LLC

Subject: Review of Analytical Methods used for (CAPVAXIVE) Drug Substance (DS) and Drug Product (DP) Lot Release

Recommendation: Approval

Executive Summary:

The following analytical methods used for lot release of CAPVAXIVE and the associated analytical method validations or qualifications, were reviewed.

1. Appearance ((b) (4) DP)
2. (b) (4)
3. (b) (4)
4. (b) (4)
5. (b) (4)
6. Polysorbate-20 content ((b) (4)) (DP)
7. (b) (4)
8. Recoverable volume (DP)

Conclusion: The analytical methods and their validations and/or qualifications reviewed for the CAPVAXIVE DS and DP were found to be adequate for their intended use.

Documents reviewed:

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

Background

MSD submitted a BLA, STN125814 for CAPVAXIVE on 19 October 2023. CAPVAXIVE is a Pneumococcal 21-valent conjugate vaccine (V116) to prevent invasive disease and pneumonia caused by *Streptococcus pneumoniae* (*S pneumoniae*) in adults 18 of age and older. *S pneumoniae* can cause meningitis, bacteremia, sepsis, bacteremic pneumonia, and septic arthritis, resulting in considerable morbidity and mortality. *S pneumoniae* remains one of the most common causes of death from infection in many regions of the world.

As a conjugate vaccine, V116 elicits a T-cell dependent immune response, and the use of a helper T-cell specific carrier protein supports specificity, functionality, and maturation of serotype-specific B cells. V116 containing all serotypes is manufactured in (b) (4) as DS. Each 0.5 mL dose of V116 DP is prepared by (b) (4) DP in sodium chloride, L-Histidine and Polysorbate 80 (PS80) for injection, supplied as a single-dose prefilled syringe to be administered intramuscularly. V116 contains purified capsular polysaccharide from *S. pneumoniae* legacy serotypes 3, 6A, 7F, 8, 9N, 10A, 11A, 12F, deOAc15B (de-O-acetylated serotype 15B), 17F, 19A, 20, 22F, 33F and novel serotypes 15A, 16F, 23A, 23B, 24F, 31, 35B. (b) (4)

V110 and V114 vaccines with legacy serotypes were previously approved by the FDA. Individual (b) (4) serotypes from V110 and V114 were used as (b) (4) for assay validations. Since analytical method validations were previously reviewed for serotypes included in V114 and these are also included in the V116 formulation, additional validations were often not needed.

1. Appearance ((b) (4) DP)

Introduction

The specification for (b) (4) (b) (4). The color specification for pneumococcal conjugate vaccine (PCV) V116 DP is (b) (4) (colorless (b) (4)). Similarly, the opalescence specification (is clear to opalescent (b) (4)) is (b) (4). The appearance tests for (b) (4) DP are performed at the MSD site at (b) (4) in (b) (4).

Method: (b) (4) the appearance test for the PCV V116 DP is performed in accordance with (b) (4) for color and (b) (4) for Degree of Opalescence of Liquids and are carried out as per test method (TM) ATM-22754 and TM ATM-22753, respectively. These are simple (b) (4) methods that require inspection and recording of the observations.

Method verification

(b) (4)

The appearance method ATM-22754 and ATM-22753 verifications were performed at (b) (4) of (b) (4) following the verification protocol (b) (4)-VAL-6360 and (b) (4)-VAL-6362, respectively. Lot (b) (4) of PCV V116 DP was tested in (b) (4); (b) (4) performed this test at each facility. All (b) (4) opalescence results at (b) (4) were clear to opalescent, meeting the acceptance criteria. Similarly, all (b) (4) results at (b) (4) were observed as colorless and met the color acceptance criteria.

(b) (4)

Conclusion:

This appearance method is appropriately verified for lot release testing of PCV V116 DP (b) (4).

(b) (4)

(b) (4)

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(b) (4)

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

(b) (4)

6. Polysorbate-20 (DP)

Introduction

PS-20 is used as an excipient in the final DP formulation. The concentration of PS-20 was evaluated in the final DP material and the final lot release test was performed at the MSD site at (b) (4) in (b) (4). The specification of PS-20 for DP is (b) (4).

Method:

The proposed method for the determination of PS-20 in DP is described in section 3.2.P.5.2.5, Control of Drug Product. Assay for PS20 is based on (b) (4)

The system suitability criteria include:

(b) (4)

[Redacted]

The description of the method is adequate.

Method Validation:

The validation study was executed according to ICH Q2 (R1) guidelines and the parameters evaluated include specificity, accuracy, linearity, precision (repeatability and intermediate precision), linearity, range, and robustness studies; (b) (4)

[Redacted]

[Redacted]

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(b) (4)



8. Recoverable volume (DP)

Introduction

The recoverable volume and syringeability specification for the PCV V116 DP are 0.50 (b) (4) mL and liquid is dispensed from the needle in an even stream with no evidence of needle blockage.

Method

This recoverable volume method is a (b) (4) method and it is performed according to (b) (4) and (b) (4) following TM -ATM-22848. Syringeability was determined as a part of recoverable volume method by (b) (4). The lot release test for recoverable volume is performed at the MSD site at (b) (4) in (b) (4).

Method Validation

The recoverable volume and syringibility method verifications for PCV V116 DP were performed at (b) (4) of (b) (4), per the verification protocol (b) (4)-VAL-6364. (b) (4)



Liquid dispensed from the needle in an even stream with no evidence of needle blockage was observed in each of the recoverable volume testing sequences at (b) (4). Hence, the recoverable volume and syringibility method is verified.

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Conclusion

This procedure is acceptable as for the determination of recoverable volume and syringibility of PCV V116 DP.