(b) (6) ANALYTICAL METHOD REVIEW MEMO

To: STN125817/0

From: (b) (6) CBER(b) (6)

Through: (b) (6), CBER(b) (6)

(b) (6), CBER(b) (6)

Product: Nuvaxovid (COVID-19 Vaccine, Adjuvanted)

Applicant: Novavax

Subject: Analytical Methods for the Lot Release of (b) (4) Drug Product

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Recommendation: Approval

Summary:
The following analytical methods used for lot release of Nuvaxovid (COVID-19 Vaccine, Adjuvanted) (b) (4) drug product (DP), Matrix-A and Matrix-C components from Novavax, and the associated validations and qualifications, were reviewed:

1. Appearance (b) (4) DP),
2. pH (b) (4) DP),
3. (b) (4)
4. (b) (4)
5. (b) (4)
6. (b) (4)
7. (b) (4)
8. (b) (4)
9. (b) (4)
10. (b) (4)
11. (b) (4)
12. (b) (4)
13. (b) (4)
14. Particle size (DP),
15. Extractable volume (DP),
16. Total protein content (DP),
17. Matrix-A/-C content (DP)

Conclusion: The analytical methods and their validations/qualifications reviewed for Nuvaxovid (b) (4) DP, Matrix-A and Matrix-C components from Novavax, were found to be adequate for their intended use.

Documents Reviewed
Information in sections of the original submission that describe control of (b) (4) DP (3.2.P.5,), including descriptions of the specifications, analytical procedures and validation of these analytical procedures for (b) (4) DP were reviewed. IR#16 was sent to the sponsor on June 12, 2024, the sponsor's Amendment 0.28 was received in reply on July 17, 2024; then IR#26 was sent to the sponsor on October 8, 2024, the sponsor's Amendment 0.44 was received in reply on November 8, 2024.

Background:
Nuvaxovid is a vaccine intended for active immunization to prevent coronavirus disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The Nuvaxovid DP is a sterile, preservative-free dispersion of SARS-CoV-2 rS protein co-formulated with Matrix-M adjuvant, presented in either multi-dose vial (five or ten doses, for prototype and variant strains), or a pre-filled syringe (PFS) of 0.5 mL (for JN.1 strain); the Nuvaxovid DS is a SARS-CoV-2 rS protein expressed in a baculovirus expression system, purified, and formulated into trimeric nanoparticles; Matrix-M adjuvant is manufactured by mixing Matrix-A and Matrix-C adjuvant components; Matrix-A and Matrix-C adjuvant components are complexes made from adjuvant active Quillaja saponin materials, Fraction-A or Fraction-C, respectively formulated into complexes with cholesterol and phosphatidylcholine.

In this memo, the lot release tests for Nuvaxovid (b) (4) DP, Matrix-A and Matrix-C components, and their validations/qualification are reviewed.

1. Appearance (b) (4) DP)
The appearance of (b) (4) DP is determined by visual inspection of the color, clarity and presence of visible particles in (b) (4) DP; the specifications for both release and stability of (b) (4) DP are the same: colorless (b) (4) for color, clear (b) (4) for clarity, and practically free of visible particles for visible particle presence. The appearance is indicated to be determined for the release of (b) (4) DP at both the (b) (4)

Method:
(b) (4)

(b) (4)



Conclusion:
Based on information provided, the appearance method has been verified for its intended use of release testing of the (b) (4) DP at the (b) (4) .

2. pH (b) (4) DP)
The pH of (b) (4) DP is determined (b) (4) ; the specifications are (b) (4) for release and stability of (b) (4), and (b) (4) for release and stability of DP. The pH is indicated to be determined for the release of (b) (4) DP at (b) (4) and for DP release at (b) (4) .

Method:
(b) (4)



Conclusion:

Based on information provided, the pH method has been verified for its intended use of release testing of the (b) (4) DP at the (b) (4)

(b) (4)





(b) (4)



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

(b) (4)

[redacted]

14. Particle size (DP)

The particle size of the DP is determined by a (b) (4) method; its specifications for both release and stability are the same: particle size, (b) (4) This method is performed for DP release at NVX-AB.

Method:

(b) (4)

[redacted]

(b) (4)

[redacted]

Conclusion:
Based on the provided information, the method has been validated for the release testing of DP at NVX-AB using volumes of (b) (4) (b) (4) .

15. Extractable volume (DP)

The specification for extractable volume for DP release is: “the volume should be such that each syringe delivers not less than stated doses”, and DP extractable volume is determined at (b) (4) .

Method:
(b) (4)





Conclusion:
Based on information provided, the extractable volume method has been verified for its intended use of release testing of DP at (b) (4) .

16. Total protein content (DP)

The total protein of the DP is determined using a (b) (4) method, its specifications for both release and stability are the same: (b) (4) . Total protein of the DP is determined for the release at (b) (4)

Method:
(b) (4)



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

(b) (4)

) DPs: no significant difference was detected between the result from both samples.

Conclusion:
Based on information provided, the total protein method has been validated for DP release testing at (b) (4)

17. Matrix-A and Matrix-C contents (DP)

Matrix-M, the adjuvant component of the DP, consists of Matrix-A and -C in the ratio of (b) (4) The Matrix-A and -C contents of DP are determined using a (b) (4) method, and their specifications for release and stability are the same: (b) (4) , respectively for Matrix-A and -C. As indicated in the submission, the (b) (4) method for the Matrix-A and -C contents is performed at both (b) (4) and NVX-AB for DP release.

Method:
(b) (4)

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(b) (4)

(b) (4)

Conclusion:
Based on information provided, the Matrix-A and Matrix-C contents by (b) (4) method has been verified for its intended use of DP release testing at both Serum Institute of India and NVX-AB (b) (4) .

Method Validation Updates for JN.1 Strain

(b) (4)

(b) (4)