Our STN: BL 125817/0

**BLA APPROVAL**
May 16, 2025

Novavax Inc.
Attention: Kathleen Callahan
700 Quince Orchard Road
Gaithersburg, MD 20878

Dear Ms. Callahan:

Please refer to your Biologics License Application (BLA) received April 1, 2024, submitted under section 351(a) of the Public Health Service Act (PHS Act) for COVID-19 Vaccine, Adjuvanted.

## LICENSING

We are issuing Department of Health and Human Services U.S. License No. 2349 to Novavax Inc., Gaithersburg, Maryland, under the provisions of section 351(a) of the PHS Act controlling the manufacture and sale of biological products. The license authorizes you to introduce or deliver for introduction into interstate commerce, those products for which your company has demonstrated compliance with establishment and product standards.

Under this license, you are authorized to manufacture the product COVID-19 Vaccine, Adjuvanted, which is indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in adults 65 years and older. Additionally, COVID-19 Vaccine, Adjuvanted is indicated for individuals 12 through 64 years who have at least one underlying condition that puts them at high risk for severe outcomes from COVID-19.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: NCT04368988, NCT04611802, NCT05463068 and NCT05372588.

## MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture COVID-19 Vaccine, Adjuvanted, which consists of recombinant full-length SARS-CoV-2 spike glycoprotein (rS) drug substance co-formulated with Matrix-M adjuvant, at the (b) (4)

You may label your product with the proprietary name NUVAXOVID and market it in single-dose (0.5 mL) pre-filled syringes, in cartons of 10 pre-filled syringes.

## ADVISORY COMMITTEE

We did not refer your application to the Vaccines and Related Biological Products Advisory Committee because our review of information submitted in your BLA, including the clinical study design and trial results, did not raise concerns or controversial issues that would have benefited from an advisory committee discussion.

## DATING PERIOD

The dating period for COVID-19 Vaccine, Adjuvanted shall be 3 months from the date of manufacture when stored at 2°C to 8°C. The date of manufacture shall be defined as the date when the filling of the formulated drug product into syringes is initiated. Following the final sterile filtration, no reprocessing/reworking is allowed without prior approval from the Agency. The dating period for your drug substance shall be (b) (4) months when stored at (b) (4)

## FDA LOT RELEASE

Please submit final container samples of the product in final containers together with protocols showing results of all applicable tests. You may not distribute any lots of product until you receive a notification of release from the Director, Center for Biologics Evaluation and Research (CBER).

## BIOLOGICAL PRODUCT DEVIATIONS

You must submit reports of biological product deviations under 21 CFR 600.14. You should identify and investigate all manufacturing deviations promptly, including those associated with processing, testing, packaging, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA 3486 to the (b) (6) , electronically through the eBPDR web application or at the address below. Links for the instructions on completing the electronic form (eBPDR) may be found on CBER's web site at https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/biological-product-deviations :

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

**MANUFACTURING CHANGES**

You must submit information to your BLA for our review and written approval under 21 CFR 601.12 for any changes in, including but not limited to, the manufacturing, testing, packaging or labeling of COVID-19 Vaccine, Adjuvanted, or in the manufacturing facilities.

**LABELING**

Under 21 CFR 201.57(c)(18), patient labeling must be referenced in section 17 PATIENT COUNSELING INFORMATION. Patient labeling must be available and may either be reprinted immediately following the full prescribing information of the package insert or accompany the prescription product labeling.

We hereby approve the draft content of labeling including: Package Insert and FDA-approved patient labeling submitted under amendment 111, dated May 15, 2025, the draft package label submitted under amendment 111, dated May 15, 2025, and the draft container label submitted under amendment 90, dated March 13, 2025.

**CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, please submit the final content of labeling (21 CFR 601.14) in Structured Product Labeling (SPL) format via the FDA automated drug registration and listing system, (eLIST) as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the Package Insert and FDA-approved patient labeling submitted on May 15, 2025. Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As* at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

**PACKAGE AND CONTAINER LABELS**

Please electronically submit final printed package and container labels identical to the package and container labels submitted on May 15, 2025, and March 13, 2025, respectively, according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm333969.pdf.

All final labeling should be submitted as Product Correspondence to this BLA,

STN BL 125817, at the time of use and include implementation information on Form FDA 356h.

**ADVERTISING AND PROMOTIONAL LABELING**

You may submit two draft copies of the proposed introductory advertising and promotional labeling with Form FDA 2253 to (b) (6) at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

You must submit copies of your final advertising and promotional labeling at the time of initial dissemination or publication, accompanied by Form FDA 2253 (21 CFR 601.12(f)(4)).

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence or substantial clinical experience to support such claims (21 CFR 202.1(e)(6)).

**ADVERSE EVENT REPORTING**

You must submit adverse experience reports in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80). In addition to the reporting requirements in 21 CFR 600.80, you must submit all adverse experience reports for myocarditis and/or pericarditis; atrial fibrillation and/or atrial flutter; cerebrovascular accident; ocular motor cranial nerve disorders (i.e., cranial nerve disorders affecting cranial nerves III, IV, or VI); cranial nerve VIII disorders (including vestibular neuronitis); cardiac failure; and cardiomyopathy as 15-day expedited reports to the Vaccine Adverse Event Reporting System (VAERS) at https://vaers.hhs.gov/. Adverse experience reports for myocarditis and/or pericarditis; atrial fibrillation and/or atrial flutter; cerebrovascular accident; ocular motor cranial nerve disorders (i.e., cranial nerve disorders affecting cranial nerves III, IV, or VI); cranial nerve VIII disorders (including vestibular neuronitis); cardiac failure; and cardiomyopathy must be submitted as 15-day expedited reports for 3 years following the date of product licensure. You must submit distribution reports as described in 21 CFR 600.81. For information on adverse experience reporting, please refer to the guidance for industry *Providing Submissions in Electronic Format —Postmarketing Safety Reports for Vaccines* at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-submissions-electronic-format-postmarketing-safety-reports-vaccines. For information on distribution reporting, please refer to the guidance for industry *Electronic Submission*

*of Lot Distribution Reports* at
http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Post-MarketActivities/LotReleases/ucm061966.htm.
For information on the postmarketing safety reporting requirements for combination products as described in 21 CFR 4, Subpart B, and the dates by which combination product applicants must comply with these requirements, please refer to the Postmarketing Safety Reporting for Combination Products webpage available at https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products.

(b) (4)

**PEDIATRIC REQUIREMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are deferring submission of your pediatric studies for ages birth to <12 years for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required under section 505B(a) of the Federal Food, Drug, and Cosmetic Act (FDCA) are required postmarketing studies. The status of these postmarketing studies must be reported according to 21 CFR 601.28 and section 505B(a)(4)(C) of the FDCA. In addition, section 506B of the FDCA and 21 CFR 601.70 require you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

Label your annual report as an "**Annual Status Report of Postmarketing Study Requirement/Commitments**" and submit it to the FDA each year within 60 calendar days of the anniversary date of this letter until all Requirements and Commitments subject to the reporting requirements under section 506B of the FDCA are released or fulfilled. These required studies are listed below:

1. Deferred pediatric study under PREA (Study 2019nCoV-503) to evaluate the safety and immunogenicity of Nuvaxovid in COVID-19 vaccine-naïve individuals 6 months to <12 years of age.
   Final Protocol Submission: March 28, 2022 (Submitted)
   Study Completion: October 28, 2025
   Final Report Submission: March 4, 2026

2. Deferred pediatric study under PREA (Study 2019nCoV-317) to evaluate the immunogenicity of Nuvaxovid in COVID-19 vaccine-naïve seropositive individuals 2 years to <12 years of age and to evaluate the safety and immunogenicity of Nuvaxovid in individuals 6 months to <2 years of age, using a contemporaneously vaccinated comparator group.
   Final Protocol Submission: April 30, 2025
   Study Completion: December 31, 2027
   Final Report Submission: July 31, 2028

3. Deferred pediatric study under PREA (Study 2019nCoV-506) to evaluate the safety and immunogenicity of Nuvaxovid in COVID-19 vaccine-naïve individuals 0 to <6 months of age.
   Final Protocol Submission: October 30, 2028
   Study Completion: March 31, 2031
   Final Report Submission: October 31, 2031

Submit the protocols to your IND 22430, with a cross-reference letter to this BLA, STN BL 125817, explaining that these protocols were submitted to the IND. Please refer to the sequential number for each study/clinical trial and the submission number as shown in this letter.

Submit final study reports to this BLA, STN BL 125817. In order for your PREA PMRs to be considered fulfilled, you must submit and receive approval of either an efficacy or a labeling supplement. For administrative purposes, all submissions related to these required pediatric postmarketing studies must be clearly designated as:

**Required Pediatric Assessments**

We note that you have fulfilled the pediatric study requirement for ages 12 years through 16 years for this application.

**POSTMARKETING REQUIREMENTS UNDER SECTION 505(o)**

Section 505(o) of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute (section 505(o)(3)(A), 21 U.S.C. 355(o)(3)(A)).

We have determined that an analysis of spontaneous postmarketing adverse events reported under section 505(k)(1) of the FDCA will not be sufficient to assess known serious risks of myocarditis and pericarditis.

Furthermore, the pharmacovigilance system that FDA is required to maintain under section 505(k)(3) of the FDCA is not sufficient to assess these serious risks.

Therefore, based on appropriate scientific data, we have determined that you are required to conduct the following studies:

4. Study 2019nCoV-402, entitled “Safety of the Novavax COVID-19 vaccine in England using a self-controlled case series design: A post-authorization safety study using data from the Clinical Practice Research Datalink (CPRD) Aurum and linked databases” to evaluate the occurrence of myocarditis and pericarditis following administration of Novavax COVID-19 Vaccine, Adjuvanted or NUVAXOVID.

   We acknowledge the timetable you submitted on March 26, 2025, which states that you will conduct this study according to the following schedule:

   Final Protocol Submission: March 30, 2022 (Submitted)
   Study Completion Date: September 30, 2027
   Final Report Submission: June 30, 2028

5. Study 2019nCoV-404, entitled "Safety Profile of the Novavax COVID-19 Vaccine, Adjuvanted in Individuals ≥ 12 Years of Age in the United States" to evaluate the occurrence of myocarditis and pericarditis following administration of Novavax COVID-19 Vaccine, Adjuvanted or NUVAXOVID.

   We acknowledge the timetable you submitted on March 26, 2025, which states that you will conduct this study according to the following schedule:

   Final Protocol Submission: June 29, 2022 (Submitted)
   Study Completion Date: September 30, 2027
   Final Report Submission: September 30, 2028

6. Study 2019nCoV-418, entitled “Post-Authorization Safety Study to Evaluate Long-Term Sequalae of Myocarditis and Pericarditis Following Vaccination” to evaluate long-term sequelae of myocarditis and pericarditis following administration of NUVAXOVID with at least 5 years of follow-up.

   We acknowledge the timetable you submitted on March 26, 2025, which states that you will conduct this study according to the following schedule:

   Final Protocol Submission: January 31, 2026
   Study Completion Date: December 31, 2031

Final Report Submission: September 30, 2032

Please submit the protocols to your IND 22430, with a cross-reference letter to this BLA, STN BL 125817, explaining that these protocols were submitted to the IND. Please refer to the sequential number for each study/clinical trial and the submission number as shown in this letter.

Please submit final study reports to the BLA STN BL 125817. If the information in the final study report supports a change in the label, the final study report must be submitted as a supplement to this BLA, STN BL 125817. For administrative purposes, all submissions related to these postmarketing studies required under section 505(o) must be submitted to this BLA and be clearly designated as:

- **Required Postmarketing Correspondence under Section 505(o)**
- **Required Postmarketing Final Report under Section 505(o)**
- **Supplement contains Required Postmarketing Final Report under Section 505(o)**

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to the FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. In addition, section 506B of the FDCA and 21 CFR 601.70 require you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

You must describe the status in an annual report on postmarketing studies for this product. Label your annual report as an **Annual Status Report of Postmarketing Requirements/Commitments** and submit it to the FDA each year within 60 calendar days of the anniversary date of this letter until all Requirements and Commitments subject to the reporting requirements of section 506B of the FDCA are fulfilled or released. The status report for each study should include:

- the sequential number for each study as shown in this letter;
- information to identify and describe the postmarketing requirement;
- the original milestone schedule for the requirement;
- the revised milestone schedule for the requirement, if appropriate;
- the current status of the requirement (i.e., pending, ongoing, delayed, terminated, or submitted); and,
- an explanation of the status for the study or clinical trial. The explanation should include how the study is progressing in reference to the original projected schedule, including, the patient accrual rate (i.e., number enrolled to date and the total planned enrollment).

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our website at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/default.htm.

We will consider the submission of your annual report under section 506B of the FDCA and 21 CFR 601.70 to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in section 505(o) and 21 CFR 601.70. We remind you that to comply with section 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to periodically report on the status of studies or clinical trials required under section 505(o) may be a violation of FDCA section 505(o)(3)(E)(ii) and could result in regulatory action.

**POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B**

We acknowledge your written commitments as described in your letters of December 5, 2024, February 3, 2025, and May 13, 2025, as outlined below:

7. Study 2019nCoV-405, entitled “Global Pregnancy and Infant Outcomes Study Using the COVID-19 Vaccines International Pregnancy Exposure Registry (C-VIPER)” to evaluate obstetric, neonatal, and infant outcomes among women vaccinated during pregnancy with Novavax COVID-19 Vaccine, Adjuvanted or NUVAXOVID.

   Final Protocol Submission: March 30, 2022 (Submitted)
   Study Completion: February 28, 2027
   Final Report Submission: June 30, 2027

8. Study 2019nCoV-402, entitled “Safety of the Novavax COVID-19 vaccine in England using a self-controlled case series design: A post-authorization safety study using data from the Clinical Practice Research Datalink (CPRD) Aurum and linked databases” to evaluate the occurrence of atrial fibrillation and cerebrovascular accident following administration of Novavax COVID-19 Vaccine, Adjuvanted or NUVAXOVID.

   Final Protocol Submission: March 30, 2022 (Submitted)
   Study Completion Date: September 30, 2027
   Final Report Submission: June 30, 2028

9. Study 2019nCoV-404, entitled "Safety Profile of the Novavax COVID-19 Vaccine, Adjuvanted in Individuals ≥ 12 Years of Age in the United States" to evaluate the occurrence of atrial fibrillation and cerebrovascular accident following administration of Novavax COVID-19 Vaccine, Adjuvanted or NUVAXOVID.

   Final Protocol Submission: June 29, 2022 (Submitted)
   Study Completion Date: September 30, 2027
   Final Report Submission: September 30, 2028

10. A study entitled “A Phase 4, Randomized, Double-Blind, Placebo-Controlled, Post-Marketing Study to Evaluate the Efficacy and Safety of a Subvariant SARS-CoV-2 rS Vaccine Adjuvanted with Matrix-M in Adults 50 to < 65 years of Age Without High-Risk Conditions for Severe COVID-19” to evaluate the clinical efficacy and safety and update the benefit-risk assessment of the intended marketed formulation of NUVAXOVID within the current epidemiological environment in a lower risk population aged 50 through 64 years.

    Study Initiation: November 30, 2025Interim Results: May 31, 2026
    Study Completion: July 31, 2026
    Final Report Submission: January 31, 2027
    Benefit-Risk Assessment Submission: May 31, 2027

Please submit the clinical protocol and Interim Results to your IND 22430, and cross-reference letters to this BLA, STN BL 125817, explaining that the protocol and interim results were submitted to the IND. Please submit the Benefit-Risk Assessment to the BLA as a PMR/PMC Submission – Correspondence Status Update. Please refer to the sequential number for each study/clinical trial and the submission number as shown in this letter.

If the information in the final study report supports a change in the label, the final study report must be submitted as a supplement. Please use the following designators to prominently label all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- **Postmarketing Commitment – Correspondence**
- **Postmarketing Commitment – Final Study Report**
- **Supplement contains Postmarketing Commitment – Final Study Report**

For each postmarketing study subject to the reporting requirements of 21 CFR 601.70, you must describe the status in an annual report on postmarketing studies for this product. Label your annual report as an **Annual Status Report of Postmarketing Requirements/Commitments** and submit it to the FDA each year within 60 calendar days of the anniversary date of this letter until all Requirements and Commitments subject to the reporting requirements of section 506B of the FDCA are fulfilled or released. The status report for each study should include:

- the sequential number for each study as shown in this letter;
- information to identify and describe the postmarketing commitment;
- the original schedule for the commitment;
- the status of the commitment (i.e., pending, ongoing, delayed, terminated, or submitted); and,
- an explanation of the status including, for clinical studies, the patient accrual rate (i.e., number enrolled to date and the total planned enrollment).

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our website at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/default.htm.

**POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B**

We acknowledge your written commitment as described in your letter of March 17, 2025, as outlined below:

11. To conduct a study entitled "Shipping Evaluation of SARS-CoV-2 rS (JN.1 Vaccine) Drug Product in Pre-Filled Syringe (PFS) Finished Good Presentation at (b) (4)" to provide objective evidence that the SARS-CoV-2 rS JN.1 Variant DP PFS finished goods presentation will maintain its quality after being exposed to shipping and distribution loads between (b) (4) and destination sites, including distributors and end users.

    Final Report Submission: July 31, 2025

We request that you submit information concerning nonclinical and chemistry, manufacturing, and control postmarketing commitments and final reports to your BLA, STN BL 125817. Please refer to the sequential number for each commitment.

Please use the following designators to prominently label all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- **Postmarketing Commitment – Status Update**
- **Postmarketing Commitment – Final Study Report**
- **Supplement contains Postmarketing Commitment – Final Study Report**

For each postmarketing commitment not subject to the reporting requirements of 21 CFR 601.70, you may report the status to FDA as a **Postmarketing Commitment – Correspondence Status Update**. The status report for each commitment should include:

- the sequential number for each study as shown in this letter;
- the submission number associated with this letter;
- a description of what has been accomplished to fulfill the non-section 506B PMC; and,
- a summary of any data collected or issues with fulfilling the non-section 506B PMC.

When you have fulfilled your commitment, submit your final report as **Postmarketing Commitment – Final Study Report** or **Supplement contains Postmarketing Commitment – Final Study Report**.

**POST APPROVAL FEEDBACK MEETING**
New biological products qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, please contact the Regulatory Project Manager for this application.

Sincerely,

(b) (6)
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(b) (6)
Center for Biologics
Evaluation and Research

David C. Kaslow, MD
Director
Office of Vaccines
Research and Review
Center for Biologics
Evaluation and Research