Chemistry, Manufacturing, and Controls Statistical Review

Application Type	Original BLA
STN	125817/0
Applicant	Novavax, Inc
Trade Name	Nuvaxovid
Pharmacologic Class	Vaccine
Indication	Active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus (SARS-CoV-2) in individuals 12 years of age and older
Review Priority	Standard
CBER Received Date	04/01/2024
Action Due Date	04/01/2025
Product Office	OVRR
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Supervisory Concurrence # 1	(b) (6)
Supervisory Concurrence # 2	(b) (6)
Supervisory Concurrence # 3	(b) (6)

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1. EXECUTIVE SUMMARY

In this original BLA, the applicant seeks approval for their adjuvanted COVID-19 vaccine, Nuvaxovid for active immunization to prevent of COVID-19 caused by SARS-CoV-2 in individuals 12 years of age and older. The applicant originally sought approval based on manufacturing data from the vaccine targeting the prototype and XBB.1.5 strains. However, since the review cycle overlapped with the 2024–2025 season, Novavax amended this BLA to include the 2024–2025 formulation (targeting the JN.1 strain). I reviewed the assay validation for drug substance (DS) and drug product (DP), the DP potency specification, and the DP shelf life establishment for all three formulations.

The applicant has provided validation study results that support use of the quantitative, non-compendial assays to monitor the DP quality. The applicant has also provided stability data that support the proposed specification and shelf life for the COVID-19 V\vaccine.

Therefore, I recommend approval of this original BLA.

2. REGULATORY BACKGROUND AND SOURCE OF INFORMATION

In this original BLA, the applicant seeks licensure of their adjuvanted COVID-19 vaccine (Nuvaxovid) for immunization of individuals 12 years of age and older to prevent COVID-19 caused by SARS-CoV-2. The vaccine is a recombinant spike protein vaccine, and the drug product (DP) is made from the SARS-CoV-2 rS Protein drug substance (DS) and the Matrix-M adjuvant, which is a mixture of Matrix-A and Matrix-C. This product was studied under IND 22430 and is authorized for emergency use under EUA 28237 in multiple final containers (multi-dose vials and pre-filled syringes) for multiple different variants. Therefore, the BLA contains manufacturing and quality information about DP for multiple variants and in final containers.

Since detailed reviews of the DP potency specifications and shelf life were conducted under the IND and EUA, this review focuses on assay validations for DS and DP, and only summarizes the DP potency justification of specifications and shelf life establishment.

Table 1 shows the CMC statistical information requests (IR) sent and responses received. In general, the responses to these IRs were acceptable. Detailed reviews of the IRs are given in Section 3, where relevant.

Table 1. BLA 125817/0 CMC Statistical Information Requests (IR) and Responses

Submission	Request Sent	Response Received	Summary
BLA 125817/0.28	06/12/2024 (IR#16, Question 4)	07/17/2024	Product reviewers requested details of assays validation
BLA 125817/0.74	02/18/2025 (IR # 51)	02/24/2025	Request clarification of study design, models, formulas, and raw data for Total Protein Content by (b) (4) and Drug Product (DP) Relative Potency by (b) (4) methods. The applicant provided the requested information.
BLA 125817/0.80	02/25/2025	02/27/2025	Request the applicant use the exact formula for the %GCV for their future submissions. The applicant acknowledged.

Source: Created from BLA 125817/0

3. Discussion of Protocols, Studies or Analyses, and Results

3.1 Drug Product (b) (4) Relative Potency (b) (4) Validation

An (b) (4) measures the potency of the (b) (4) DP. The validation study assessed the precision, accuracy, linearity, range, and robustness.

(b) (4)

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(b) (4)

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(b) (4)

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3.2 Drug Product (b) (4) Validation

This method determines the (b) (4) of the DP at release and during stability studies. The validation study assessed the accuracy, precision (repeatability and IP), range, and robustness.

3.2.1 Study Design and Acceptance Criteria

To assess accuracy, (b) (4)

(b) (4)

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

3.3 Drug Product Total Protein by (b) (4) Assay Validation

The (b) (4) method measures the total protein concentration for DP. The validation study assessed accuracy, linearity, precision, limit of quantitation (LOQ), range, and confirmed that testing of the Wuhan variant produced similar assay validation results.

3.3.1 Study Design and Acceptance Criteria

To assess linearity and accuracy, (b) (4)

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(b) (4)

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Overall, the BCA method was verified as precise and accurate across a range of 5–50 µg/ml.

Reviewer's Comment: *The range is acceptable and covers the specification range:* (b) (4)

3.4 Drug Product and Adjuvant Matrix-A and Matrix-C Content Validation

The (b) (4) method is used to quantify the amount of Matrix-A and Matrix-C in the adjuvant and DP. Two validation studies were performed (validation reports QAG_07911 and QAG_04964), along with a supplemental validation study for the XBB.1.5 and JN.1.

Reviewer's Comment: *The first and second validation study appear to both use prototype variant (i.e. original strain) DP, based on the location of the report in the eCTD. The difference between these two studies was not explained.*

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3.5 Matrix-A and C Supplemental Validation for XBB.1.5 and JN.1 DP

Supplementary validation studies were performed for the DP for the XBB.1.5 and JN.1 variants. These two supplementary validations assessed the accuracy and repeatability.

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3.7 Stability

For different variants and final containers, the applicant proposed different shelf lives:

- Prototype DP in 5- or 10-dose vials: (b) (4) months at 2–8°C
- XBB.1.5 DP in 5-dose vials: 9 months at 2–8°C
- JN.1 DP in pre-filled syringes: 3 months at 2–8°C.

3.7.1 Prototype Drug Product in 5- or 10-Dose Vials

(b) (4)

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

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(b) (4)

4. CONCLUSIONS

The applicant has provided validation study results that support use of their quantitative non-compendial assays to monitor the quality of their COVID-19 vaccine. The applicant has also provided stability data that support the proposed DP potency specification and shelf life.

Therefore, I recommend approval of this original BLA.