World Health Organization	REGULATION AND PREQUALIFICATION DEPARTMENT
	Vaccines & Immunization Devices Team (VAX)

WHO PUBLIC ASSESSMENT REPORT (WHOPAR)

Nuvaxovid™
COVID-19 Vaccine (recombinant, adjuvanted)
NOVAVAX CZ a.s., Czech Republic

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What is Nuvaxovid™?

Nuvaxovid is a vaccine for preventing coronavirus disease (COVID-19) in people aged 12 years and older. The recommended Nuvaxovid™ contains a version of a protein found on the surface of SARS-CoV-2 (the virus that causes COVID-19).

Nuvaxovid™ has been adapted to target the most recent strains of the virus. This helps maintain protection against COVID-19. In this case Nuvaxovid contains a version of the protein from the Omicron JN.1 subvariant of SARS-CoV-2.

Nuvaxovid™ is a dispersion for injection presented in a single dose vial (2R USP Type 1). The vaccine is adjuvanted. The dispersion is ready to use after a gentle agitation.

Each dose of vaccine (0.5 mL) contains:

Active components and quantity per dose	
SARS-CoV-2 spike protein (recombinant)	5 µcg
Adjuvant	
Matrix-M	50 µcg
Excipients	
Active component and adjuvant are co-formulated with formulation buffer (containing sodium phosphate heptahydrate, monohydrate, sodium chloride and polysorbate 80)	

Nuvaxovid™ (JN.1) will be available for UN purchase in a carton box containing 10 vials. Each vaccine vial consists of 1 dose of 0.5 mL of vaccine. The vaccine should be administered by intramuscular injection only, preferably in the deltoid muscle of upper arm.

The vaccine is filled in a 2R USP Type 1 glass siliconized vial. The vial closure system is complemented with a bromo butyl rubber stopper with aluminum – flip off seal of blue pantone colored.

The stability data submitted by the prequalification holder supports a shelf life of 9 months when the vaccine is stored between 2°C to 8°C. The vaccine should be shipped and stored at this recommended temperature, and it should not be frozen. With the data today available, the prequalification (PQ) holder does not have the ability to apply VVM as part of their labelling and packaging processes. Novavax is working to pursue a solution for providing a VVM as part of the labelling and packaging process of the vaccine to comply with this programmatic characteristic.

Nuvaxovid™ in its presentation of one dose per vial, is manufactured for Novavax CZ a.s., by Siegfried Hameln GmbH Langes Field 13 31789, Hamel, Germany.

What is Nuvaxovid™ used for?

Data have shown that Nuvaxovid™ and its adapted vaccines cause the production of antibodies against SARS-CoV-2 that can protect against COVID-19. The immune response to the vaccine is similar in adolescents and adults. It is indicated for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 12 years of age and older. The use of this vaccine should be in accordance with official recommendations.

Nuvaxovid™ was originally given an "emergency use" recommendation (EUL) because there was more evidence to come about the vaccine. The PQ holder has provided comprehensive information, including data on the pharmaceutical quality of the vaccine. As a result, the EUL status has been switched to a standard prequalification.

How is Nuvaxovid™ used?

Nuvaxovid™ is given in accordance with official recommendations issued at national level by public health bodies.

Nuvaxovid™ (JN.1) is administered intramuscularly as a single dose (0.5 mL) for individuals 12 years of age and older regardless of previous vaccination status.

For individuals who have previously been vaccinated with a COVID-19 vaccine, Nuvaxovid™ (JN.1) should be administered at least 3 months after the most recent dose of a COVID-19 vaccine. Additional doses may be administered to individuals who are severely immunocompromised in accordance with national recommendations. Safety and efficacy of Nuvaxovid™ (JN.1) in children aged less than 12 years have not yet been established. No data are available.

No dose adjustment is required in elderly individuals ≥ 65 years of age.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of an adverse reaction (e.g., anaphylactic reaction) following the administration of the vaccine.

What are the vaccine characteristics?

Nuvaxovid™ (JN.1) is a dispersion for injection, it is colourless to slightly yellow, clear to mildly opalescent. It must be stored as recommended by the manufacturer, between 2°C to 8°C. Under this recommended storage condition, the vaccine is stable for 9 months from the date of manufacture.

The vaccine does not contain preservative.

Cold chain volume per dose is 16.96 cm^3/dose in the secondary packaging.

Who is the regulatory authority responsible for its oversight vis a vis WHO?

Nuvaxovid™ (JN.1) is under the regulatory oversight of the European Medicines Agency (EMA). This is the regulatory agency of record for this vaccine.

How has Nuvaxovid™ (JN.1) been studied from the clinical point of view?

Novavax has developed an adapted severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) recombinant (r) spike (S) protein nanoparticle vaccine (SARS-CoV-2 rS) with Matrix-MTM adjuvant for the proposed indication of active immunization for the prevention of coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2. The composition of the Novavax COVID-19 vaccine has been updated for the 2024-2025 vaccination season to a monovalent JN.1-based vaccine. The safety and effectiveness of the JN.1 candidate vaccine are further inferred from safety, immunogenicity, and efficacy data gathered in adults and

adolescents for the original Wuhan-based vaccine as well as from safety and immunogenicity data gathered in adults for monovalent candidate Omicron BA.1 and BA.5 subvariant vaccines and from the authorized Omicron XBB.1.5 subvariant vaccine, Nuvaxovid™ XBB.1.5.

The immunogenicity of the vaccine was evaluated in following clinical trials. Immunogenicity assessments comprised serum anti-S protein binding IgG, angiotensin converting enzyme 2 (ACE2) receptor binding inhibition, neutralizing antibodies, and cell-mediated immunity (CMI) by intracellular cytokine staining (ICCS).

Study 2019nCoV-101, a phase 1/2, first-in-human, randomized, observer-blinded, placebo-controlled trial evaluating the safety and immunogenicity of 5 μg and 25 μg SARS-CoV-2 rS with or without 50 μg Matrix-M1 adjuvant, administered 21 days apart on Days 0 and 21 as a bedside mixture, was done at two sites in Australia and US in healthy adult participants between ages18 and 59 years of age who were seronegative to SARS-CoV-2 at baseline. 134 participants were enrolled in part 1 and 1,288 participants enrolled in part 2.

Study 2019nCoV-501 (11) is a Phase 2a/b, randomized, observer-blinded, placebo-controlled trial evaluating the efficacy, safety and immunogenicity of NVX-CoV2373, administered 21 days apart on Days 0 and 21 as a coformulation, in healthy adult HIV-negative participants 18 to 84 years of age and medically stable adult HIV-positive participants 18 to 64 years of age who were seronegative to SARS-CoV-2 at baseline. A total of 4,419 participants were randomized.

Study 2019nCoV-302 (12) is a Phase 3, randomized, observer-blinded, placebo-controlled trial evaluating the efficacy, safety, and immunogenicity of NVX-CoV2373, administered 21 days apart on Days 0 and 21 as a coformulation, in healthy and medically stable adult participants 18 to 84 years of age who were seronegative to SARS-CoV-2 at baseline. This study includes a Seasonal Influenza Vaccine Substudy, where approximately 400 participants received an additional IM injection of a licensed seasonal influenza vaccine on Day 0 in the opposite deltoid. A total of 15,185 participants were randomized (1:1) into Study 2019nCoV-302, with 15,138 receiving at least 1 dose of study vaccine (n = 7,568) or placebo (n = 7,570) and 14,930 receiving both doses of study vaccine (n = 7,467) or placebo (n = 7,463).

Study 2019nCoV-301, a phase 3, randomized, observer-blinded, placebo-controlled trial evaluating the efficacy, safety and immunogenicity of NVX-CoV2373, administered 21 days apart on Days 0 and 21 as a coformulation, in adult participants ≥ 18 years with a pediatric expansion in adolescents (12 to < 18 Years) is ongoing at multiple study sites in the US and Mexico. A total of 29,949 participants were randomized, out of which 19,965 were in the NVX-CoV2373 group and 9,984 were in the placebo group.

Study 2019nCoV-311 Part 1: Part 1 of Clinical Study 2019nCoV-311 is a Phase 3, randomized, placebo-controlled, observer blinded study evaluating the safety and immunogenicity of a single dose of Omicron BA.1 subvariant (NVX-CoV2515) and bivalent SARS-CoV-2 rS vaccines (NVX-CoV2373 and NVX-CoV2515) in adults previously vaccinated with other COVID-19 vaccines. A total of 953 participants were enrolled in the study.

Clinical Study 2019nCoV-311 Part 2: Part 2 of Clinical Study 2019nCoV-311 is a Phase 3, randomized, observer-blinded study evaluating the safety and immunogenicity of 2 doses of Omicron BA.5 subvariant (NVX-CoV2540) vaccine and bivalent vaccine (NVX-CoV2540 and NVX-CoV2373), given 90 days apart, in adults who were vaccinated with ≥ 3 doses of COVID-19 mRNA vaccines administered ≥ 90 days previously. 766 participants were randomly assigned to treatment groups.

Study 2019nCoV-313 (Omicron XBB.1.5): A 2-Part Phase 2/3 Open-Label Study to Evaluate the Safety and Immunogenicity of an XBB.1.5 (Omicron Subvariant) SARS-CoV-2 rS Vaccine

Booster Dose in Previously mRNA COVID-19 Vaccinated and Baseline SARS-CoV-2 Seropositive COVID-19 Vaccine Naïve Participants. The co-primary objectives in Part 1 were 1) to determine if NVX-CoV2601 booster induced superior antibody responses to the Omicron XBB.1.5 subvariant compared to the antibody responses of a historical control of NVX-CoV2373 and 2) to determine if NVX-CoV2601 booster induced non-inferior seroresponse rates (SRRs) compared to SRRs of a historical control of NVX-CoV2373 in participants who previously received ≥ 3 mRNA COVID-19 vaccinations.

The co-primary endpoints of the study were achieved as the Omicron XBB.1.5 subvariant vaccine NVX-CoV2601 induced a superior response in adjusted GMTs (ID50) against the Omicron XBB.1.5 subvariant virus along with a non-inferior SRR versus the historical control prototype Novavax vaccine NVX-CoV2373 at Day 28 following booster administration in participants previously vaccinated with ≥ 3 doses of the Moderna and/or Pfizer-BioNTech COVID-19 mRNA vaccines.

Immunogenicity Nuvaxovid™ JN.1 (Omicron-adapted Nuvaxovid): The efficacy of Nuvaxovid JN.1 is inferred from the efficacy data of the Nuvaxovid™ (Original, Wuhan strain) vaccine and immunogenicity data from the adapted vaccine of the Omicron BA.5 strain.

Safety summary: The safety of Nuvaxovid™ JN.1 is inferred from the safety data of the Nuvaxovid (Original, Wuhan strain) vaccine and the safety data from the adapted Omicron BA.5 vaccine.

A booster dose of the Nuvaxovid™ monovalent Omicron BA.5 and bivalent Original/ Omicron BA.5 vaccines evaluated in a Phase 3 study in participants 18 years of age and older (2019nCoV-311 Part 2). The overall safety profile for the Nuvaxovid™ monovalent Omicron BA.5 booster doses was similar to that seen after the Nuvaxovid™ (Original, Wuhan strain) booster dose.

Other information about evaluation of Nuvaxovid™ (JN.1)

In line with regulatory oversight of the European Medicines Agency (EMA), documentation for Nuvaxovid™ contains information on multi-dose (5-dose vials and 10-dose vials) presentations as well.

The transit from EUL to a standard prequalification is based on a vaccine prequalification dossier submitted in compliance with a CTD format.

The evaluation of Nuvaxovid™ (JN.1) prequalification application was based on the review of the information submitted to WHO by NOVAVAX CZ s.a., Czech Republic.

The recommendation of this vaccine is based on the review of the information submitted to WHO by NOVAVAX, which included certifications (e.g., European Union Good Manufacturing Practices certificates), and an array of different assessment reports as well as the acceptable responses to regulatory commitments and recommendations.