CMC REVIEW MEMO

Date: March 24, 2025

From: (b) (6) Adventitious Agents

Subject: Review of Adventitious Agents Safety for Novavax SARS-CoV-2 rS Vaccine

Product Name: Novavax COVID-19 Vaccine, Adjuvanted

Proprietary Name: Nuvaxovid

Applicant Name: Novavax Inc.

To: FILE STN 125817

Through: (b) (6)

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EXECUTIVE SUMMARY

The Novavax COVID-19 vaccine, Adjuvanted contains the SARS-CoV-2 recombinant full-length spike glycoprotein (rS), adjuvanted with Matrix-M. The SARS-CoV-2 spike protein drug substance (DS), is produced by recombinant DNA technology using a baculovirus expression system in an insect cell line that is derived from Sf9 cells of the *Spodoptera frugiperda* species.

The Original (prototype) monovalent vaccine (NVX-CoV2373) contained the rS of the Wuhan strain. Subsequent SARS-CoV-2 variant vaccines were developed containing the rS antigen of various strains, including Omicron BA.1, Omicron BA.2, Omicron BA.5, Omicron XBB.1.5, and Omicron JN.1. The Original monovalent Wuhan vaccine (2022-2023 Formula, NVX-CoV2373), the Omicron XBB.1.5 variant vaccine (2023-2024 Formula; NVX-CoV2601) and the Omicron JN.1 variant vaccine (2024-2025 Formula; NVX-CoV2705) were authorized for emergency use under EUA 28237 on July 13, 2022, October 3, 2023, and August 30, 2024, respectively. The viral safety data for these 3 vaccines has been submitted in the Chemistry, Manufacturing, and Controls (CMC) information for STN 125817 to support a marketing authorization request for Nuvaxovid.

(b) (4)







(b) (4)



REVIEWER'S RECOMMENDATION

On the basis of the information submitted and evaluation of the viral safety package demonstrating absence of adventitious agents, I recommend approval of the license application for Nuvaxovid.

FULL REVIEW: NUVAXOVID

Novavax COVID-19 Vaccine, Adjuvanted

OVERVIEW

My review focused on demonstrating product safety based on: I) the adventitious agents testing of the (b) (4) used to generate the Drug Substances for manufacturing the COVID-19 rS vaccines; and II) the viral clearance studies performed to demonstrate removal/inactivation of adventitious viruses, (b) (4) by the manufacturing process.

Other CMC information has been reviewed in (b) (6) as follows:

- (b) (6) rS antigen Drug Substance and Drug Product
- (b) (6) Adjuvant
- (b) (6) Biopharmaceutical studies

My memo contains:

- Review of the information in the BLA original submission and amendments (indicated in **Table 1**)
- Related submissions to support the BLA, indicated in **Table 2**
- Review of the Applicant's responses to following **IR Letters**:
  - Amendment 63: IR dated Jan 2, 2024
  - Amendment 63: IR dated Feb 5, 2025
  - Amendment 70: IR dated Feb 13, 2025
  - Amendment 71: IRs dated Feb 13, 2025, and Feb 19, 2025
  - Amendment 73: IR dated Feb 13, 2025 – follow-up.

Table 1. Review of BLA submissions.

Amend No.	Serial No.	Section	Review Information
0	0001	3.2.S.2.3 (rS)	(b) (4)

			(b) (4)
	0001	3.2.S.2.4. (rS)	
4	0005	2.3.A	
		3.2.S.2.3 (rS variant)	
		3.2.S.2.4 (rS variant)	
42	0044	3.2.S.2.3 (rS JN.1)	

			(b) (4)
		3.2.S.4.3 (rS JN.1)	
		3.2.S.2.4 (rS JN.1)	
52	0054	1.11.1	
63	0065	1.11.1	
		3.2.S.2.3 (rS JN.1)	
70	0072	3.2.S.2.3 (rS JN.1)	
		3.2.S.2.4 (rS JN.1	
71	0073	3.2.S.2.3 (rS JN.1)	
73	0075	1.11.1	

3.2.A.2. APPENDICES – ADVENTITIOUS AGENTS SAFETY EVALUATION

0, 42	001, 0044	3.2.A.2	(b) (4)
0, 52	001, 0054		
52	0054	3.2.A.2	

Table 2. Other regulatory submissions supporting SARS-CoV-2-rS BLA 12817

Type	EUA 28237 Amendments	IND 22430 Amendments
rS		214, 474, 525, 590, 595,597,641, 645,653, 656, 660, 661,656, 661, 682,683,691,698, 705, 709, 714, 716
2022-2023 formulation-Wuhan original		64, 68121, 214, 238,247, 253,272, 291,299-301, 303, 313, 320, 326
2023-2024 formulation-XBB.1.5	130, 135, 138, 146, 148, 154	389, 401

2024-2025 formulation-JN.1	177, 183, 191, 194, 222, 224, 246, 277, 278	

Additional documents providing support: **IND** (b) (4) (Novavax), **MF** (b) (4) (Novavax) and **MF** (b) (4) support the BLA.

CMC REVIEW

The detailed review of the derivation and adventitious agents testing of the (b) (4) and (b) (4) used for the manufacturing of the DP lots have been provided in my memos for the EUA 2022-2023 formulation of the Wuhan strain dated July 22 2022; for the EUA 2023-2024 formulation of the Omicron XBB.1.5 strain dated October 10, 2023; and included in the memo from the CMC Product Reviewer dated August 31, 2024 for the EUA 2024-2025 formulation of the Omicron JN.1 strain. Additionally, viral clearance studies and assessment of the (b) (4) were reviewed in my EUA memo dated July 22, 2022. This memo provides a summary of the previously reviewed information, and details of the updated information submitted to the BLA and its amendments.

I. ADVENTITIOUS AGENTS TESTING

(b) (4)

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

(b) (4)

<u>REVIEWER'S COMMENT.</u> The overall results of the viral clearance and assessment studies demonstrated that the SARS-CoV-2 purification process is a robust process to remove both endogenous and relevant viruses that may present during manufacturing, resulting in DS with an acceptable trace amounts of viral process contaminants.